Klinik für Allgemein- und Viszeralchirurgie

CHIRURGISCHE FORSCHUNGS-TAGE 2022

„Surgeon Scientists – die akademische Chirurgie ist wichtiger denn je"

PROGRAMM

20.– 22. OKTOBER 2022

Historisches Kaufhaus
Münsterplatz 24 | 79098 Freiburg

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Erzeugt bei offenen Verfahren ein einheitliches Beleuchtungsmuster, das scharfe Bilder und eine zuverlässige Messung gewährleistet

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INHALTSVERZEICHNIS

GRUSSWORT

Liebe Kolleginnen und Kollegen,

die Chirurgischen Forschungstage haben lange Tradition und stehen diesjährig unter dem Motto **„Surgeon Scientist – die akademische Chirurgie ist wichtiger denn je“**. Die Verbindung von klinischer Tätigkeit und wissenschaftlicher Weiterentwicklung unserer Fachgebiete muss an akademischen Institutionen Hand in Hand intensiv gelebt werden.

Die 25. Chirurgischen Forschungstage umfassen alle Fachgesellschaften der Deutschen Gesellschaft für Chirurgie und in den Sitzungen werden Ihnen exzellente Vorträge zu experimenteller Grundlagenwissenschaft, translationaler Forschungsstrategien und klinischen Studien präsentiert.

Am Schlusstag der Chirurgischen Forschungstage wird dieses Programm mit chirurgisch technischen Videobeiträgen komplettiert werden.

Die 25. Chirurgischen Forschungstage werden vom 20. bis 22. Oktober in den schönen Räumlichkeiten des Historischen Kaufhauses am Münstermarkt in Freiburg stattfinden - ein hervorragender Ort für persönliche Begegnungen und intensive akademische Diskussionen.

Am Samstagvormittag, 22.10. von 8:30 Uhr bis 12:00 Uhr laden wir Sie ein, an unserem viszeral-chirurgischen Symposium zu Gastrointestinalen Anastomosen teilzunehmen. Hier werden wir Ihnen anhand von intraoperativen Videos eine Übersicht offener und minimalinvasiver Anastomosen-und OP-Techniken präsentieren.

Ich freue mich sehr, Sie in Freiburg begrüßen zu dürfen

und verbleibe mit freundlichen kollegialen Grüßen

Prof. Dr. med. Stefan Fichtner-Feigl

Ärztlicher Direktor der Klinik für Allgemein- und Viszeralchirurgie am Universitätsklinikum Freiburg

WISSENSCHAFTLICHE LEITUNG

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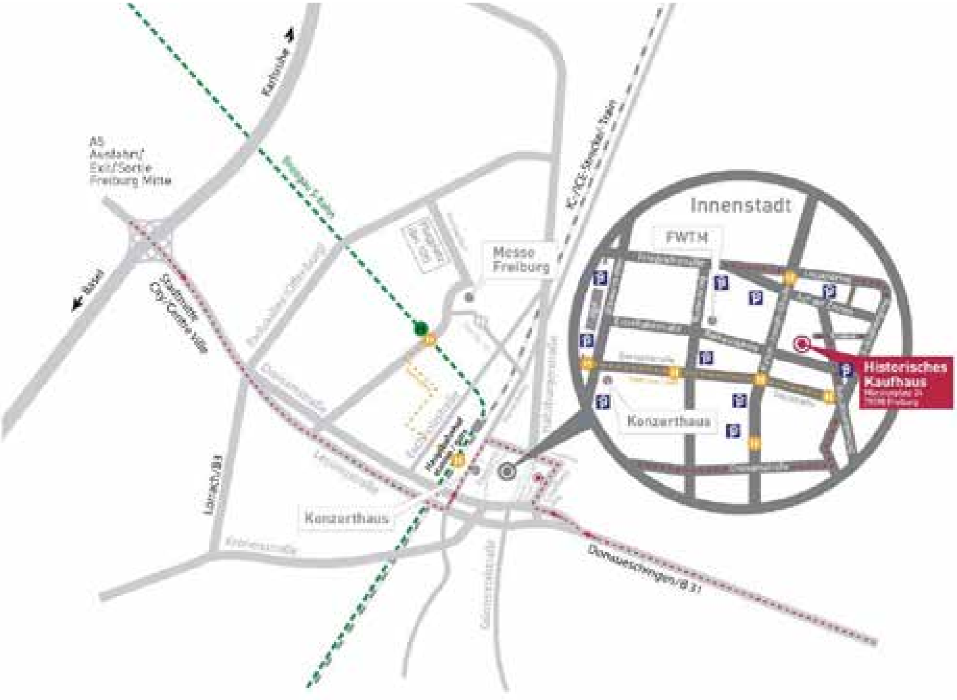
Dr. Dietrich A. Ruess
Allgemein- und Viszeralchirurgie

PROGRAMMKOMITEE

Prof. Dr. Hannes Neeff
Allgemein- und Viszeralchirurgie (viszeralchirurgisch-klinisches Symposium)
Prof. Dr. Hagen Schmal
Orthopädie/Unfallchirurgie
Prof. Dr. Steffen Eisenhardt
Plastische Chirurgie
Prof. Dr. Dr. Wolfgang Jungraithmayr
Thoraxchirurgie
Prof. Dr. Oliver Schnell
Neurochirurgie
Prof. Dr. Martin Czerny
Herz-/Gefäßchirurgie

VERANSTALTUNGSORT UND WEGBESCHREIBUNG

Historisches Kaufhaus in Freiburg
Münsterplatz 24 | 79098 Freiburg



CFT 2022 FREIBURG: „SURGEON SCIENTISTS – DIE AKADEMISCHE CHIRURGIE IST WICHTIGER DENN JE"

DO 20.10.

SAAL 1 (Kaisersaal)		SAAL 2 (Kaminsaal)	
14:00	Begrüßung		
14:15 – 15:45	Molekulare Onkologie I	14:15 – 15:45	Translational I (Orthopädie / Unfallchirurgie 1): Bench-to-bedside - Knorpel-chirurgie
16:00 – 17:30	Molekulare Onkologie II	16:00 – 17:30	Translational II (Plastische Chirurgie): Sarkome
17:45 – 19:15	Molekulare Onkologie III	17:45 – 19:15	Translational III (Viszeralchirurgie 1)

FR 21.10.

8:30	Begrüßung		
8:30 – 10:00	Klinische Studien II	8:30 – 10:00	Translational IV (Herz- / Gefäßchirurgie 1)
10:15 – 11:45	Entwicklung und Planung klinischer Studien	10:15 – 11:45	Translational V (Herz- / Gefäßchirurgie 2)
12:50 – 14:20	Sitzung für den Surgeon Scientist Nachwuchs	12:50 – 14:20	Translational VI (Thoraxchirurgie)
14:35 – 16:05	Klinische Studien III	14:35 – 16:05	Translational VII (Neurochirurgie)
16:20 – 17:50	Molekulare Onkologie IV	16:20 – 17:50	Translational VIII (Viszeralchirurgie 2)
18:00 – 19:00	Preisträgersitzung		
19:30	Gesellschaftsabend		

CFT 2022 FREIBURG: „SURGEON SCIENTISTS – DIE AKADEMISCHE CHIRURGIE IST WICHTIGER DENN JE"

DO 20.10.

SAAL 3 (Rokokosaal)		CEMT facilities	
16:00 – 17:30	Klinische Studien I	16:00 – 17:30	Workshop: Techniken der Lungentransplantation im Mausmodell (I)

FR 21.10.

8:30 – 10:00	Sektion Chirurgische Forschung – Vorstandssitzung	8:30 – 10:00	Workshop: Techniken der Lungentransplantation im Mausmodell (II)
10:15 – 11:45	Sektion Chirurgische Forschung – Mitgliederversammlung		
14:35 – 16:05	Transplantation (Interdisziplinär)		
16:20 – 17:50	Inflammation und Innate Immunity in der Chirurgie		

CFT 2022 FREIBURG: „SURGEON SCIENTISTS – DIE AKADEMISCHE CHIRURGIE IST WICHTIGER DENN JE"

SAAL 1 (Kaisersaal)		**SAAL 2** (Kaminsaal)	
SA 22.10.			
8:30 – 12:00	Viszeralchirurgisch-Klinisches Symposium: Videositzung: Gastrointestinale Anastomosen von der Speiseröhre bis zum Rektum.	8:30 – 10:00	Translational IX (Orthopädie / Unfallchirurgie 2)
		10:15 – 11:45	Interdisziplinäre Gewebeersatzforschung
12:00 – 12:30	Verabschiedung		

14:10	Begrüßung (Kaisersaal)
14:15-15:45	**Molekulare Onkologie I** *Vorsitz: Dr. René Thieme, Leipzig;* *Prof. Dr. Stefan Fichtner-Feigl, Freiburg*
14:15-14:25	182: Establishing esophageal adenocarcinoma organoids and paired cancer associated fibroblasts for in vitro tumor growth monitoring and drug screening *Fan Ningbo, Köln*
14:25-14:35	139: Quantification of surface proteins on serum exosomes of oral squamous cell carcinoma patients *Prof. Dr. Ute Warnecke-Eberz, Köln*
14:35-14:45	175: High hydrostatic pressure enables head and neck cancer devitalization and induction of immunogenic cell death *Thoralf Kleitke, Rostock*
14:45-14:55	166: Carvacrol exerts anti-angiogenic effects against triple-negative breast cancer *Tianci Tang, Homburg*
14:55-15:05	170: Extracellular vesicles derived from activated-pancreatic stellate cells enhance the chemoresistance and plasticity of pancreatic adenocarcinoma in the tumor microenvironment *Xiaolin Wu, Köln*
15:05-15:15	197: Untersuchung und Abgrenzung des Energiestoffwechsel in proliferierenden Hepatozyten und Hepatozellulären Karzinomzellen *Julia Nerusch, Leipzig*
15:15-15:25	195: Der protoonkogene Effekt der Tyrosinkinasen Axl, Mer and Tyro 3 im kolorektalen Karzinom *Naita Maren Wirsik, Köln*
15:25-15:35	156: Molekulare Veränderungen nach Resektion von kolorektalen Lebermetastasen *Dr. Jost Lünstedt, Freiburg*
15:35-15:45	Offene Fragen / Diskussion
15:45-16:00	**PAUSE**

16:00-17:30	**Molekulare Onkologie II** *Vorsitz: Dr. Henrik Nienhüser, Heidelberg;* *Dr. Dr. Christopher Berlin, Freiburg*
16:00-16:25	KEYNOTE: Nicht-kanonische Mutationen im Tumorgenom ***Prof. Dr. Sven Diederichs, Freiburg***
16:25-16:35	198: Herunterregulation der ADP-Ribosylierung und Deacylierung als Bindeglied zwischen genotoxischer Schädigung und akzelerierter Gewebsalterung ***Dr. Michael Haase, Dresden***
16:35-16:45	113: The prognostic role of co-inhibitory receptor ligands on circulating tumor cells and T cells in gastrointestinal tumors ***Dr. Leonie Konczalla, Hamburg***
16:45-16:55	202: Linking Cancer Cell Plasticity to Resistance in Esophageal Cancer by Integrative Single-cell RNA-sequencing ***Nellie Horstmann, Köln***
16:55-17:05	138: Hereditary homozygosity and allelic imbalance of HLA as common immune escape mechanisms in oesophago-gastric adenocarcinoma ***Dr. Maria Alejandra Garcia Marquez, Köln***
17:05-17:15	104: Organization, function and gene expression of tertiary lymphoid structures in pancreatic cancer resembles lymphoid follicles in secondary lymphoid organs and their abundance is related to superior survival ***Jonas Lehmann, Köln***
17:15-17:25	144: ECM-receptor signature is associated with basal-like subtype and immune exclusion in pancreatic ductal adenocarcinoma ***Dr. Yifeng Sun, Ulm***
17:25-17:45	**PAUSE**

17:45-19:15	**Molekulare Onkologie III** *Vorsitz: PD Dr. Hans Anton Schlößer, Köln;* *Dr. Jost Lünstedt, Freiburg*
17:45-18:05	KEYNOTE: The molecular faces of multivisceral stage IV CRC *Dr. Dr. Christopher Berlin, Freiburg*
18:05-18:15	145: Arp2/3 complex-mediated fibroblast migration signature is associated with poor prognosis of pancreatic cancer *Dr. Yifeng Sun, Ulm*
18:15-18:25	146: mTORC1 promotes the formation of immunosuppressive microenvironment in pancreatic ductal adenocarcinoma *Dr. Chao Fang, Ulm*
18:25-18:35	147: Phenotypic and molecular characterization of duct- and acinar-derived pancreatic ductal adenocarcinoma *Jingxiong Hu, Ulm*
18:35-18:45	159: Proteinkinase-inhibition augments the response against multidrug chemotherapy in pancreatic cancer *Danilo Hackner, Erlangen*
18:45-18:55	167: Pharmacologic inhibition of the IRE1α-XBP1s pathway impairs PDAC cell growth in vitro *Annabelle Schmitt, Heidelberg*
18:55-19:05	151: Non-canonical Wnt pathway member Frizzled 5 is downregulated in gastric cancer *Sarah Zimmer, Heidelberg*
19:05-19:15	168: Cancer-specific differences of cellular and humoral immune responses against tumor associated antigens *Ella Preugszat, Köln*

14:15-15:45	**Translational I (Orthopädie / Unfallchirurgie 1): Bench-to-bedside – Knorpelchirurgie** *Vorsitz: Prof. Dr. Kaywan Izadpanah, Freiburg;* *Prof. Dr. Hagen Schmal, Freiburg*
14:15-14:30	Versorgungskonzepte in der Knorpelchirurgie – heute und morgen *Dr. Andreas Fuchs, Freiburg*
14:30-14:45	Neue Methoden zur Beurteilung des Knorpels und Planung von Eingriffen *Dr. Markus Siegel, Freiburg*
14:45-15:00	Zellinstruktive Materialdesigns zur Kontrolle des degenerativen Phänotyps humaner Chondrozyten *Prof. Dr. Bernd Rolauffs, Freiburg*
15:00-15:15	Möglichkeiten zur biologischen Augmentation der autologen Chondrozytentransplantation *PD Dr. Johanna Kubosch, Freiburg*
15:15-15:30	Modellgestützte Vorhersage der Knorpeloberflächen-Entropie und des zellulären Überlebens *Mischa Selig, Freiburg*
15:30-15:45	Patientenindividuelle Modellierung von Kniegelenksverletzungen zur Therapieplanung und -umsetzung *PD. Dr. Kaywan Izadpanah, Freiburg*
15:45-16:00	**PAUSE**
16:00-17:30	**Translational II (Plastische Chirurgie): Sarkome** *Vorsitz: Prof. Dr. Andreas Leithner, Graz;* *Prof. Dr. Björn Behr, Bochum*
16:00-16:20	KEYNOTE: Update Knochensarkome *Prof. Dr. Andreas Leithner, Graz*
16:20-16:30	Der freie Fibulatransfer für die Rekonstruktion dia- und epiphysärer Knochendefekte in der interdisziplinären Plastischen Chirurgie *Dr. Jurij Kiefer, Freiburg*

16:30-16:40	121: Relevant knowledge of the general and abdominal surgeon on plastic surgery *Armin Kraus, Magdeburg*
16:40-16:50	115: Einfluss von Tamoxifen auf die Genexpression der Tumorgenese in adipogenen Stammzellen, epithelialen Brustdrüsenzellen und Mammakarzinomzelllinien – eine in vitro Studie *Dr. Frederik Schlottmann, Hannover*
16:50-17:00	162: Etablierung der Hautbank Hannover: Sterile Abnahme- und Prüfprotokolle zur Generierung vitaler, kryokonservierter allogener Hauttransplantate von lebenden Spendern *Dr. Frederik Schlottmann, Hannover*
17:00-17:10	Liquid biopsy bei myxoiden Lipsarkomen *Adrian Schmid, Freiburg*
17:10-17:20	165:Non-invasive monitoring of soft-tissue sarcoma response to neoadjuvant radiotherapy through quantification of circulating tumor DNA and multiparametric MRI *Dr. Alexander Runkel, Freiburg*
17:20-17:30	In vitro visualization of C-reactive protein (CRP)-mediated monocyte infiltration during the acute allograft rejection in a VCA model *Dr. Jurij Kiefer, Freiburg*
17:30-17:45	**PAUSE**
17:45-19:15	**Translational III (Viszeralchirurgie 1)** *Vorsitz: Prof. Dr. Nicolas Schlegel, Würzburg;* *PD Dr. Philipp-Alexander Neumann, München*
17:45-17:55	143: The protein kinase CK2: A novel regulator of glucagon expression in α-cells *Mandy Pack, Homburg*
17:55-18:05	120: Role of plakophilins in the regulation of intestinal barrier function in vitro and in vivo *Dr. Catherine Kollmann, Würzburg*

18:05-18:15	140: Anti-inflammatorische Medikamente zeigen unterschiedliche direkte Effekte auf Caco2 Zellen und Enteroide *Dr. Michael Meir, Würzburg*
18:15-18:25	142: Low postoperative carbon dioxide levels are associated with impaired healing of intestinal anastomoses *Dr. Moritz Strowitzki, Heidelberg*
18:25-18:35	164: Verbesserung der intestinalen Anastomosenheilung im murinen Kolitis-Modell durch niedrigdosierte Prednisolon-Therapie *Dr. Marie-Christin Weber, München*
18:35-18:45	174: Glial cell line-derived neurotrophic factor improves intestinal wound healing by upregulation of proliferative pathways *Dr. Sven Flemming, Würzburg*
18:45-18:55	194: Targeting the canonical WNT signaling pathway – a potential novel therapy in Crohn´s associated fibrosis *Annalisa Buck, München*
18:55-19:15	KEYNOTE: Neues zu Mechanismen der intestinalen Barrieredysregulation bei entzündlichen Erkrankungen des Gastrointestinaltraktes *Prof. Dr. Nicolas Schlegel, Würzburg*

16:00-17:30	**Klinische Studien I (interdisziplinär)** *Vorsitz: PD Dr. Emrullah Birgin, Mannheim;* *Dr. Dietrich Ruess, Freiburg*
16:00-16:10	123: Novel Aspects & Trends on the Investigated Interdisciplinary Pain Management in Abdominal Surgery - Data Obtained in a Systematic Clinical Observational Study by an Interdisciplinary Research Group in a Tertiary Center *Dr. Michael Brinkers, Magdeburg*
16:10-16:20	155: 3D PRINTING OF MINIPORTS FOR MICROLAPAROSCOPIC SURGERY USED IN NEWBORNS AND PREMATURE INFANTS *Salmai Turial, Magdeburg*
16:20-16:30	127: Depression in coronary heart disease & tumor lesions as representative examples of somatic diseases with considerable relevance for morbidity & mortality *Dr. Michael Brinkers, Magdeburg*
16:30-16:40	108: Operative Versorgung von Patienten ab 65 Jahren mit proximaler Humerusfraktur – Ein Beispiel aus der alterstraumatologischen Versorgungsforschung *Dr. Jeanette Köppe, Münster*
16:40-16:50	126: Role of depression in tumor and non-tumor patients *Dr. Michael Brinkers, Magdeburg*
16:50-17:00	161: Stoma placement and quality of life in paraplegic patients with extensive sacral pressure ulcers: a retrospective case series *Marco Torri, Ludwigshafen*
17:00-17:10	124: Currently recommended Cannabis use in daily surgical as well as broad clinical practice (initial systematic results) - proper handling, control measures & indicated trends *Dr. Michael Brinkers, Magdeburg*
17:10-17:20	125: What is better in neuropathic pain(?): Anticonvulsives or Antidepressants *Dr. Michael Brinkers, Magdeburg*
17:20-17:30	Offene Fragen / Diskussion

PROGRAMM | DONNERSTAG 20.10.2022
CENTER FOR EXPERIMENTAL MODELS AND TRANSGENIC SERVICE (CEMT)

16:00-17:30	Workshop: Techniken der Lungentransplantation im Mausmodell (I) *Prof. Dr. Dr. Wolfgang Jungraithmayr, Freiburg* *Dr. Birte Ohm, Freiburg*

PROGRAMM | FREITAG 21.10.2022
KAISERSAAL

8:20	Begrüßung (Kaisersaal) *Prof. Dr. Stefan Fichtner-Feigl, Freiburg* *Dr. Dietrich A. Ruess, Freiburg*
8:30-10:00	**Klinische Studien II** *Vorsitz: Prof. Dr. Christoph Reißfelder, Mannheim;* *Prof. Dr. Markus Diener, Freiburg*
8:30-8:40	172: LAMS (lumen-apposing metal stent) dislocation as complication of EUS-GE (Endoscopic Ultrasound-guided GastroEnteroanastomosis) - representative case report on the complication management by interventional re-endoscopy *Viliam Masaryk, Gera*
8:40-8:50	196: Acquisition and Preprocessing of Robotic Assisted Minimal Invasive Esophagectomy Video Data at a High-volume Center *Yinan Xu, Köln*
8:50-9:00	173: Atypical site of the papilla of Vater is challenging with regard to the endoscopic management of cholangiolithiasis and cholangitis *Viliam Masaryk, Gera*
9:00-9:10	107: Maschinelles Lernen zur Prädiktion postoperativer Komplikationen nach onkologischen Ösophagusresektionen *Dr. Jin-On Jung, Köln*
9:10-9:20	112: Klinische Relevanz des oralen Sicherheitsabstandes beim Ösophaguskarzinom *Dr. Karl Knipper, Köln*

9:20-9:30	119: The CARDIA-trial: Comparing transthoracic esophagectomy with transhiatal extended gastrectomy in adenocarcinoma of the gastroesophageal junction (GEJ) type II in a multinational and prospective randomized clinical trial *Dr. Stefanie Brunner, Köln*
9:30-9:40	129: Improved survival by blockade of adrenergic signaling in patients with gastric signet ring carcinoma *Sarah Zumsande, Heidelberg*
9:40-10:00	Offene Fragen / Diskussion
10:00-10:15	**PAUSE**
10:15-11:45	**Entwicklung und Planung klinischer Studien - INTERAKTIV** *SDGC/Chir-Net team:* *Prof. Dr. Markus Diener* *PD Dr. Rosa Klotz* *PD Dr. Johan Lock*
11:45-12:50	**PAUSE mit industriegefördertem Lunchsymposium**
12:50-14:20	**Sitzung für den Surgeon Scientist Nachwuchs** *Vorsitz: Prof. Dr. Stefan Fichtner-Feigl, Freiburg;* *Dr. Dietrich Ruess, Freiburg*
12:50-13:05	KEYNOTE: Warum chirurgische Forschung unerlässlich ist *Prof. Dr. Christoph Reißfelder, Mannheim*
13:05-13:15	122: What must a(n) academic surgeon know about medical library system? *Manuela Röhner, Magdeburg*
13:15-14:05	Personal insights from young Surgeon Scientists – “The road to independence and success – opportunities, caveats, tips and tricks” *Dr. Henrik Nienhüser, Heidelberg* *Dr. Tim Berger, Freiburg* *PD Dr. Hans Anton Schlößer, Köln* *PD Dr. Johanna Kubosch, Freiburg* *PD Dr. Gernot Lang, Freiburg* *PD Dr. Dirk Henrik Heiland, Freiburg* *PD Dr. Patrick Plum, Leipzig*

14:05-14:20	KEYNOTE: Förderprogramme und Antragstellung bei der Deutschen Forschungsgemeinschaft – Sichtweise aus dem Fachkollegium *Prof. Dr. Steffen Eisenhardt, Freiburg*
14:20-14:35	**PAUSE**
14:35- 16:05	**Klinische Studien III** *Vorsitz: Prof. Dr. Andreas Schnitzbauer, Frankfurt* *PD Dr. Patrick Plum, Leipzig*
14:35-14:45	180: The validity of an App-based risk scoring defining an aerobic endurance prehabilitation program (Patronus Prehab App) in patients undergoing elective major surgery: The prospective, interventional PROTEGO MAXIMA Trial *Dr. Svenja Sliwinski, Frankfurt*
14:45-14:55	149: The safety and validity of an App-based prehabilitation program (Patronus Prehab App) in patients undergoing elective major surgery: The prospective, interventional PROTEGO MAXIMA Trial *Fatima Faqar-Uz-Zaman, Frankfurt*
14:55-15:05	153: Gender-specific differences in the perioperative management, early postoperative and long-term oncosurgical outcome in gastric cancer (Ca) - results of a prospective multicenter observational study *Pirashanna Mahendran, Magdeburg*
15:05-15:15	154: Impact of basic disease (chronic pancreatitis [Pan.] vs. pancreatic head cancer [Ca]) and perioperative immune status onto early postoperative outcome in pylorus-preserving pancreatic head resection by Traverso-Longmire (PPPD) *Nikolas Scholz, Magdeburg*
15:15-15:25	157: Outcome der Pankreatoduodenektomie nach chirurgischer T-Drainagen-Anlage versus ERCP und Stenteinlage bei Verschlussikterus *Miklos Peter Berente, Heidelberg*
15:25-15:35	160: Clinical characteristics and oncological outcomes of surgically treated early onset gastric adenocarcinoma *Dr. Ingmar Rompen, Heidelberg*

15:35-15:45	184: Surgical Audio Guidance (SURAG) macht das Einbringen der Veress-Nadel sicherer *Dr. Salmai Turial, Magdeburg*
15:45-15:55	185: Composition of the oral and gastrointestinal microbiome in patients with Barrett's esophagus and esophageal adenocarcinoma *Yi Liao, Köln*
15:55-16:05	189: Endoskopische Vakuumtherapie versus Stentbehandlung von Ösophagusanastomosen (ESOLEAK): Studienprotokoll für eine prospektive randomisierte Phase-2-Studie *Dr. Seung-Hun Chon, Köln*
16:05-16:15	**PAUSE**
16:15-17:45	**Molekulare Onkologie IV** *Vorsitz: PD Dr. Dr. Lena Conradi, Göttingen;* *Prof. Dr. Stefan Brunner, Regensburg*
16:15-16:25	190: CytoskeletonAssociated Protein 4 (CKAP4) is critical for esophageal adenocarcinoma cells *Dr. René Thieme, Leipzig*
16:25-16:35	179: Aldo-Keto Reductase 1C3 enhances radioresistance in esophageal adenocarcinoma cells via inhibiting ferroptosis *Feng Ju, Köln*
16:35-16:45	191: Identification and classification of tumor cells in specimens of patients with Barrett's carcinoma by Hyperspectral imaging (HSI) *Dr. René Thieme, Leipzig*
16:45-16:55	171: Translational Research Approach to Improve Individualized Pancreatic Tumor Therapy *Benedikt J. Wagner, Regensburg*
16:55-17:05	192: Characterization of PD-L1 in an esophageal adenocarcinoma cell culture model *Dr. René Thieme, Leipzig*
17:05-17:15	188: Phenotypic characterization of colorectal liver metastases: capsule versus no capsule and the potential role of epithelial mesenchymal transition *Prof. Dr. Stefan Brunner, Regensburg*

17:15-17:35	KEYNOTE: Molekulare Unterschiede zwischen angiogenen und Blutgefäß-kooptierenden kolorektalen Lebermetastasen ***PD Dr. Dr. Lena Conradi, Göttingen***
17:35-17:45	Offene Fragen / Diskussion
17:45-18:00	**PAUSE**
18:00-19:00	**Preisträgersitzung** ***Vorsitz: Prof. Dr. Stefan Fichtner-Feigl, Freiburg;*** ***Sektion Chirurgische Forschung:*** ***Prof. Dr. Matthias Laschke, Homburg***
18:00-18:50	Preisträger-Vorträge 109:Herz-/Gefäßchirurgie: Functional alterations of neutrophil granulocytes during major cardiac surgery ***Pascal Lessing, Ulm*** 248: Thoraxchirurgie: Zero Echo Time Lungen-MRT in der präoperativen Planung pädiatrischer Patienten mit Tracheobronchialer Stenose ***Nadja Kocher, Zürich*** 137: Plastische Chirurgie: Untersuchungen zur Rolle von C-reaktivem Protein in der Abstoßungsreaktion im Hinterlauftransplantationsmodell der Ratte ***Laura Schneider, Freiburg*** 106: Viszeralchirurgie: Immune responses against shared antigens are common in esophago-gastric cancer and can be enhanced using CD40-activated B cells ***Martin Thelen, Köln (vertreten durch PD Dr. Hans Anton Schlößer)*** 118: Viszeralchirurgie: The EVIglance trial: the new gold standard for answering a clinical question – a randomised controlled trial ***PD Dr. Rosa Klotz***
18:50-18:55	Vergabe Hans-Jürgen Bretschneider Preis
18:55-19:00	Einladung zu den CFT 2023 Mannheim ***Prof. Dr. Christoph Reißfelder, Mannheim***

8:30-10:00	**Translational IV (Herz- / Gefäßchirurgie 1):** Moderne Behandlungskonzepte der Herz- und Gefäßchirurgie *Vorsitz: Prof. Dr. Bartosz Rylski, Freiburg;* *Luc Claeys, Freiburg*
8:30-8:40	141: Von der Fokussierung auf Röntgenbefunde zurück zum diagnostischen Blick und der stabilisierenden operativen Therapie: Venöse Kompressionssyndrome und das hypermobile EHLERS-DANLOS Syndrom *Prof. Dr. Wilhelm Sandmann, Düsseldorf*
8:40-9:00	Moderne Aortenbogenchirurgie *Dr. Tim Berger, Freiburg*
9:00-9:20	Moderne endovaskuläre Aortenchirurgie *Dr. Stoyan Kondov, Freiburg*
9:20-9:40	Moderne Konzepte der extrakorporalen Perfusion *Prof. Dr. Georg Trummer, Freiburg*
9:40-10:00	Moderne Behandlungskonzepte der terminalen Herzinsuffizienz *Dr. David Schibilsky, Freiburg*
10:00-10:15	**PAUSE**
10:15-11:45	**Translational V (Herz- / Gefäßchirurgie 2):** *Vorsitz: Dr. Stoyan Kondov, Freiburg;* *Dr. Tim Berger, Freiburg*
10:15-10:30	110: Piloting flow-cytometry based immunomonitoring in patients with major cardiac surgery *Dominik Hüsken, Ulm*
10:30-10:45	136: The iliopsoas muscle as a main clinical focus of a rare pathological lesions and indicati “symptom muscle“ of retroperitoneal vascular surgical diseases as well as various differential diagnoses to be delineated *Udo Barth, Burg*
10:45-11:00	186: Infraschallexposition kann die Kraft-Frequenz-Beziehung am isolierten atrialen menschlichen Myocard ändern *Prof. Dr. Christian Vahl, Mainz*
11:00-11:15	187: No Reduction of Contractile Isometric Performance in Human Atrial Myocardium at Infrasound Levels of 80 and 90 dB *Prof. Dr. Christian Vahl, Mainz*

11:15-11:45	Offene Fragen / Diskussion
11.45 - 12.50	**PAUSE mit industriegefördertem Lunchsymposium**
12:50-14:20	**Translational VI (Thoraxchirurgie)** *Vorsitz: Prof. Dr. Dr. Wolfgang Jungraithmayr, Freiburg* *Dr. David Schibilsky, Freiburg*
12:50-13:20	KEYNOTE: Lange nicht-kodierende RNAs im NSCLC *Prof. Dr. Sven Diederichs, Freiburg*
13:20-13:35	103: Establishment of a novel test method to analyze in vitro biofilm development with 3D organotypic co-culture *Dr. Peggy Stock, Leipzig*
13:35-13:50	116: Die Entzündungsantwort der Niere während TRAKI nach experimentellem Thoraxtrauma mit hämorrhagischem Schock *Lorena Schult, Ulm*
13:50-14:05	169: Prognostic factors for long-term survival following complete resection by lobectomy in stage I non-small cell lung cancer *Dr. Davor Stamenovic, Mainz*
14:05-14:20	177: Blutungsmanagement nach Verletzung des linken Vorhofes durch Ballonokklusion – eine experimentelle Studie *Prof. Dr. Andreas Kirschbaum, Marburg*
14:20-14:35	**PAUSE**
14:35- 16:15	**Translational VII(Neurochirurgie):** *Vorsitz: Prof. Dr. Jürgen Beck, Freiburg*
14:35-14:55	Der Operationssaal zwischen klinischer Versorgung und translationaler Forschung *Prof. Dr. Oliver Schnell, Freiburg*
14:55-15:15	Extent of resection reloaded: a new classification for glioblastoma by the RANO resect group *Dr. Philipp Karschnia, München*
15:15-15:30	132: Die miR-29b, ein neuer Regulator der NG2-Expression im Glioblastom *Anne-Sophie Böwe, Homburg*

15:30-15:45	Liquid Biopsy in Glioma: The role of extracellular vesicles as tumor surrogates *Amanda Salviano da Silva, PhD, Hamburg*
15:45-16:00	Real-time imaging of glutamate transients in acute brain slices *PD Dr. Sebastian Brandner, Erlangen*
16:00-16:15	Spatially resolved multi-omics in glioblastoma *PD Dr. Dirk Henrik Heiland*
16:15-16:20	**PAUSE**
16:20-17:50	**Translational VIII (Viszeralchirurgie)** *Vorsitz: Prof. Thomas Schmitz-Rixen, Frankfurt;* *Prof. Dr. Markus Diener, Freiburg*
16:20-16:30	111: Gastric bypass surgery weight loss-independently induces gut Il-22 release in association with improved glycemic control in Zucker Fatty rats *Rebecca Springer, Würzburg*
16:30-16:40	117: Soluble VE-cadherin disrupts endothelial barrier function via VE-PTP/RhoA signalling *Dr. Natalie Burkard, Würzburg*
16:40-16:50	178: Einschätzung der lateralen Wärmeausbreitung während der bipolaren Gefäßversiegelung an einem ex vivo Modell *Prof. Dr. Andreas Kirschbaum, Marburg*
16:50-17:00	128: NLRP3 inflammasome activation in leucocytes drives hepatic stellate cell activation and fibrosis in non-alcoholic steatohepatitis *Dr. Benedikt Kaufmann, München*
17:00-17:10	148: Metabolic profiling of the rat liver after portal vein ligation *Prof. Dr. Bruno Christ, Leipzig*
17:10-17:20	158: The significance of metabolic reprogramming during hepatic fibrosis *Christopher Tuffs, Heidelberg*

17:20-17:30	181: Lipidomic Characterization of Liver Regeneration after Portal Vein Ligation using Rapid Evaporation Ionisation Mass Spectrometry (REIMS) *Julian Connor Eckel, Leipzig*
17:30-17:50	KEYNOTE: Pooled human bone marrow-derived Mesenchymal Stromal Cells improve dermal wound healing in diabetic rats by accelerated vascularization and dynamic recruitment of M2-like macrophages *Prof. Dr. Thomas Schmitz-Rixen, Frankfurt*

PROGRAMM | FREITAG 21.10.2022
ROKOKOSAAL

8:30-10:00	Sektion Chirurgische Forschung - Vorstandssitzung
10:15-11:45	Sektion Chirurgische Forschung - Mitgliederversammlung
11:45-12:50	**PAUSE mit industriegefördertem Lunchsymposium**
14:35- 16:05	**Transplantation (interdisziplinär)** *Vorsitz: Prof. Dr. Uta Dahmen, Jena;* *Dr. Bernd Jänigen, Freiburg/ Dr. Philipp Holzner, Freiburg*
14:35-14:45	Increased incidence of thromboembolism after lung transplantation - need for an individualized prophylaxis? *Dr. Isabelle Moneke, Freiburg*
14:45-14:55	CD26-inhibition is associated with absence of Chronic Lung Allograft Dysfunction *Dr. Isabelle Moneke, Freiburg*
14:55-15:05	133: The generation of insulin producing cells (IPC)-spheroids from microvascular fragments (MVF) *Cedric Wilden, Homburg*

15:05-15:15	134: Co-transplantation of pancreatic islets and microvascular fragments effectively restores normoglycemia in diabetic mice *Selina Wrublewsky, Homburg*
15:15-15:25	150: Mesenchymal stromal cells attenuate liver damage after partial hepatectomy in the mouse by mitigating thrombospondin-1, TGF-b, and epithelial-mesenchymal transition (EMT) *Dr. Lysann Tietze, Leipzig*
15:25-15:35	163: Anzahl und Funktion von myeloiden Suppressorzellen (MDSCs) bei Patienten nach Lebertransplantation *Isabella Baur, Tübingen*
15:35-16:05	KEYNOTE: Computational Liver Surgery *Prof. Dr. Uta Dahmen, Jena*
16:05-16:20	**Pause**
16:20-17:50	**Inflammation und Innate Immunity in der Chirurgie** *Vorsitz: Prof. Dr. Markus Huber-Lang, Ulm;* *Dr. Katrin Richter, Giessen*
16:20-16:40	KEYNOTE: Molekulare Gefahrenantwort nach Trauma *Prof. Dr. Markus Huber-Lang, Ulm*
16:40-16:50	Vom Mechanismus zur Therapie: Entwicklung einer neuen immunmodulierenden Compound zum „therapeutic targeting“ der angeborenen Immunantwort *Prof. Dr. Steffen Eisenhardt, Freiburg*
16:50-17:00	114: Transplantatengineering humaner allogener Keratinozyten durch US11-Proteine – Perspektive zur reduzierten Transplantatabstoßung bei Fremdhaut-Allotransplantationen *Dr. Frederik Schlottmann, Hannover*
17:00-17:10	130: Aus Fettstammzellen isolierte Exosomen induzieren proapoptotische Gene in einer Brusttumorzellinie *Dr. Oliver Felthaus, Regensburg*
17:10-17:20	131: Einfluss des mTOR-Signalwegs auf die Hyperproliferation bei der Multiplen Symmetrischen Lipomatose *Lukas Prantl, Regensburg*

PROGRAMM | FREITAG 21.10.2022
ROKOKOSAAL

17:20-17:30	152: Evaluation of IL-33R and Galectin-3 as new Biomarkers of Cardiac Damage after Polytrauma – Association with Cardiac Comorbidities and Risk Factors ***Dr. Birte Weber, Frankfurt***
17:30-17:40	183: Effect of combined C5/CD14 immunomodulators on the liver of polytrauma injured pigs after 72h ***Dr. Yang Li, Ulm***
17:40-17:50	193: Cholinergic control of trauma-mediated cytokine release by innate immune cells in endothelial NO synthase activation and P2X7 receptor modification ***Dr. Katrin Richter, Giessen***

PROGRAMM | FREITAG 21.10.2022
CENTER FOR EXPERIMENTAL MODELS AND TRANSGENIC SERVICE (CEMT)

8:30-10:00	Workshop: Techniken der Lungentransplantation im Mausmodell (I) ***Prof. Dr. Dr. Wolfgang Jungraithmayr, Freiburg*** ***Dr. Birte Ohm, Freiburg***

HISTORISCHER BURSENKELLER – Uniseum Freiburg

Ab 19:30	Gesellschaftsabend

8:30-12:00	**Viszeralchirurgisch-Klinisches Symposium i.R.d. CFT 2022** Videositzung: Gastrointestinale Anastomosen von der Speiseröhre bis zum Rektum
8:30-9:00	Ösophagus/Magen *Prof. Dr. Markus Diener, Freiburg*
9:00-9:30	Bariatrische Operaionen *Prof. Dr. Goran Marjanovic, Freiburg*
9:30-10:00	Pankreas *Prof. Dr. Uwe Wittel, Freiburg*
10:00-10:30	**PAUSE**
10:30-11:00	Leber/Gallenwege *Dr. Philipp Holzner, Freiburg*
11:00-11:30	Dünndarm/Rechtskolon *PD Dr. Gabriel Seifert, Freiburg*
11:30-12:00	Linkskolon/Rektum *Prof. Dr. Hannes Neeff, Freiburg*
12:00-12:15	Verabschiedung und nochmalige Einladung zu den CFT 2023 Mannheim *Prof. Dr. Stefan Fichtner-Feigl, Freiburg* *Dr. Dietrich A. Ruess, Freiburg* *Prof. Dr. Christoph Reißfelder, Mannheim*

8:30-10:00	**Translational IX (Orthopädie / Unfallchirurgie 2):** *Vorsitz: PD Dr. Gernot Lang, Freiburg,* *Prof. Dr. Hagen Schmal, Freiburg*
8:30-8:40	Intervertebral disc regeneration – fact or fiction? *PD Dr. Gernot Lang, Freiburg*
8:40-8:50	Neuromuskuläre Leistungsdiagnostik nach offener Achilles-sehnen-Rekonstruktion *Dr. Saskia Maletzke, Freiburg*
8:50-9:00	199: Serum levels of GFAP and NfL are related to the neurological impairment and spinal edema after traumatic spinal cord injury *Dr. Iris Leister, Murnau*
9:00-9:10	200: An effective prehospital management after traumatic cervical spinal cord injury can positively influence the neurological as well as the functional outcome *Dr. Christof Wutte, Murnau*
9:10-9:20	Regeneration von Mechanik und Funktion nach lateraler Bandruptur am Sprunggelenk *Charlotte Kurtz, Freiburg*
9:20-9:30	Neuromuskuläre Regeneration nach VKB-Hamstring-Plastik *Dr. Dr. Markus Wenning, Freiburg*
9:30-9:40	Neuromuskuläre Regeneration nach Muskelfaserverletzung *Jonas Bender, Freiburg*
9:40-9:50	Genderspezifische Verletzungsanalyse und Prävention im Frauenprofifußball *Dr. Lisa Bode, Freiburg*
9:50-10:00	Offene Fragen / Diskussion
10:00-10:15	**PAUSE**

10:15-11:45	**Interdisziplinäre Gewebeersatzforschung** *Vorsitz: Prof. Dr. Bernd Rolauffs, Freiburg,* *Prof. Dr. Günter Finkenzeller, Freiburg*
10:15-10:35	KEYNOTE: Chirurgische Forschung oder wie kommt Tissue Engineering und Biofabrikation in die klinische Anwendung – die Sicht des Plastischen Chirurgen ***Prof. Dr. Dr. h.c. Raymund E. Horch, Erlangen***
10:35-10:45	101: Diet-induced obesity in mice improves the vascularization capacity of microvascular fragments from subcutaneous adipose tissue ***Friederike C. Meßner, Homburg***
10:45-10:55	102: Fibroblast growth factor (FGF)21 is crucial for the revascularization of white adipose tissue grafts ***Ettore Limido, Homburg***
10:55-11:05	105: Acceleration of cutaneous wound healing by adipose tissue-derived microvascular fragments ***Melina C. Dinter, Homburg***
11:05-11:15	Bioprinted Endothelial Cells in Bone Tissue Form Functional Blood Vessels In Vivo ***PD Dr. Filip Simunovic, Freiburg***
11:15-11:25	135: Cell Enriched Lipotransfer – Die Auswirkung von mechanischer Aufbereitung auf Lipoaspirat und dessen Fettstammzellen ***Andreas Eigenberger, Regensburg***
11:25-11:35	In vivo gezüchtete axial vaskularisierte Bindegewebs-lappenplastiken eignen sich zur Transplantation und stabilen Defektrekonstruktion im Großtiermodell des Schafes ***Dr. Florian Falkner, Freiburg***
11:35-11:45	Cell Morphology as a Biological Fingerprint for Describing the Phenotype of Cells ***Assoc. Prof. Dr. Melanie Hart, Freiburg***

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ABSTRACTS

20.– 22. OKTOBER 2022

Historisches Kaufhaus
Münsterplatz 24 | 79098 Freiburg

ID: 101
Topics: Andere, Basic+Translational

Diet-induced obesity in mice improves the vascularization capacity of microvascular fragments from subcutaneous adipose tissue

Meßner, Friederike C. (1); Metzger, Wolfgang (2); Marschall, Julia E. (1); Bickelmann, Caroline (1); Menger, Michael D. (1); Laschke, Matthias W. (1)

1: Institute for Clinical and Experimental Surgery, Saarland University, 66421 Homburg, Germany; 2: Department of Trauma, Hand and Reconstructive Surgery, Saarland University, 66421 Homburg, Germany,

Background: Microvascular fragments (MVF) are intact vessel segments, which are isolated from adipose tissue and serve as vascularization units in tissue engineering. The functionality of these MVF may be determined by the quality of the fat source. Therefore, we compared the vascularization capacity of MVF from subcutaneous adipose tissue of diet-induced obese mice and healthy controls.
Methods: C57BL/6J mice were exposed to a high-fat or standard diet (control) for 12 weeks. Subsequently, MVF were enzymatically isolated from their subcutaneous adipose tissue and seeded onto collagen-glycosaminoglycan matrices. The MVF-seeded matrices were characterized by scanning electron microscopy or implanted into full-thickness skin defects within the dorsal skinfold chamber of recipient mice ($n = 10$ per group) to analyze their vascularization over 14 days using intravital fluorescence microscopy. All values were expressed as means ± SEM. Statistical significance was accepted for $p < 0.05$.
Results: The vascularization of matrices seeded with MVF from obese mice was improved when compared to controls, as indicated by a significantly higher functional microvessel density (81 ± 15 cm/cm² vs. 32 ± 11 cm/cm²) on day 14 after implantation. Scanning electron microscopy of freshly seeded matrices revealed that MVF isolates from obese mice were almost free of connective tissue, whereas MVF isolates from control mice contained large amounts of undigested collagen fibers. They clogged the pores of the matrices and prevented the reassembly of MVF into blood-perfused microvascular networks.
Conclusion: Subcutaneous adipose tissue from obese mice is more suitable for the isolation of connective tissue-free MVF isolates, which also exhibit an improved vascularization capacity when compared to controls. If this finding is transferable to humans, it indicates that particularly adipose patients may benefit from MVF-based vascularization strategies in future clinical practice.

ID: 102
Topics: Plastische Chirurgie, Basic+Translational

Fibroblast growth factor (FGF)21 is crucial for the revascularization of white adipose tissue grafts

Limido, Ettore (1); Weinzierl, Andrea (1,2); Ampofo, Emmanuel (1); Harder, Yves (3,4); Menger, Michael D. (1); Laschke, Matthias W. (1)

1: Institute for Clinical and Experimental Surgery, Saarland University, 66421 Homburg, Germany; 2: Department of Plastic Surgery and Hand Surgery, University Hospital Zurich, 8006 Zurich, Switzerland; 3: Department of Plastic, Reconstructive and Aesthetic Surgery, Ospedale Regionale di Lugano, Ente Ospedaliero Cantonale (EOC), 6900 Lugano, Switzerland; 4: Faculty of Biomedical Sciences, Università della Svizzera Italiana, 6900 Lugano, Switzerland,

Background: Autologous fat grafting is widely used for soft tissue augmentation in reconstructive and aesthetic surgery. The clinical outcome of this procedure is crucially determined by a rapid and sufficient blood supply of the grafts, which prevents volume loss due to resorption. Therefore, we analyzed in this study the function of fibroblast growth factor (FGF)21, a hepatokine with metabolic and pro-angiogenic activity, in the revascularization process of white adipose tissue grafts.
Methods: Subcutaneous white adipose tissue was harvested from 4 FGF21-knockout (KO) mice and 4 C57BL/6J wild-type (WT) control mice and cut into fat samples of standardized dimensions (0.5 x 0.5 x 0.5 mm). These samples were transplanted into the dorsal skinfold chambers of corresponding FGF21-KO (n = 8) and WT (n = 8) recipient animals to study their revascularization by means of repeated intravital fluorescence microscopy over 14 days. All values were expressed as means ± SEM. Statistical significance was accepted for $p < 0.05$.
Results: The revascularization of transplanted white adipose tissue was delayed in FGF21-KO mice, as indicated by a significantly reduced perfused graft area (1.6 ± 0.9%) on day 6 when compared to controls (12.4 ± 5.1%). This resulted in a significantly lower final functional microvessel density within the grafts (249 ± 11 cm/cm² vs. 361 ± 15 cm/cm²). Moreover, vessel maturation was also impaired in FGF21-KO mice, as shown by larger diameters of newly formed graft microvessels on day 14 (13.1 ± 0.3 µm vs. 11.7 ± 0.1 µm).
Conclusion: Our findings indicate that FGF21 is crucial for the revascularization of white adipose tissue grafts. Hence, this hepatokine represents a promising target for the development of novel vascularization strategies to increase the clinical success rates of fat transplantation.

ID: 103
Topics: Thoraxchirurgie, Basic+Translational

Establishment of a novel test method to analyze in vitro biofilm development with 3D organotypic co-culture

Kurow, Olga; Metelmann, Isabella; Krämer, Sebastian; Stock, Peggy; Steinert, Mathias; Langer, Stefan

Universitätsklinikum Leipzig, Deutschland,

Background/ Purpose
Bacterial pleura infections are an important healthcare challenge and pleural empyema is still associated with high mortality. A severe complication and factor leading to the lack of treatment progress may be that the bacteria encase themselves in a protective coating thus organizing in biofilms. The aim of the present study was to develop a three-dimensional (3D) organotypic model for investigation of infection of the pleural mesothelium.
Methods
Human pleural mesothelial cells (HPMCs) were used together with fibroblasts to set up the 3D organotypic co-culture model of pleura. For the experimental infection, 3D tissue model was exposed to bacterial culture of S. aureus. Permeability of the 3D model was determined by measuringof the concentration of FITZ-labeled dextran. Cell supernatants were processed for cytokine secretion by ELISA and cell viability was assessed using a LHD-assay. Microscopy of 3D tissue sections, quantification of tissue penetration and bacterial accumulation in 3D tissue was performed.
Results
Our 3D model of pleura shares key characteristics with the origin organ (pleura), by expression of the phenotypic markers (vimentin, α-SMA and PHD1). The permeability of 3D co-culture was dependent on the mesothelial cell layer and significantly increased in infection group ($p=0.008$).S. aureus-activated HPMCs release VEGF, TNF-α, MMP-1 and IL-1β in a time-dependent manner. Experimental S. aureus infection showed tissue dissemination throughout the whole 3D model, induction of severe injury, disruption of mesothelial and sub mesothelial connective tissue and dynamic development of the total bioburden with increased CFU counts over time.
Conclusions
Our, novel, non-animal, 3D organotypic co-culture model of pleura can be used in biofilm diagnostics. The experimental in vitro set-up may add a structured approach to testing antiseptics prior to clinical trials, since adding complexity and possibly relevance to recent testing.

ID: 104
Topics: Viszeralchirurgie, Basic+Translational

Organization, function and gene expression of tertiary lymphoid structures in pancreatic cancer resembles lymphoid follicles in secondary lymphoid organs and their abundance is related to superior survival

Lehmann, Jonas (1); Thelen, Martin (1); Schran, Simon (1); Preugszat, Ella (1); Wennhold, Kerstin (1); Garcia-Marquez, Maria A. (1); Lohneis, Philipp (2); Löser, Heike (2); Popp, Felix (3); Kruger, Stephan (4); Boeck, Stefan (4); Ormanns, Steffen (5); Rudelius, Martina (5); Heinemann, Volker (4); von Bergwelt-Baildon, Michael (1,4,6); Bruns, Christiane J. (1,3); Quaas, Alexander (2); Schlößer, Hans A. (1,3)

1: Center for Molecular Medicine Cologne, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 2: Institute of Pathology, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 3: Department of General, Visceral, Cancer and Transplantation Surgery, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 4: Department of Internal Medicine III, University Hospital, Ludwig Maximilians University, Munich, Germany; 5: Institute of Pathology, University Hospital, Ludwig Maximilians University, Munich, Germany; 6: German Cancer Consortium (DKTK), Heidelberg, Heidelberg, Germany,

Background: Tertiary lymphoid structures (TLS) are ectopic B cell clusters in tumor microenvironment (TME) in a variety of cancer types and their abundance is related to cancer-specific. TLS in the TME are assumed to represent hotspots for tumor-specific humoral and cellular immune responses. We aim to identify shared and distinct features of TLS and secondary lymphoid organs (SLOs) to elucidate their functional overlap.
Methods: We performed immunohistochemistry staining of 163 primary pancreatic ductal adenocarcinoma (PDAC) patients to analyze spatial distribution of tumor-infiltrating lymphocytes. Comparison of structural components of lymphoid follicles between TLS and SLOs was done by 5-color immunofluorescence staining. Laser microdissection of TLS, PDAC, SLOs and normal pancreatic tissue for Nanostring-based RNA expression analysis was conducted. B cell receptor sequencing of TLS and SLOs will be performed.
Result: TLS found in 95 % of all analyzed patients were mainly localized in a 2000 µm invasive tumor margin, but in also 49 % of samples intratumoral TLS were present. High abundance of TLS inside and surrounding the tumor led to significantly improved overall survival. Immunofluorescence revealed high similarities regarding composition and spatial distribution of immune cells and structural components. Nanostring analysis confirmed functional similarities of TLS and SLOs by largely overlapping expression patterns in a variety of immune related gene clusters.
Conclusion: Our results confirm beneficial impact of TLS abundance in the TME on the clinical outcome of PDAC patients. The largely overlapping composition, structural organization and gene expression patterns of SLOs and TLS in PDAC further suggest similar function. Our results indicate a role of TLS in cancer immunosurveillance of PDAC, which may be susceptible to therapeutic targeting in this highly aggressive and immunotherapy-resistant disease.

ID: 105

Topics: Plastische Chirurgie, Basic+Translational

Acceleration of cutaneous wound healing by adipose tissue-derived microvascular fragments

Dinter, Melina C.; Bickelmann, Caroline; Nickels, Ruth M.; Menger, Michael D.; Laschke, Matthias W.

Institute for Clinical and Experimental Surgery, Saarland University, 66421 Homburg, Germany,

Background: Cutaneous wound healing is crucially dependent on an adequate vascularization of the skin defect site. In this study, we analyzed whether this can be achieved by the transplantation of microvascular fragments (MVF). MVF are a mixture of fully functional arteriolar, capillary and venular vessel segments, which can be harvested in large amounts from adipose tissue and exhibit a high angiogenic activity.
Methods: MVF were enzymatically isolated from the epididymal fat pads of 5 transgenic green fluorescent protein (GFP)-positive C57BL/6J donor mice. Subsequently, 5,000 MVF were suspended in 10 µL murine platelet-rich plasma (PRP) as carrier and transferred into full-thickness skin wounds with a diameter of 4 mm within dorsal skinfold chambers of C57BL/6J wild-type mice (n = 8). Empty wounds (n = 8) and wounds solely filled with PRP (n = 8) served as controls. Wound healing was repeatedly analyzed throughout 14 days by means of stereomicroscopy, histology and immunohistochemistry. All values were expressed as means ± SEM. Statistical significance was accepted for a value of $p < 0.05$.
Results: The MVF survived within the wounds and markedly contributed to their significantly improved vascularization (microvessel density on day 14: 363 ± 63 mm-2 (MVF/PRP) vs. 95 ± 23 mm-2 (PRP) and 80 ± 35 mm-2 (empty)), as indicated by a fraction of >85% GFP/CD31-positive microvessels within the wounds on day 14. Moreover, planimetric assessment of wound epithelialization over time revealed a significantly accelerated healing of MVF/PRP-filled wounds (non-epithelialized wound area on day 10: 45 ± 6%) when compared to PRP-filled (69 ± 5%) and empty (68 ± 6%) controls.
Conclusion: MVF are potent vascularization units, which effectively promote wound healing. Hence, in future clinical practice, autologous MVF-loaded PRP may serve as a promising biological wound dressing, particularly under poor healing conditions, such as diabetes or post-radiation therapy.

ID: 106
Topics: Andere, Basic+Translational

Immune responses against shared antigens are common in esophago-gastric cancer and can be enhanced using CD40-activated B cells

Thelen, Martin (1); Keller, Diandra (1); Lehmann, Jonas (1); Wennhold, Kerstin (1); Weitz, Hendrik (1); Bauer, Eugen (2); Gathof, Birgit (2); Brüggemann, Monika (3); Kotrova, Michaela (3); Quaas, Alexander (4); Mallmann, Christoph (5); Chon, Seung-Hu (5); Hillmer, Axel (1,4); Bruns, Christiane (5); von Bergwelt-Baildon, Michael (6,7); Garcia-Marquez, Maria (1); Schlößer, Hans (1,5)

1: Center for Molecular Medicine Cologne, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 2: Institute of Transfusion Medicine, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 3: Klinik für Innere Medizin II, Universitätsklinikum Schleswig-Holstein, Campus Kiel, Germany; 4: Institute of Pathology, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 5: Department of General, Visceral, Cancer and Transplantation Surgery, University of Cologne, Faculty of Medicine and University Hospital Cologne, Cologne, Germany; 6: Department of Internal Medicine III, University Hospital, Ludwig Maximilians University, Munich, Germany; 7: German Cancer Consortium (DKTK), Heidelberg, Heidelberg, Germany,

Background Specific immune response is a hallmark of cancer immunotherapy and shared tumor-associated antigens (TAAs) are important targets. Recent advances using combined cellular therapy against multiple TAAs renewed the interest in this class of antigens. Our study aims to determine the role of TAAs in esophago-gastric adenocarcinoma (EGA).
Methods RNA expression was assessed by NanoString in tumor samples of 41 treatment-naïve EGA patients. Endogenous T cell and antibody responses against the 10 most relevant TAAs were determined by FluoroSpot and protein-bound bead assays. Digital image analysis was used to evaluate the correlation of TAAs and T-cell abundance. T-cell receptor sequencing, in-vitro expansion with autologous CD40-activated B cells (CD40Bs) and in-vitro cytotoxicity assays were applied to determine specific expansion, clonality and cytotoxic activity of expanded T cells.
Results 68.3% of patients expressed ≥5 TAAs simultaneously with co-regulated clusters, which were similar to data from The Cancer Genome Atlas (n=505). Endogenous cellular or humoral responses against ≥1 TAA were detectable in 75.0% and 53.7% of patients, respectively. We found a correlation of T-cell abundance and the expression of TAAs and genes related to antigen-presentation. TAA-specific T-cell responses were polyclonal, could be induced or enhanced using autologous CD40Bs and were cytotoxic in-vitro. Despite the frequent expression of TAAs co-occurrence with immune responses was rare.
Conclusions We identified the most relevant TAAs in EGA for monitoring of clinical trials and as therapeutic targets. Antigen-escape rather than missing immune response should be considered as mechanism underlying immunotherapy resistance of EGA.

ID: 107
Topics: Viszeralchirurgie, Basic+Translational

Maschinelles Lernen zur Prädiktion postoperativer Komplikationen nach onkologischen Ösophagusresektionen

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Hintergrund
Die präoperative Vorhersage von Komplikationen nach onkologischen Resektionen der Speiseröhre ist nach wie vor ein relevantes Problem der Ösophaguschirurgie. Methoden des Maschinellen Lernens (ML) können jedoch komplexe Zusammenhänge effizienter und adäquater erfassen. Ziel dieser Arbeit war die Anwendung solcher Algorithmen zur verbesserten Prädiktion von chirurgischen Komplikationen nach Clavien-Dindo Grad ≥3a.
Methodik
In einer prospektiv geführten Datenbank wurden alle onkologischen Resektionen von Adenokarzinomen oder Plattenepithelkarzinomen des Ösophagus bzw. des ösophagogastralen Übergangs erfasst, welche im Zeitraum von 2016 bis 2021 am Universitätsklinikum Köln durchgeführt wurden. Zu den getesteten ML-Algorithmen gehörten: Logistische Regression (LR) auf Grundlage aller Prädiktoren inklusive Recursive Feature Elimination (RFE), Random Forest (RF), K-Nearest Neighbor (KNN), Support Vector Machine (SVM) und Neuronales Netzwerk (NN). Die ML-Algorithmen wurden vergleichend mit dem Kölner Risikoscore analysiert.
Ergebnisse
Von 864 Operationen lag bei 457 Fällen ein Clavien-Dindo Grad ≥3a vor (52,9% versus 407 Fälle mit Clavien-Dindo Grad 0, 1 oder 2). Nach 3-facher Imputation und 3-facher Cross-Validierung wurden die Accuracy und die 95%-Konfidenzintervalle (95%-KI) der Algorithmen folgendermaßen berechnet:
LR + RFE 0.528 (95%-KI: 0.512 - 0.544), RF 0.535 (95%-KI: 0.515 - 0.555), KNN 0.491 (95%-KI: 0.474 - 0.507), SVM 0.511 (95%-KI: 0.502 - 0.520), NN 0.688 (95%-KI: 0.666 to 0.710) und Kölner Risikoscore 0.510 (95%-KI: 0.492 - 0.528).
Konklusion
Die vorliegende Arbeit zeigt, dass es trotz ML-Methoden schwierig ist, eine klinisch praktikable Prädiktion des Clavien-Dindo-Grades anhand der einbezogenen präoperativen Variablen vorzunehmen. Allerdings konnte das Neuronale Netzwerk im Vergleich zu den anderen Algorithmen statistisch die höchste Accuracy erzielen. Für die Zukunft werden größere und möglicherweise aufwendigere Datenbanken benötigt.

ID: 108
Topics: Orthopädie/Unfallchirurgie, Andere

Operative Versorgung von Patienten ab 65 Jahren mit proximaler Humerusfraktur – Ein Beispiel aus der Alterstraumatologischen Versorgungsforschung

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1) Hintergrund/Fragestellung
Die proximale Humerusfraktur (PHF) ist die dritthäufigste altersassoziierte Fraktur, deren Versorgung – insbesondere im Hinblick auf die durch den demographischen Wandel steigende Inzidenz – in Zukunft eine enorme Herausforderung an das Gesundheitssystem stellen wird. Aktuell herrscht selbst unter Experten kein Konsens über eine optimale Therapiestrategie. In den letzten Jahren zeichnet sich ein deutlicher Trend von der gängigen Versorgung mittels winkelstabiler Plattenosteosynthese (WPO) hin zur Versorgung mittels inverser Schulterendoprothese (ISE) ab. Ziel der Analyse lag darin, beide Verfahren hinsichtlich ihres Kurz- und Langzeitoutcomes zu vergleichen.
2) Methodik
Abrechnungsdaten der AOK wurden retrospektiv analysiert. Alle Patienten ab 65 Jahren, die mittels ISE oder WPO in einem Zeitraum von 2010 – 2018 stationär versorgt wurden, wurden in die Studie eingeschlossen. Das Outcome während der initialen Versorgung und im weiteren Verlauf (52 Monate mediane Beobachtungszeit) in Abhängigkeit der Behandlungsgruppe wurde adjustiert auf das Patientenprofil über multivariable logistische bzw. Cox Regressionen evaluiert.
3) Ergebnisse
55.070 Patienten (medianes Alter 79 Jahre, 84% Frauen) wurden in die Studie eingeschlossen, von denen 75 % eine WPO erhielten. Nach Adjustierung auf die bekannten Komorbiditäten war die ISE mit einem höheren Risiko für schwere unerwünschte Ereignisse (SUEs; OR 1,41, 95% CI 1,29 - 1,54, p<0,001) und einem höheren Risiko für chirurgische Komplikationen (OR 1,14, 95% CI 1,06 - 1,21, p<0,01) während des Indexaufenthalts verbunden [1]. Es wurden jedoch keine Unterschiede bei der 30-Tage-Mortalität festgestellt (p>0,05). Im Langzeitverlauf (53.971 Patienten) nach Entlassung war die ISE mit einem höheren Gesamtüberleben (HR 0,92, 95% CI 0,87 - 0,96), einem geringeren Risiko für SUEs (HR 0,92, 95% CI 0,89 - 0,95) und einem geringeren Risiko für chirurgische Komplikationen (HR 0,50, 95% CI 0,46 - 0,55, alle p<0,001) verbunden [2].
4) Konklusion
Eine individuelle Therapieentscheidung unter Berücksichtigung der in dieser Gruppe häufig verkommenden Multimorbidität scheint essentiell. Zudem zeigt sich das Potential der Analyse solcher Daten in Hinblick auf Patientensicherheit im realen Klinikalltag.
Literatur:
[1] J. Koeppe et al, Clin Orthop Relat Res. 2021.
[2] J. Stolberg-Stolberg et al, Dtsch Arztebl Int, 2021

ID: 109
Topics: Herz-/Gefäßchirurgie, Basic+Translational

Functional alterations of neutrophil granulocytes during major cardiac surgery

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Background
Proper neutrophil function is vital to combat pathogens and to clear cellular debris. Excessive stimulation of neutrophils, e.g., during trauma, may alter their functional activity, which in turn puts the host at risk of secondary complications such as infections. Therefore, this study analyses the function of neutrophils regarding phagocytosis, their interaction with platelets, and the generation of radical oxygen species (ROS), in patients prior, during, and after cardiac surgery with extracorporeal circulation (ECC).
Methods
After ethical approval (#452/21) and informed written consent, blood was drawn from patients with cardiac surgery the day before surgery, 45 min after the beginning of ECC intraoperatively as well as 24, 48, and 120 hours postoperatively and analyzed by flow cytometry. Data are reported as mean ± SD from currently five patients with a total planned sample size of 14.
Results
Phagocytotic activity of neutrophils remained stable prior (26.5±4.4%), during (24.3±8.6%) as well as 24 (26.1±8%), 48 (35.1±13.7%), and 120 hours (37.5±16.7%) postoperatively. While 10.4±7.2% neutrophils formed complexes with platelets (PNC) before surgery, PNC formation decreased to 1.8±1.2% intraoperatively, but relapsed to 5.1±2.9% at 24 hours, 6.8±3.9% 48 hours, and 12.6±7.1% 120 hours postoperatively, respectively. Stimulation of ROS-generation (baseline: 100%) by exposure to 1µM PAF was 302±262% preoperatively in comparison to 124±13.4% intraoperatively. Over the course, ROS generation was 143±7% at 24 hours, 179±47.4% at 48 hours, and 198±56% at 120 hours after surgery.
Conclusion
Despite major surgery and related tissue injury, phagocytotic activity remained largely unchanged. However, the cellular function of pathogen clearance through the generation of ROS, as well as the formation of PNCs were reduced. Further studies need to clarify the relevance of the decreased PNC formation and its implications to the host's immunocompetence.

ID: 110
Topics: Herz-/Gefäßchirurgie, Basic+Translational

Piloting flow-cytometry based immunomonitoring in patients with major cardiac surgery

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Background
Major cardiac surgery with extracorporeal circulation triggers systemic inflammation, which in turn affects organ function and increases the susceptibility to infections. However, the analysis of standard parameters such as interleukin 6 (IL6) or C-reactive protein (CRP) lags to the current magnitude of inflammation. Therefore, this study evaluates the activation of neutrophil granulocytes as potential immunomonitoring in patients with aortic valve replacement pre-, intra-, and postoperatively.
Methods
After ethical approval (#452/21) and informed written consent, blood was drawn the day before major cardiac surgery, 45 min after the beginning of extracorporeal circulation intraoperatively as well as 24, 48, and 120 hours postoperatively and analyzed by flow cytometry. Data are reported as mean ± SD from currently five patients with a total planed sample size of 14.
Results
Neutrophil expression of CD10 (+108±114%), CD11b (+589±249%), CD66b (+146±38%) and CD35 (+170±92%) increased intraoperatively normalized to the respective baseline values (0%) while CRP (preoperatively 3.1±1.8 mg/l vs 1.6±0.9 mg/l intraoperatively) and IL6 (preoperatively 3.8±2.2 pg/ml vs 9.8±3.1 pg/ml intraoperatively) remained largely unchanged. However, after 24 hours, the activation status of neutrophils returned close to the preoperative status (CD10: −57±22%, CD11b: +77±117%, CD66b: +63±42%, CD35: +37±38%). In contrast, CRP and IL6 showed a delayed increase reaching their maximum at day 5 and 3, respectively. Other neutrophil markers like CD64 and CD14 showed also a delayed and longer upregulation.
Conclusion
Immunomonitoring of neutrophils by flow cytometry may have potential advantages regarding the delay and the reverberation of clinically established humoral inflammatory markers. Further studies with larger groups including patients with infectious complication are warranted to elucidate the benefits of a neutrophil-based immunomonitoring, e.g., by detection a rising sepsis early.

ID: 111
Topics: Andere, Basic+Translational

Gastric bypass surgery weight loss-independently induces gut Il-22 release in association with improved glycemic control in Zucker Fatty rats

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Introduction
Gastric bypass surgery (GBS) leads to significantly improved glycaemic control in patients with morbid obesity beyond the effects of weight loss alone. Interleukin-22 (Il-22) is an anti-inflammatory cytokine produced by gut immune cells and has beneficial metabolic effects when administered exogenously in preclinical studies. We therefore asked whether GBS induces gut Il-22 release to improve glycaemic control.
Materials and methods
Genetically obese and glucose-intolerant adult male Zucker Fatty rats were assigned to sham-operated ad libitum fed (AL), Roux-en-Y gastric bypass-operated (RYGB) or sham operated body weight-matched to RYGB (BWM) groups. Body weight and food intake were measured for four weeks post-surgery. Oral glucose tolerance test (OGTT) was performed on day 27, rats were sacrificed on day 28. Samples were collected from throughout the gut for Il-22 mRNA expression analysis by RT-qPCR. Portal vein and systemic plasma samples were collected for Il-22 quantification by ELISA. Correlation analysis was performed between systemic/portal vein Il-22 levels and phenotypic measures.
Results
Body weights of RYGB and BWM rats were significantly less than AL rats ($P < 0.0001$). The RYGB group had better oral glucose tolerance than the AL ($P < 0.0001$) and BWM ($P < 0.01$) groups. In the RYGB group, Il-22 mRNA expression in the upper jejunum was approximately 100-fold higher than in the AL group ($P < 0.01$). Il-22 was detectable in portal vein (29.2 ± 8.6 pg/mL) and systemic (46.9 ± 10.5 pg/mL) plasma samples taken from the RYGB group, but not in samples taken from AL and BWM groups. Systemic Il-22 levels negatively correlated with the OGTT AUC ($r = - 0.68$, $P = 0.09$) in the RYGB group.
Conclusion
GBS induces gut Il-22 expression and release in a weight loss-independent manner. This may provide the link between postoperative changes in gut microbiota and improvements in glycaemic control. These findings also support the use of Il-22 to treat obesity-associated insulin resistance.

ID: 112
Topics: Viszeralchirurgie, Klinische Studien

Klinische Relevanz des oralen Sicherheitsabstandes beim Ösophaguskarzinom

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Hintergrund
Die chirurgische Therapie mittels Ösophagusresektion stellt eine der Haupttherapiesäulen des Ösophaguskarzinoms dar. Multiple Risikofaktoren für ein schlechteres Überleben, wie ein erhöhtes TNM-Stadium, wurden identifiziert. Auch mit der Resektion zusammenhängende Faktoren, wie tumorfreie Absetzungsränder, sind Faktoren, die das Überleben der Patienten beeinflussen. Die Länge des oralen Sicherheitsabstandes ist seit den Anfängen der Ösophaguschirurgie umstritten.
Methodik
Es wurden 857 Patienten aus einer prospektiv geführten Datenbank eingeschlossen, die an der Universitätsklinik Köln zwischen 2013 und 2019 mit einer Ivor-Lewis-Ösophagusresektion mit Magenhochzug bei Ösophaguskarzinom in kurativer Intension operiert wurden. 80% der Patienten (682/175) wurden neoadjuvant behandelt. Der makroskopische Abstand des Tumors zum Absetzungsrand wurde durch unabhängige Pathologen nach Fixierung des Präparates erfasst. Wir verglichen die klinisch-pathologischen Variablen mit dem Gesamtüberleben der Patienten.
Ergebnisse
Wir teilten die Gesamtpopulationen in vier Subgruppen (0-20, 20-40, 40-60, >60 mm) auf. Patienten mit einem Absetzungsrand zwischen 20 und 40 mm zeigten das beste Gesamtüberleben (63,5 Monate, 95%CI: 58,9-68,1). Sowohl mit einem kürzeren als auch mit einem längerem Absetzungsrand zeigte sich ein schlechteres Überleben (G1: 54,4, G2: 63,5, G3: 53,8, G4: 44,7 Monate). In multivariaten Cox-Regressionsanalysen ist die Subgruppe 20-40 mm ein signifikanter Faktor für ein besseres Überleben ($p=0,003$, HR: 0,648). Andere Variablen wie das T-, das N-Stadium und der Clavien-Dindo-Score zeigten sich als unabhängige Risikofaktoren für ein schlechteres Überleben ($p=0,045$, $p<0,001$, $p=0,014$).
Konklusion
Zusammenfassend lässt sich sagen, dass ein Mindestabstand von 20 mm zu empfehlen ist. Bei größeren Sicherheitsabständen haben andere klinisch-pathologische Variablen, wie das TNM-Stadium oder das Auftreten von Komplikationen einen höheren Einfluss auf das Überleben.

ID: 113
Topics: Viszeralchirurgie, Basic+Translational

The prognostic role of co-inhibitory receptor ligands on circulating tumor cells and T cells in gastrointestinal tumors

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Background:
Individual cancer cells can escape from the primary tumor to the bloodstream, where many immune cells are present. To date, the immune escape mechanisms of these circulating tumor cells (CTCs) are poorly understood, but there is an urgent need since exploring the key mechanisms of CTC surveillance may lead to new therapeutic strategies to prevent cancer cell proliferation, metastasis, and tumor recurrence. We hypothesize that one mechanism is the expression of co-inhibitory receptors such as PDL-1, which lead to decreased immune cell activity and thereby immune escape of CTCs.
Methods:
CTC detection by CellSearch and PBMC characterization by multiparametric FACS analysis of 98 GI cancer patients with different TMN stage.
Result:
In total, 17,28% of all screened patients, CTCs were detected and 35,71% of the CTCs showed robust PDL-1 expression. Interestingly, all of the PDL-1+ CTC patients appeared with distant metastases or local recurrence, while patients with PDL-1- CTCs showed smaller frequency of had distant metastases with only 44,4%. However, PDL-1+ CTC patients occur to have higher frequency of PBMCs with especially significantly upregulated frequency of regulatory T cells (TREG). Moreover, we could detect a higher expression of PD-1 on cytotoxic CD8+ T cells and tumor fostering TREG.
Conclusion:
Expression of PDL-1 on CTCs appears as a prognostic marker for enhanced metastasis and thereby reduced outcome. This could be explained by a PDL-1/PD-1 mediated tumor escape of CTCs in the blood stream. Whether the expression con PDL-1 on CTCs and primary cancer and metastasis tissue needs further investigation. However, addressing the PDL-1/PD-1 axis by immunotherapy could help to reduce CTCs and their metastatic potential. PDL-1+ CTCs can be used as prognostic marker in GI cancer patients. Furthermore, immunotherapies may be able to reduce the metastases in these patients.
Disclosure Statement: The authors declare no conflict of interest.

ID: 114

Topics: Plastische Chirurgie, Basic+Translational

Transplantatengineering humaner allogener Keratinozyten durch US11-Proteine – Perspektive zur reduzierten Transplantatabstoßung bei Fremdhaut-Allotransplantationen?

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Autologe Spalthauttransplantationen stellen in der Plastischen Chirurgie einen Goldstandard in der Behandlung Schwerbrandverletzter dar, bedeuten jedoch aufgrund des Mangels geeigneter Entnahmestellen bei ausgedehnten Hautdefekten häufig auch eine Herausforderung im Behandlungsansatz. Die Verwendung glycerol- oder kryokonservierter allogener Spenderhaut ist daher eine der Standardtherapien zur vorübergehenden Wundabdeckung, birgt jedoch die Risiken einer sekundären Transplantatabstoßung. Somit wäre eine Immunmodulation allogener Hauttransplantate wünschenswert, ohne in die Gesamtimmunantwort des Empfängerorganismus einzugreifen. Einen möglichen experimentellen Therapieansatz stellt das humane Cytomegalievirus dar, das verschiedene Strategien nutzt, um der Immunantwort des Empfängerorganismus zu entgehen. So hat unteranderem das kodierende US11-Gen sowie das zugehörige Protein eine Schlüsselrolle in der Immunevasion.

Basierend auf den bisherigen Erkenntnissen wurden humane primäre Keratinozyten mit US11-Vektoren transfiziert oder mit einem rekombinanten US11-Protein als Biopharmazeutikum behandelt, um eine Verringerung der MHC-I-Expression zu erzielen und somit die Alloreaktivität der humanen primärer Keratinozyten zu reduzieren. Die Reduktion der MHC-I-Expression wurde mittels Western Bloting, real-time PCR und Durchflusszytometrie quantifiziert. Um das in-vivo Potenzial der mit US11 stimulierten Keratinozyten zu bewerten, wurde eine Ko-Kultur mit humanen PBMC durchgeführt, die in ELISA-Tests verringerte IFN-Gamma-Konzentrationen zeigten. In einem weiteren Schritt wurde menschliche Spenderhaut mit rekombinanten US11-Proteinen behandelt und zeigte nach 7 Tagen eine reduzierte MHC-I-Expression.

Zusammenfassend stellt die genetische Modifikation humaner primärer Keratinozyten mittels Transfektion oder die Behandlung mit rekombinantem US11-Protein als Biopharmazeutikum einen vielversprechenden Ansatz zur Verringerung der Alloreaktivität dar.

ID: 115

Topics: Plastische Chirurgie, Basic+Translational

Einfluss von Tamoxifen auf die Genexpression der Tumorgenese in adipogenen Stammzellen, epithelialen Brustdrüsenzellen und Mammakarzinomzelllinien – eine in vitro Studie

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Das Mammakarzinom stellt eine der häufigsten bösartigen Tumorerkrankungen bei Frauen dar. Die multimodalen Behandlungsansätze umfassen neben der chirurgischen Therapie eine adjuvante Radiatio, eine Chemotherapie sowie eine Antikörper- und Hormontherapie. Dabei hat sich Tamoxifen als antiöstrogene Substanz bewährt. Das Behandlungsspektrum sekundärer Brustrekonstruktionen reicht von autologen Fettinfiltrationen bis hin zu komplexen mikrochirurgischen Eingriffen mit freien Lappenplastiken. Im Rahmen von autologen Fettinfiltrationen werden auch adipogene Fettstammzellen (ASC) transferiert. In der Literatur wird der Einfluss von ASC auf das Tumorbett und eine dadurch möglicherweise erhöhte Rezidivrate kritisch diskutiert. Zudem gibt es derzeit keine abschließende Empfehlung bezüglich Tamoxifen behandelter Patientinnen und autologer Fettinfiltrationen.
Ziel der vorliegenden Studie war es die Wirkung von Tamoxifen auf die Genexpression einer Vielzahl von Genen, die an der Tumorentstehung und -transformation beteiligt sind, zu untersuchen. Dazu wurden eine Brustepithelzellen sowie Mammakarzinomzellen mit Tamoxifen in vitro behandelt sowie mit ASC kokultiviert. Die Genexpression an der Tumorentstehung beteiligter Pathways wurde mittels PCR Arrays quantifiziert und zeigte in den Ko-Kulturen von ASC und Mammakarzinomzellen mit zunehmender Zeit der Behandlung und Konzentration von Tamoxifen eine vermehrte Genexpression, so dass hier eine möglicherweise erhöhte Tumorrezidivrate durch autologes Fettgrafting postuliert werden könnte. Aufgrund einer vermehrten Expression proangiogener Gene scheint Tamoxifen jedoch die Einheilung eines autologer Fetttransplantate nicht zu beeinträchtigen, sondern viel mehr zu begünstigen. Insgesamt können die vorgelegten Daten als Ergänzung in der kontroversen Diskussion über die Beziehung zwischen ASC und Mammakarzinomzellen angesehen werden. Alle Ergebnisse zusammengenommen sind weitere Studien erforderlich, um Ergebnisse abschließend zu beurteilen.

ID: 116
Topics: Andere, Basic+Translational

Die Entzündungsantwort der Niere während TRAKI nach experimentellem Thoraxtrauma mit hämorrhagischem Schock

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Fragestellung
Körperliche Traumata und deren Folgen sind eine häufige Todesursache, wobei das Thoraxtrauma (TXT) und der hämorrhagische Schock (HS) eine zentrale Rolle einnehmen. Rund 24% der Intensivpatienten entwickeln ein akutes Nierenversagen (AKI). Die morphologisch-dynamische Antwort der Niere ist noch weitgehend unbekannt.
In dieser Studie wurden die molekularen Schädigungsmuster der Niere räumlich und zeitlich untersucht.
Methodik
Bei C57BL/6J Mäusen wurde ein TXT+HS (MAP 30 ± 5 mmHg) erzeugt. Eine Stunde nach Induktion des HS erfolgte die Retransfusion. Nach 4 h, 24 h und 5 d erfolgte die Versuchsterminierung mit Entnahme von Blut, Urin und Organen. Zytokine, Chemokine und Organ-Schadensmarker wurden mittels ELISAs bestimmt. In qPCR-Analysen, histologischen Färbungen und mittels Elektronenmikroskopie (EM) wurden die Nieren vergleichend untersucht.
Parallel erfolgte die in vitro-Untersuchung muriner Zellen des distalen Tubulus sowie des Sammelrohrs, welche mit traumarelevanten Stimuli versetzt wurden. Die Auswertung erfolgte durch One-Way-ANOVA mit post-hoc-Testing. Das Signifikanzniveau war auf $p < 0{,}05$ festgelegt.
Ergebnisse
In den Nieren der TXT+HS-Tiere fand sich 24 h nach Trauma eine signifikante Erhöhung der Expression von Neutrophilengelatinase-assoziiertes Lipocalin (NGAL) und Kidney Injury Molecule-1. Im Plasma der TXT+HS-Mäuse zeigte sich ein signifikanter Anstieg von NGAL und der Komplementaktivierungsprodukte C3a und C5a. EM-Analysen ergaben Hinweise auf strukturelle Veränderungen im tubulären System. Die in vitro-Exposition der Tubuluszellen mit C3a und C5a zeigte eine signifikante Reduktion der Expression von C3 und IL-6.
Konklusion
Es ergaben sich klare Hinweise auf die Ausbildung eines TRAKI nach TXT+HS. Räumlich konzentrierte es sich primär auf den proximalen Tubulus, insbesondere 24 h post Trauma. Eine frühe systemische Komplementaktivierung konnte nachgewiesen werden, die in in vitro-Versuchen an Tubuluszellen die Entzündungsantwort supprimierte.

ID: 117
Topics: Andere, Basic+Translational

Soluble VE-cadherin disrupts endothelial barrier function via VE-PTP/RhoA signalling

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Background:
Increased levels of soluble Vascular endothelial (VE)-cadherin fragments (sVE-cadherin) have previously been linked with inflammation-induced loss of endothelial barrier function. Here we tested whether sVE-cadherin is critically involved in the onset of endothelial barrier dysfunction independent of pro-inflammatory stimuli.
Methods and results:
Recombinant human sVE-cadherin (extracellular domains EC1-5) was generated and verified by sequencing and immunoblotting. Application of sVE-cadherinEC1-5 on human microvascular endothelial cells (HDMECs) dose-dependently induced loss of endothelial barrier function. In vivo application of sVE-cadherinEC1-5 resulted in loss of endothelial barrier function and reduced microcirculatory flow. Immunostaining and Western blot analysis revealed that the functional effects of sVE-cadherinEC1-5 were paralleled by decreased VE-cadherin, reduction of alpha-/beta-/gamma-catenin and tight junction-associated protein ZO-1 at the cell borders. While induction of endothelial cell death was not observed, sVE-cadherinEC1-5 interfered homophilic VE-cadherin interaction. In addition, sVE-cadherinEC1-5 perturbed VE-protein tyrosine phosphatase (VE-PTP)/VE-cadherin interaction as revealed by molecular modelling and loss of VE-cadherin/VE-PTP at cell borders indicating activation of VE-PTP under these conditions. Accordingly, VE-PTP inhibitor AKB9778 blunted all sVE-cadherinEC1-5-induced effects in vitro and in vivo. Downstream effects involve VE-PTP-dependent RhoA activation, which was attenuated by AKB9778. Rho-kinase inhibitor Y27632 blocked sVE-cadherinEC1-5-induced loss of endothelial barrier function.
Conclusion:
In summary, sVE-cadherin disrupts endothelial barrier function by dismantling the VE-cadherin complex at the cell borders via VE-PTP-dependent RhoA activation. This uncovers a novel pathophysiological role of sVE-cadherin in the context of endothelial barrier dysfunction in inflammation.

ID: 118
Topics: Viszeralchirurgie, Klinische Studien

The EVIglance trial: the new gold standard for answering a clinical question – a randomised controlled trial

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Background/Objective
Profound literature search is a vital element of evidence-based medicine for clinicians and researchers. Yet, daily increasing numbers of publications and limited time resources make it hard to identify high-quality evidence. The objective of this randomised controlled trial (RCT) was to demonstrate the superiority of the “Evidence Map of Pancreatic Surgery” (via EVIglance) compared to conventional literature search via PubMed for answering clinically relevant questions in pancreatic surgery.
Methods
We performed a single-centre, cross-over RCT including medical students, residents and consultants. Participants conducted literature searches with two predefined PICO (Patient, Intervention, Control, Outcome) questions, one with PubMed and the other with EVIglance. Order of the search tools and selection of the two questions were randomised. Primary endpoint was time in minutes until a synopsis was made regarding the PICO question. The synopsis was characterised by the direction of the effect and the certainty of evidence.
Results
Each 28 students, residents and consultants were randomised and analysed. A synopsis for the PICO question was found with PubMed after 10.8 minutes and with EVIglance after 1.7 minutes (95%-CI for difference: 9.9 to 8.3 minutes; p<0.001). EVIglance answered the PICO significantly faster in all groups even after Bonferroni correction. Participants were able to guess the direction of the effect (95% vs 48%; p<0.001) and the certainty of evidence (99% vs 30%, p<0.001) better with EVIglance. The correct number of RCTs to answer the PICO question was found more often with EVIglance compared to PubMed (99% vs 15%; p<0.001).
Conclusion
EVIglance is faster and more reliable to support physicians in their literature search finding high-quality evidence. Given the advantages of EVIglance it may be considered the new gold standard for finding best available evidence. Therefore, evidence maps regarding further topics are urgently needed.

ID: 119
Topics: Viszeralchirurgie, Klinische Studien

The CARDIA-trial: Comparing transthoracic esophagectomy with transhiatal extended gastrectomy in adenocarcinoma of the gastroesophageal junction (GEJ) type II in a multinational and prospective randomized clinical trial

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Adenocarcinoma of the GEJ type II can be resected using two surgical approaches: transthoracic esophagectomy or transhiatal extended gastrectomy. Both allow for a complete tumor resection, yet there is an ongoing controversy about which surgical approach is superior with regard to quality of life and oncological outcomes.
The CARDIA study is a non-blinded, multinational, multicenter, prospective, randomized clinical superiority trial. Patients (n = 262) with a GEJ type II tumor resectable by both transthoracic esophagectomy and transhiatal extended gastrectomy will be enrolled in the trial. Patients with tumor stages cT3-4a N0/N+ M0 receive a perioperative chemotherapy according to the FLOT regimen and will be randomized to either study group during restaging. The primary endpoint is overall survival. Secondary endpoints are disease-free survival, quality of life, histopathological complete resection (R0), post-operative complications, number and localization of infiltrated lymph nodes after dissection. Postoperative survival, disease- free survival and quality of life will be followed-up for 24 months after discharge. Further survival follow-up will be conducted up to 60 months.
In this ongoing study we were able to initiate nine German study centers (Cologne, Mainz, Berlin, Heidelberg, Munich, Leipzig, Freiburg, Würzburg and Lübeck) and two international study centers (Utrecht and Stockholm). Up to date, we were able to include 48 patients in the trial. At the University Hospital of Cologne, 28 patients were included so far. The average hospital stay was 15 days. We performed 50% of the operations as conventional open surgery, 28,6% as a hybrid operations and 21,4% as MIS. All patients survived until discharge, no SAEs occurred.
This is the first international prospective randomized clinical trial exploring the best surgical strategy for GEJ type II tumors regarding overall survival and quality of life.

ID: 120

Topics: Viszeralchirurgie, Basic+Translational

Role of plakophilins in the regulation of intestinal barrier function in vitro and in vivo

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Background: Previous data provide evidence for a critical role of desmosomes to stabilize intestinal epithelial barrier function. The contribution of desmosomal plaque proteins plakophilins (PKP) in the intestinal epithelium remains unexplored.
Methods: The expression of PKP1-3 in human gut specimens, human intestinal organoids and Caco2 cells was analyzed. Using siRNA, knockdown of PKP1-3 in Caco2 cells was induced and intercellular adhesion, expression of junctional proteins and epithelial barrier function was evaluated. Immunostaining, proximity ligation assays and co-immunoprecipitation were used to investigate the effect on Proteinkinase C (PKC). An inducible enterocyte-specific knockout for PKP2 was generated (VilCreERT2 PKP2-/-).
Results: The intestinal expression of PKP2 and PKP3 was verified in gut specimens whereas PKP1 was not detected. Loss of PKP2 and PKP3 was observed in samples from patients with inflammatory bowel disease. Knockdown of PKP2 in Caco2 cells resulted in loss of intercellular adhesion and attenuated barrier formation. This was paralleled by changes of the whole desmosomal complex. In addition, tight junction proteins claudin1 and claudin4 were reduced following the loss of PKP2. Loss of PKP3 did not change intercellular adhesion and barrier function in Caco2 cells, while loss of both PKP2 and PKP3 augmented the changes observed for reduced PKP2 alone. Further investigations revealed a direct interaction between PKP2 and PKC suggesting that PKP2 is involved in the regulation of PKC. Preliminary data from an inducible enterocyte-specific knockout mouse suggest an increased susceptibility of intestinal barrier function under inflammatory conditions.
Conclusion: Our data suggest that PKP2 and PKP3 are involved in the pathogenesis of inflammatory bowel diseases. In vitro analyses revealed that PKP2 but not PKP3 is essential for intestinal barrier function by providing a signaling hub for PKC-mediated expression of tight junction proteins.

ID: 121
Topics: Plastische Chirurgie, Andere

Relevant knowledge of the general and abdominal surgeon on plastic surgery

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Aim & Method: Short & compact review based on i) a selection of relevant references from the medical scientific literature & ii) surgical experiences obtained in daily work.
Results (selected corner points): 1) Biological protection procedures in vascular surgery by flap coverage after meticulous debridement w/ or w/o autogenic vascular reconstruction are used to overcome infection of a vascular prosthesis.
2) Fistula treatment for aorto-tracheal/-duodenal fistulas, a big challenge for the referring general surgeon, can be treated by flap coverage, such as by using the interposition of a pectoralis-major flap & the omentum-majus flap, resp.
3) W/ regard to nerve surgery, encouraging results after early microsurgical recurrent laryngeal nerve repair w/ improved subjective voice quality or concerning reconstitution of respiratory capacity in diaphragmatic palsy has been reported.
4) Lymphatic surgery for lymphedema can be indicated, e.g., for surgical repair of the lymphatic pathway by the i) interrupted lymph system can be reconstructed by an interposition, or ii) lymphatic fluid can be drained extraanatomically (e.g., by a lymphatico-venous anastomosis).
5) Mass reduction such as dermolipectomy w/ subsequent split-thickness is a valuable option, which provides excellent volume reduction.
6) Defect coverage: A. Split- or full-thickness skin grafts.
B. Further methods are local & free fascio- & musculocutaneous flaps.
7) Abdominal wall hernia closure w/ instable skin coverage, flap closure, either alone or in combination w/ mesh is superior to mesh closure only.
8) Free flaps: If there is no option for a local or pedicled flap availabe, free flaps can well be used for abdominal wall defect closure.
Conclusion: Plastic surgery is an indispensable partner for specific surgical problems & clinical situations of general & abdominal surgery w/ its great options & surgical techniques, which modern plastic surgery can provide to achieve best outcome & quality of life for the patients.

ID: 122
Topics: Andere, Andere

What must a(n academic) surgeon know about medical library system?

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A scientific medical school library provides not only printed literature to the staff in research, teaching & patient care, it also offers a broad profile of services.
Method: Overview on the performance spectrum of a medical library w/ regard to the clinical work of a surgeon, e.g., as i) available experiences of the librarians, & ii) evaluation of novel, selected publications associated w/ specific topics.
Results (corner points): The interested surgeon should be familiar with the various services of a scientific medical school library, which he might need for up-coming scientific searches of factual knowledge + for individual advanced training (aquisition of novel knowledge) as part of his activities comprising clinical care, science, education & publication + clinical review. For this purpose, the surgeon should be able to handle electronic presentations, such as websites & to be oriented in the building of the library but he should also know the main tools for literature search, such as the library catalog, the electronic library of journals ("EZB") & the bibliographic data base "PubMed". Even the order of specific literature from other libraries (interlibrary loan) should be sufficiently known to use them as addition of the missing body of literature locally. Thus, the path from literature search to available printed media should not be further considered a persisting barrier. In addition, administrative literature software can be used supporting efficient scientific work. The surgeon gets to know consecutively the supporting options, which the library can provide in its role as service provider either for assistance in literature search or an offer for a training course.
Conclusion: Medical library can be considered an essential service provider for the surgeon acting as clinician, scientist, tutor, publisher & reviewer. It provides important accesses to expert information & services to make surgeon's work easier & to support him that he can reach his aims.

ID: 123
Topics: Andere, Klinische Studien

Novel Aspects & Trends on the Investigated Interdisciplinary Pain Management in Abdominal Surgery - Data Obtained in a Systematic Clinical Observational Study by an Interdisciplinary Research Group in a Tertiary Center

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Aim/Method:
To summarize the results of an interdisc. clin. work & research group of a pain outpatient clinic & abdominal surgery department at a tertiary institution in a representative overview to reflect on upcoming research topics & current trends in the field.
Results:
- The creation & implementation of an institutional pain management SOP represents a worthwhile & promising endeavor.
- For quality assurance, the consults for pain patients are supervised by the senior physicians of the outpatient pain division.
- Abdominal surgery poses an increased risk for the occurrence of back pain in later years.
- Own studies provide also reliable data showing effective pain therapy w/ Novaminsulfon/NSAIDs & Piritramid up to a postop. duration of 8d; especially for cancer pats., sustained-release opioids + psychotropic drugs should be considered thereafter.
- Medications are then selected based on the pat.'s classification of pain quality, which is complained about.
- In clin. practice, the level of pain is not a basis for assessing the medication required; pain level of the individual pat. is used solely to assess the course of therapy.
- The consults are not solely for the purpose of administering opioids to every pat. requested; the aim is rather the dissemination of the SOP, its internalization by the ward staff &, based on this, the implementation of a therapy adapted to the individual case - therefore, it seems necessary to increase the No. of consults in the long run to get more & appropriate information.
- The goal is to provide consultation beyond the normal consultative case, not to the indiv. physician but to the ward team. In this context, the pain service is more involved in the inpatient case &, in return, the team is more actively involved in pain management.
Conclusions:
Our own experience with a postop. algorithm shows that a continuation of the administration or combination of NSAIDs/Dipidolor not only for 3 but for 8d postoperatively is possible & effective.

ID: 124
Topics: Andere, Klinische Studien

Currently recommended Cannabis use in daily surgical as well as broad clinical practice (initial systematic results) - proper handling, control measures & indicated trends

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W/ the 2017 legislation, a different approach to cannabis prescribing became possible. At the same time, however, the question arised as to where the benefits & dangers of cannabis medication exist now, in particular, in that the public is being given the option to legally use cannabis.
Methods: Data provided by & obtained from:
- Health insurance companies, the medical association, the “Medical Service of the Health Insurance Companies“ (German abbreviation, “MdK“) on previously approved uses (e.g., in case of tumor cachexia & spasticity in MS).
- Chamber of Pharmacists, professional organization & umbrella group. in particular, on self-purchased cannabis preparations were used.
W/ regard to possible & identifiable consequences, wich can lead to derive reasonable new regulations, the use of cannabis was compared with that of opioids.
Results: 3 various types of administration behaviors exist: Physicians
- using cannabis for "confirmed" indications such as tumor cachexia, nausea, & spastic pain in MS;
- who also "try cannabis!" for up to 50 other indications;
- who use cannabis as a bridging measure because they do not have an idea for a particular pain situation (even though there would be other options).
In contrast, there are 3 types of cannabis preparation:
- As tablet, as flower, as a tetrahydrocannabinol(THC)-free preparation on a green prescription.
A comparison in tabular form shows that a danger of addiction in cannabis medication, which also exists with opioids, originates in the uncritical expansion of indications as well as in the use of flowers against “everything“.
Conclusion: Addiction to opioid intake has been already known for a long time. Therefore, countermeasures, such as stricter indications & quantity limits in non-cancer patients were taken. Against a possibly threatening wave of addiction to cannabis, a further development as well as careful & approved extension of indications, as well as adequate control over flower users, appear indicated.

ID: 125
Topics: Andere, Klinische Studien

What is better in neuropathic pain(?): Anticonvulsives or Antidepressants

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Aim/Method: In a retrospective unicenter observational study, pain therapy (Tx) was investigated & compared with regard to AC & AD in a consecutive patients (Pats.) cohort of a representative No. over a defined study period.
Results: In total, 403 Pats. were registered from 2015-2019: Prior to admission to the hospital, 95 subjects (23.6%) received AC (n=72 alone, n=23 together with AD).
After admission, n=15 individuals did not receive any further AC, n=57/95 Pats. (n=39 alone, n=18 together with AD; 60%) received an AD instead of AC (47.4% of Pats. became better). Out of the 41 cases, in whom AC administration was continued (n=23 alone, n=18 together with AD), 41.5% became better.
It is crucial, in which dosage of AC the 57 Pats. were switched to AD:
- In the 6 Carbamazepin-Pats., n=3 received minimally 600 mg.
- In the 21 Gabapentin-Pats., n=19/21 received minimally 900 mg. If the 39 Pats. with AD alone were evaluated, this was confirmed.
- Only in Pregabalin-Pats.: If Pats. with a low dosage were presented w/ unsuff. pain Tx regimen, it was switched to AD by the Pain Therapy Outpatient Clinic - in n=13/26 w/ a maximum of 150 mg/d.
Conclusion: Out of the Pats. who had been switched from AC to AD by the pain therapists, only a trend of Pats. became better by the switch of the drugs. It has to be taken into account that in 22 of 57 Pats., a suff. AC dosage had been administered but the Pats. had not become better. Only the switch to AD led to Tx success, namely, improvement of pain.
It is also important to clarify whether all Pats. with neuropathic pain have received an appropriate medication (AC or AD) - this is actually not the case.
At admission, 252 Pats. had neither AC nor AD but after admission, there were only 145 Pats. w/ no AC or AD medication left. This means that in 107 cases, Tx of the neuropathic pain was overlooked & these 107 subjects are 1/4 of all investigated Pats. (n=107/403) & 71.3% more than the No. of Pats. w/ psychic drugs at admission (n=107/151).

ID: 126
Topics: Andere, Klinische Studien

Role of depression in tumor and non-tumor patients

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Aim/Method: Overview on the level of knowledge regarding recent study activities on the topic, in particular, the correlation of depressions & benign/malignant diseases, in the case number (No.) at a tertiary center - i) as part of a systematic prospective unicenter observational study (design) of an interdisciplinary clinical research group (pain therapy & abdominal surgery of the reporting hospital) in a consecutive patient cohort with a representative case No. over a defined study period to reflect daily clinical practice (“real-world data“) & ii) for further topic-related investigations.
Results (corner points):
- The degree of severity of F3-depressions has decreased over time, during which the portion of mentally normal non-Tu-patients has increased from 33.3 up to 47.5%.
- In Tu-patients, there was an increase of psychic diagnoses (selective Tu-diseases) over the years of survival. The portion of acute patients with psychic diagnoses in case of an underlying Tu-disease of the urogenital tract increased from 37.2-74.1% in long-term survivors.
- In non-Tu-patients, the portion of F3-diagnoses was appr. the same (only a moderately increasing trend from 15.5-17.1%) despite a decreasing No. of psychic disorders - in Tu-patients, the portion inceased from 2.3-14.8%.
- In Tu-patients, even depressive symptoms of the subsyndromal quality were found. So, in mentally normal Tu-patients there was a significantly more frequent occurence of depressive symptoms (reduced facial expression, cheerlessness, social retreat) than compared to mentally normal non-Tu-patients.
- In addition, in the spectrum of non-Tu-diagnoses - e.g., in the non-operative orthopedics - subsyndromal depressions could be detected.
Conclusion: Based on the importance of depressions for somatic diseases, screening of depressive symptoms in Tu- & non-Tu-patients appears recommendable in each case (e.g., by routineous use of the suitable “Hospital and Anxiety Scale“ [HADS] approved in clinical practice).

ID: 127
Topics: Andere, Andere

Depression in coronary heart disease & tumor lesions as representative examples of somatic diseases with considerable relevance for morbidity & mortality

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Aim: To present the problem of comorbid depression in cardiac & cancer patients based on our own clinical experience from patient care & selected references from the topic-related literature.
Method: Narrative compact brief review.
Results: Triggered by increased stress response - not adequate to the situation - & the associated overload of the stress systems themselves with massive catecholamine release up to depletion of the noradrenaline-producing cells, it comes to the thus missing protection of the brain from the simultaneous cortisol release. The result is cell destruction on a considerable scale, especially in the limbic system. These failures ultimately lead to the depressive symptomatology, which thus forms the final stage of the overload of the stress systems. The destruction of the stress systems is flanked by the release of proinflammatory substances such as IL-2 & IL-6.
The path to overload is formed here by the 2 disease areas under consideration (myocardial infarction, selected tumor diseases).
Conclusion: The pathway from massive stress to depressive symptomatology is manifold & is to be considered separately depending on the clinical specialty. So far, this has been done solely in the context of psychiatry. By demonstrating the comorbidity of myocardial infarction & various cancer types with depression, the depression’s importance is also introduced into somatic medicine. This is reinforced by the fact that somatic (painful & nonpainful) symptoms can also indicate depression. Thus, depression is not a disorder to be concerned about because it belongs to a non-somatic specialty. In all areas of anesthesia & surgery (operative or perioperative medicine, intensive care on the ITS/IMC, emergency medicine, pain therapy), somatic physicians encounter patients with cardiac &/or cancer diseases, in whom a depression requiring treatment is present, which contributes to the patient's prognosis & which must be treated or at least diagnosed by them.

ID: 128

Topics: Viszeralchirurgie, Basic+Translational

NLRP3 inflammasome activation in leucocytes drives hepatic stellate cell activation and fibrosis in non-alcoholic steatohepatitis

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease worldwide showing a rapidly rising prevalence among all age groups. Key characteristics of the pathogenesis of NAFLD are inflammation, cellular death, and liver fibrosis. The NLRP3 inflammasome, a multiprotein complex promoting activation of caspase-1 as well as interleukin 1β (IL-1β) release, was identified as a key driver of these characteristics. The cell-specific contribution of the activation of the NLRP3 inflammasome in leucocytes in NAFLD remains unknown. Methods: After NLRP3 inflammasome stimulation monocytes were co-cultured with hepatic stellate cells (HSC) and HSC activation analysed. A conditional Nlrp3 knock-out mouse was generated and bred to mice expressing Cre under the control of Lysozyme to investigate the role of NLRP3 inflammasome dependent cell death in myeloid cells, liver inflammation and fibrosis. A chronic (choline-deficient, L-amino acid-defined high-fat diet (CDAA-HFAT)) liver injury model was used to induce in vivo NLRP3 activation and fibrotic-non-alcoholic steatohepatitis (NASH). Cell death, liver inflammation and fibrosis were analysed. Results: Co-culture of monocytes after NLRP3 inflammasome stimulation with HSCs led to an increase of HSCs activation markers. In contrast, monocytes deficient for NLRP3 were not capable to activate HSCs after NLRP3 inflammasome stimulation. NASH-associated cell death and hepatic inflammation was ameliorated in myeloid-specific Nlrp3 knock-out mice in the CDAA-HFAT model. In addition, fibrosis and hepatic stellate cell activation were decreased in myeloid-specific Nlrp3 knock-out mice. Conclusion: This study provides new insights in the role of NLRP3 activation in myeloid cells in the pathogenesis of NAFLD and identifies myeloid specific NLRP3 inflammasome activation as crucial for the progression of NAFLD to fibrotic-NASH.

ID: 129
Topics: Viszeralchirurgie, Klinische Studien

Improved survival by blockade of adrenergic signaling in patients with gastric signet ring carcinoma

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Despite improved multimodal therapy, the prognosis for patients with esophagogastric adenocarcinoma (EGA) remains poor. Overall survival rates after 5 years range from 30-40%. Recent studies in various cancers have shown a potential benefit for the intake of beta-blockers resulting in higher survival and lower recurrence and metastasis rates. This is supported by several preclinical and in vitro studies showing that adrenergic activation modulates apoptosis, angiogenesis, and other cancer hallmarks. This study was performed to elucidate the potential benefit of beta-blockadeon EGAs.
We analyzed 364 patients that underwent resection of a gastric and AEG III carcinoma. Histopathological regression, overall and disease-free survival of 395 patients with neoadjuvant treated adenocarcinoma of the esophagogastric junction type III and stomach (cT2N+ and/or cT3/cT4) were analyzed from a prospective database to evaluate the impact of beta-blocker intake during their multimodal treatment.
Patients with an intestinal EGA and beta-blocker intake during and after their oncological treatment (n=127) had a significant impaired overall survival (84 months vs. 48 months, p=0.016). This subgroup showed significant differences in the ASA classification (0.017), age (0.040), severe comorbidities (<0.001) and tumor regression according to Becker (0.050). Patients with signet ring cell carcinoma (n=122) had a significant better disease-free survival if taking beta-blockers, (44 months vs. 69 months, p=0.022). Severe comorbidities (0.005) and clinical response (0.026) differed significantly in this subgroup. The multivariate analysis identified beta-blockers as independent prognostic factor for a better disease-free survival in those patients (p=0.049).
Beta-blockers show a potential beneficial effect in addition to chemotherapy in selected patients and deserve more attention in the treatment of diffuse EGA. Future molecular studies investigating the precise mechanism of action are needed to fully elucidate the therapeutic effect of this drug.

ID: 130
Topics: Plastische Chirurgie, Basic+Translational

Aus Fettstammzellen isolierte Exosomen induzieren proapoptotische Gene in einer Brusttumorzellinie

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Hintergrund/Fragestellung
Der autologe Fetttransfer zählt zu den häufigsten Eingriffen in der Plastischen Chirurgie. Viele Indizien sprechen dafür, dass eine Anreicherung mit Fettgewebsstammzellen (ADSCs) zu einer verbesserten Überlebensrate des Gewebes führt. Bei Weichgewebsaugmentationen nach Tumorresektion wird aber der pro-proliferative Einfluss der ADSCs als erhöhtes Risiko für ein Tumorrezidiv angesehen. ADSCs könnten aber auch einen negativen Einfluss auf das Tumorwachstum ausüben. In dieser Studie wurde der Einfluss isolierter Exosomen auf die Mammakarzinomzelllinie MCF-7 untersucht.
Methodik
Primäre ADSCs wurden in serumfreiem Medium kultiviert. Mittels Magnetic Activated Cell Sorting wurden Exosomen aus dem konditionierten Medium gewonnen. Die Exosomen wurden mittels Western Blot identifiziert. MCF-7 wurde mit den Exosomen oder konditionierten Medien kultiviert. Anschließend wurden Zellvitalitäts- und Zelltoxizitätstests durchgeführt und die relative Genexpression von Proliferations-, Apoptose-, und Angiogenesemarkern mittels RT-PCR bestimmt.
Ergebnisse
Gegenüber den konditionierten Medien wirken die Exosomen von ADSCs konzentrationsabhängig proliferationsinhibierend und zytotoxisch auf MCF-7-Zellen. Während die Expression pro-apoptotischer Gene durch die Exosomen gegenüber den Zellen im konditionierten Medium hochreguliert wurden, wurden anti-apoptische Gene herunterreguliert. Darüber hinaus wurden auch pro-proliferative Gene und angiogenetische Faktoren durch die Kultivierung mit den Exosomen im Gegensatz zu den konditionierten Medien herunterreguliert.
Konklusion
ADSCs haben durch die sezernierten Wachstumsfaktoren und Zytokine einen positiven Einfluss auf die Proliferation der Zellen in ihrer Umgebung. Die sezernierten Exosomen hingegen haben auch antiproliferative und pro-apoptotische Wirkung auf Tumorzellen. Dementsprechend sollte der Einsatz von autologem Fett zur Weichgewebsdeckung auch nach Tumorresektionen nicht grundsätzlich ausgeschlossen werden.

ID: 131
Topics: Plastische Chirurgie, Basic+Translational

Einfluss des mTOR-Signalwegs auf die Hyperproliferation bei der Multiplen Symmetrischen Lipomatose

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1) Hintergrund/Fragestellung
Die Multiple Symmetrische Lipomatose (MSL, Morbus Madelung) ist eine seltene Erkrankung, die durch das exzessive Wachstum von Fettgewebe charakterisiert ist. Es existieren verschiedene Subtypen, die sich durch die betroffenen Körperareale unterscheiden. Die Ursache der Erkrankung ist ungeklärt. Es existiert keine pharmakologische Therapie, so dass die chirurgische Entfernung des Gewebes die einzige Option darstellt. Während frühere Arbeiten eine gestörte Lipolyse als ursächlich betrachtet haben, setzt sich zuletzt die die Hypothese einer Stammzellhyperproliferation durch. In früheren Arbeiten dieser Arbeitsgruppe konnte gezeigt werden, dass in Fettgewebsstammzellen aus betroffenen und unbetroffenen Geweben bestimmte Gencluster differentiell exprimiert werden.
2) Methodik
Fettstammzellen aus betroffenem und unbetroffenem Gewebe wurden mit Inhibitoren des mTOR-Signalwegs kultiviert. Der Effekt der mTOR-Inhibition wurde mittels Vitalitätstests, Durchflusszytometrie, Differenzierungsassays, Western Blots und Real-Time RT-PCRs untersucht. Zusätzlich wurden die Gewebe histologisch untersucht.
3) Ergebnisse
Zellen aus betroffenem Gewebe proliferieren schneller und differenzieren schlechter als Zellen aus unbetroffenem Gewebe. Gene des mTOR-Signalwegs werden in Zellen aus betroffenem und unbetroffenem Gewebe differentiell exprimiert. Inhibition des mTOR-Signalwegs bewirkt eine Angleichung der Proliferation und teilweise auch der Genexpression. Betroffenes Gewebe zeigt einige Eigenschaften von braunem Fettgewebe.
4) Konklusion
Die Ursache der seltenen Erkrankung MSL ist noch nicht verstanden. Die Ergebnisse unserer Studien legen nahe, dass es sich um einen hyperproliferativen Mechanismus mit Störungen im mTOR-Signalweg handelt. Unsere Daten unterstützen die Hypothese, dass der Ursprung des betroffenen Gewebes im braunen Fettgewebe liegen könnte.

ID: 132
Topics: Andere, Basic+Translational

Die miR-29b, ein neuer Regulator der NG2-Expression im Glioblastom

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Das Glioblastom ist der häufigste astrozytäre Tumor des zentralen Nervensystems und ist aufgrund des invasiven Wachstums mit einer schlechten Prognose assoziiert. Neuere Studien zeigen, dass an diesem Prozess das Nerve/Glial Antigen (NG)2 beteiligt ist. Allerdings sind die molekularen Mechanismen hierzu weitestgehend unbekannt. In der vorliegenden Studie wurde erstmalig die miR-29b als Regulator der NG2-Expression im Glioblastom identifiziert.
Der Einfluss der miR-29b auf die NG2-Expression wurde in den humanen Glioblastomzelllinien A1207 und U87 mittels quantitativer Echtzeit (q)PCR, Durchflusszytometrie und Western Blot analysiert. Reportergenanalysen wurden durchgeführt, um eine direkte miR-29b-abhängige Regulation der NG2-Expression zu überprüfen. Zudem wurde die Zellproliferation und Zellmigration unter Verwendung verschiedener Methoden bestimmt. Des Weiteren wurden regulatorische Mechanismen der miR-29b Expression mittels qPCR, Durchflusszytometrie, Western Blot und Reportergenanalysen analysiert.
Die Überexpression der miR-29b führt zu einer signifikant reduzierten NG2-Expression. Die miR-29b bindet spezifisch im 3'UTR der NG2-mRNA, wodurch der mRNA-Abbau posttranskriptionell initiiert wird. Nach miR-29 Überexpression wurde eine signifikant reduzierte Zellproliferation und Zellmigration in den Glioblastomzelllinen detektiert. Weiterführende Analysen zeigten, dass dies hervorgerufen ist durch eine Extracellular Signal-regulated Kinase (ERK)1/2-abhängige Signaltransduktion. Zudem konnten mit dem Onkogen c-Myc und der long non-coding (lnc)RNA H19 zwei Faktoren identifizierten werden, welche die miR-29b Expression reprimieren.
In dieser Studie konnte sowohl die miR-29b als neuer Regulator der NG2-Expression im Glioblastom bestimmt werden als auch eine reduzierte Zellproliferation und Zellmigration nach miR-29b Überexpression detektiert werden. Somit könnte die miR-29b eine geeignetes Zielmolekül in der Therapie des Glioblastoms darstellen.

ID: 133
Topics: Transplantation, Basic+Translational

The generation of insulin producing cells (IPC)-spheroids from microvascular fragments (MVF)

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Pancreatic islet transplantation represents a promising therapeutic approach to improve glycometabolic control in type 1 diabetes mellitus (T1DM) patients. However, the insufficient revascularization and donor shortage are major hurdles of islet transplantation. To overcome these problems, we here established a novel strategy by the differentiation of adipose tissue-derived stem cells (ADSC) within microvascular fragment (MVF)-spheroids to insulin producing cell (IPC)-spheroids.
We first established a protocol to generate and subsequently differentiate MVF-spheroids to IPC-spheroids. For this, MVF were isolated from adipose tissue of C57/BL6 mice and spheroids were formed by means of liquid overlay technique. To determine the optimal cultivation conditions and numbers of MVF for the generation of viable spheroids, we performed flow cytometric analyses of propidium iodide (PI)/Annexin V stainings. The spheroids were then cultivated for additional 28 days in a specific differentiation medium to trigger the development of IPC. The efficiency of the differentiation was assessed by immunohistochemistry, qRT-PCR and western blot analysis.
We found that the cultivation of 1,000 MVF in high glucose medium leads to roundly shaped and viable spheroids. Immunohistochemical analyses on days 0, 7, 14, 21 and 28 demonstrated that they contain a dense microvascular network consisting of CD31- and α-SMA-positive cells. The gene expression of specific β-cell markers such as PDX-1, NKX6-1 and PAX6 were significantly upregulated on days 7 and 14 during the differentiation process. Furthermore, we detected the highest number of IPC on day 14, which could be confirmed by additional Western blot analyses and qRT-PCR.
In this proof-of-concept study, we show that not only ADSC within MVF-spheroids can be differentiated to IPC, but also IPC-spheroids exhibit a dense microvascular network. Accordingly, IPC-spheroids may have the potential to improve the outcome of islet transplantation.

ID: 134
Topics: Transplantation, Basic+Translational

Co-transplantation of pancreatic islets and microvascular fragments effectively restores normoglycemia in diabetic mice

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Background and aims: Insufficient revascularization of pancreatic islets is one of the major obstacles impairing the success of islet transplantation. To overcome this problem, we introduce in the present study a straightforward strategy to accelerate the engraftment of isolated islets. For this purpose, we combined adipose tissue-derived microvascular fragments (MVF) with pancreatic islets and co-transplanted this mixture in streptozotocin (STZ)-induced diabetic mice.
Methods: Islets were isolated from wild type (WT) donor mice and cultured for 24 hours. MVF were also isolated from WT mice immediately before co-transplantation. We co-transplanted 250 islets and 20,000 MVF under the kidney capsule as well as 500 or 1,000 islets and 40,000 MVF into the subcutaneous space of diabetic mice. The endocrine function of the grafts were determined by blood glucose measurements twice a week and by an intraperitoneal glucose tolerance test (IPGTT) at the end of the entire observation period. The grafts' morphology, viability, cellular composition and insulin content were analyzed using immunohistochemistry and enzyme-linked immunosorbent assay (ELISA).
Results: We found that the co-transplantation of islets and MVF markedly accelerates the restoration of normoglycemia in diabetic recipients when compared to the transplantation of islets alone. In fact, the co-transplantation of 250 islets and 20,000 MVF under the kidney capsule as well as the subcutaneous transplantation of 500 or 1,000 islets and 40,000 MVF reversed diabetes in 88% and 100% of mice, respectively. At the end of the in vivo experiments, immunohistochemical analyses of the grafts revealed a significantly higher number of islet cells and microvessels in the co-transplantation groups.
Conclusion: Our findings demonstrate that the co-transplantation of islets and MVF is a promising strategy to improve the success rate of islet transplantation, which could be easily implemented into future clinical practice.

ID: 135

Topics: Plastische Chirurgie, Basic+Translational

Cell Enriched Lipotransfer –Die Auswirkung von mechanischer Aufbereitung auf Lipoaspirat und dessen Fettstammzellen

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1) Hintergrund/Fragestellung

Lipofilling des Sphinkters, der Stimmlippen oder bei Morbus Dupuytren sind Beispiele dafür, dass das Verfahren heutzutage von unterschiedlichen Fachbereichen angewendet wird. Für ein optimales Ergebnis sollte das Gewebe gereinigt und die Konzentration an Vorläufer- und Stammzellen erhöht werden. Statt zeit- und kostenintensivem enzymatischen Verdau sollte dies auch durch mechanische Prozessierung möglich sein. Die Auswirkungen der mechanischen Aufbereitung auf das Lipoaspirat wird im Rahmen dieser Studie untersucht.

2) Methodik

Lipoaspirat wurde mechanisch aufbereitet und die Histologie des Gewebes bei jedem Teilschritt untersucht. Zusätzlich wurden Fettstammzellen aus dem Gewebe isoliert, gezählt und hinsichtlich ihrer Vitalität, ihres Differenzierungspotentials und ihres Sekretoms untersucht. Im Rahmen einer klinischen Langzeitstudie wurde die Einheilungsrate des mechanisch aufbereiteten Lipoaspirates exemplarisch für die Behandlung von Falten im Gesichtsbereich untersucht.

3) Ergebnisse

Durch die mechanische Aufbereitung wird die Konzentration der Stammzellen im Lipoaspirat signifikant gesteigert. Die dabei auf das Gewebe wirkenden Scherkräfte sorgen für ein Aufbrechen großer Adipozytenverbände aber nicht für eine Veränderung der verbleibenden Adipozyten. Die Differenzierungseigenschaften oder das Sekretom der Stammzellen werden durch die mechanische Belastung nicht verändert. Die Langzeitstudie zeigt, dass nach einem Jahr der wrinkle severity score weiterhin besser ist als präoperativ.

4) Konklusion

Durch die mechanische Aufbereitung von Lipoaspirat kann die Stammzellenkonzentration erhöht werden, ohne dass die Sekretom- oder Differenzierungseigenschaften manipuliert werden. In der Klinik zeigen sich sogar in mechanisch beanspruchtem Gewebe zufriedenstellende Langzeitergebnisse. Da das Verfahren intraoperativ und ohne größere Medizinprodukte durchgeführt werden kann, ist es auch für Einrichtungen mit einer geringen Fallzahl gut geeignet.

ID: 136
Topics: Herz-/Gefäßchirurgie, Andere

The iliopsoas muscle as a main clinical focus of a rare pathological lesions and indicating “symptom muscle“ of retroperitoneal vascular surgical diseases as well as various differential diagnoses to be delineated

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Introduction: The iliopsoas muscle appears as a symptom-indicating muscle of retroperitoneal lesions. Rare pathologies at the muscle can be considered a great challenge to the investigating clinician.
Method:Exemplary demonstration of two unusual case histories illustrating the importance of the iliopsoas muscle.
Results:1) Assessment of a 78-y.-old female patient due to persisting pain in the left groin. Duplex ultrasonography excluded a pathological lesion of the left femoral vessels. Laboratory analysis revealed minimally elevated inflammatory parameters. Contrast-enhanced CT scan showed suspicion of a small abscess . MRI revealed suspected abscessation of the soft tissues of the hip and osteomyelitis of the proximal femur. Puncture and histopathological investigation showed diagnosis of a rare hip joint ganglion.
2) Admission of a 64-y.-old patient because of pain and older flat hematoma in the left groin. The patient had already received a suprarenal aortic replacement. Due to a new covered rupture of a penetrating aortic ulcer at the level of the SMA, the aortic segment was replaced using a tubular prosthesis and selective bypasses to the left and right renal arteries as well as reimplantation of the SMA and the coeliac trunk using. Subsequent CT angiography of the abdomen was favored: There was a strong suspicion of a covered aortic rupture with marked fluid collection around the aorta and complete burst fracture of lumbar vertebra 1.
Conclusion: In case of extensive hematoma or pain in the groin without previous trauma and vascular interventions, retroperitoneal lesion or bleeding in the (peri-)aortic area should be considered. Unclear clinical symptomatology and pathologies in the region of the iliopsoas muscle i) have a much wider range of further differential diagnoses, ii) often cannot be clearly clarified on the basis of complex radiological diagnostics, iii) not infrequently require image-guided puncture or surgical diagnostics and therapy.

ID: 137
Topics: Plastische Chirurgie, Basic+Translational

Untersuchungen zur Rolle von C-reaktivem Protein in der Abstoßungsreaktion im Hinterlauftransplantationsmodell der Ratte

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Hintergrund:
Monozyten rücken in ihrer Schlüsselposition zwischen angeborenem und adaptivem Immunsystem in der Transplantatabstoßung zunehmend in den Fokus der Forschung. In vitro konnte bereits eine Mediatorenrolle von Monozyten bei der Aktivierung von T-Zellen durch C-reaktives Protein (CRP) gezeigt werden. CRP wird daher als pathogenetischer Faktor und mögliches therapeutisches Target für die chronische Transplantatabstoßung angenommen.
Methoden:
Zur Simulation einer chronischen Abstoßungsreaktion werden allogene Hinterlauftransplantationen sowie als Kontrolle autologe Replantationen mit bzw. ohne zusätzliche Gabe von CRP in der Ratte durchgeführt. Während des Versuchszeitraumes bei klinischer Abstoßungsreaktion ggf. eine Immunsuppression durchgeführt. Blut- und Gewebeproben werden über 90 Tage nach Transplantation bzw. Replantation auf Zusammensetzung und Monozytenaktivität durchflusszytometrisch und schließlich histologisch analysiert. Multiphotonenmikroskopie wird zur Visualisierung der monozytären Migration und Entstehung der chronischen Transplantatvaskulopathie gennutzt.
Ergebnisse:
Vorläufige Ergebnisse bestätigen die Hinterlauftransplantation bzw. –replantation mit intermittierender Immunsuppression als Modell der chronischen Transplantatabstoßung. Die akute Abstoßungsreaktion wird durch eine subtypenspezifische, CRP induzierte Monozytenaktivation verstärkt. Vorläufige Ergebnisse zeigen, dass dies auch direkt die Entstehung der chronischen Transplantatabstoßung begünstigt.
Diskussion:
Die Rolle von CRP in der Aktivierung des angeborenen Immunsystems ist komplex und vorwiegend über monozytäre Zellen vermittelt. Dabei scheint nicht nur die akute Abstoßungsreaktion durch CRP aggraviert zu sein, sondern CRP auch zu einer höheren Transplantatvaskulopathie und damit chronischer Abstoßung zu führen.

ID: 138

Topics: Viszeralchirurgie, Basic+Translational

Hereditary homozygosity and allelic imbalance of HLA as common immune escape mechanisms in oesophago-gastric adenocarcinoma

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Background: The human leukocyte antigen (HLA) genotype of an individual defines the repertoire of peptides which can be presented to T cells. This study aims to elucidate the role of hereditary HLA-I homozygosity in oesophago-gastric adenocarcinoma (EGA) and to demonstrate its impact on the repertoire of immunogenic peptides derived from tumour associated antigens (TAAs) or mutation-associated neoantigens (MANAs). Materials and methods: High-resolution HLA-genotypes combined with the sequences of either TAAs or MANAs were used to predict good-affinity binders using an in-silico approach for MHC-binding (IEDB.org). RNAseq data was used to detect imbalanced or loosed expression of HLA-A/B/C alleles. Results: Frequency of HLA homozygosity in EGA patients was significantly higher than in the control population. MHC-binding predictions showed a reduced set of good-affinity binders (both TAA- and MANAs) in the homozygous cohort. Artificial restoration of the genotype of homozygous patients to a heterozygous genotype, resulted in a set of predicted good-binding peptides of comparable size to the heterozygous cohort. Quantification of allele-specific expression of HLA-I revealed altered expression in 9/12 heterozygous patients. 3 of these patients showed complete loss of heterozygosity, whereas the others had altered expression of one or two HLA-I molecules. The allelic imbalance was significantly higher in heterozygous compared to homozygous were only 2 patients showed altered expression of one HLA-I molecule. Conclusions: The high frequency of genomic HLA-I homozygosity observed in EGA patients suggests that limitation of neoantigen presentation might have a role during EGA development and may reflect an increased cancer risk for these patients. The results herein highlight that despite having a complete set of HLA-I alleles on a genomic level, the majority of EGA patients carry allelic imbalance that limit the repertoire of neoantigens for presentation to immune cells.

ID: 139
Topics: Andere, Basic+Translational

Quantification of surface proteins on serum exosomes of oral squamous cell carcinoma patients

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Introduction: The incidence of oral squamous cell carcinoma (OSCC) increases, especially in younger patients. Living cells secrete extracellular vesicles (EVs) as part of intercellular communication. Formation and cargo of exosomes released by tumor cells into body fluids have a major impact on carcinogenesis. Exosomes transfer their “oncogenic cargo” to non-transformed cells, influencing oncogenic field effects. We aim to exploit tumor-indicative proteins on the exosomal surface for liquid biopsy diagnostics to improve prognosis.
Methods: We applied time-resolved immunofluorescence (TRIFIC), and ExoView arrays (Nanoview, GB), visualizing single serum-exosomes without prior isolation, for quantification of exosomal surface proteins. Nanotracking analysis (NTA) was used for quality control and quantification of size and concentration of EVs.
Results: Serum-exosomes of OSCC patients compared to gender and age-matched healthy blood donors were analyzed for tumor-identifying markers on their surfaces. Exosomes were captured by tetraspanines, and tumor-associated proteins survivin and Caveolin-1 on Exoview arrays. EMMPRIN, EpCAM, Survivin, Caveolin-1 were localized on exosomal surfaces without significant difference between tumor and healthy. Claudin-4 has been identified as a tumor-indicative marker candidate (claudin presenting particles: tumor mean 4 717 vs healthy mean 1 417, survivin captured; tumor 6 933 vs healthy 1 583, Caveolin-1 captured). Co-localization with CD9 on exosomal surfaces has been visualized. Higher concentrations of total antibody-captured exosomes and of exosomal CD9 in tumor patients‘ sera have been detected, in addition.
Conclusion: Capture of exosomes via surface protein claudin-4 may allow the isolation of tumor-derived exosomes from serum-exosomes of different origins to simplify the identification of additional exosomal surface proteins for design of a liquid biopsy-based tumor-indicative signature.

ID: 140
Topics: Viszeralchirurgie, Basic+Translational

Anti-inflammatorische Medikamente zeigen unterschiedliche direkte Effekte auf Caco2 Zellen und Enteroide

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Hintergrund:
Eine Störung der intestinalen epithelialen Barriere ist ein entscheidender Schritt in der Pathogenese der chronisch-entzündlichen Darmerkrankungen (CED). Eine Vielzahl der CED Patienten erhalten aus diesem Grund anti-inflammatorische Medikamente wie Glukokortikoide, TNFα Blocker oder Mesasalazine. Während die immun-modulatorischen Effekte dieser Medikamente gut dokumentiert sind, sind direkte Effekte dieser Medikamente auf Enterozyten nur wenig untersucht.
Methoden:
Wir verwendeten Caco2 Zellen und Mausenteroide um die Effekte von 100ng/ml anti-TNFα Antikörper Infliximab, 1mM Prednisolon and 5mM Mesasalazine auf Enterozyten zu untersuchen. Inflammatorische Veränderungen der Darmbarriere wurden durch die Applikation von Cytomix (TNFα, Interleukin 1 beta und Interferon gamma) simuliert. Es erfolgten Messungen des transepithelialen elektrischen Widerstandes, der Permeabilität von 4kDa Fitc Dextran im Transwell Modell, sowie Untersuchungen der Claudin Expression und - Lokalisation durch Western Blots und Immunfluoresezenzen
Ergebnisse:
Cytomix führt zu einem Zusammenbruch der intestinalen Barrierfunktion in Caco2 Zellen und in Mausenteroiden. Während Infliximab zu einer Stabilisierung der Barrierefunktion führt und Mesasalazine in beiden Modellen keine Effekte aufweist, zeigen sich für Prednisolon divergente Ergebnisse. In Caco2 Zellen führt die Applikation von Prednisolon mit Cytomix zu einer Stabilisierung der Barrierefunktion. In Mausenteroiden führt die gleichzeitige Gabe von Prednisolon und Cytomix hingegen zu einer zusätzlichen Verschlechterung der Barrierefunktion.
Zusammenfassung:
Anti- TNFα Antikörper und Glukokortikoide zeigen direkte Effekte auf Enterozyten. Während Prednisolon im klassischen Tumorzellmodell mit Caco2 Zellen protektive Effekte aufweist, führt es in Mausenteroiden zu einem Zusammenbruch der Barrierfunktion.
Unsere Ergebnisse unterstreichen die Wichtigkeit der Verwendung von Enteroiden für Untersuchungen der Darmbarriere.

ID: 141
Topics: Herz-/Gefäßchirurgie, Andere

Von der Fokussierung auf Röntgenbefunde zurück zum diagnostischen Blick und der stabilisierenden operativen Therapie: Venöse Kompressionssyndrome und das hypermobile EHLERS-DANLOS Syndrom.

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Die Therapie venöser Kompressionssyndrome (VKS)(Nussknacker-(NKS),MAY-THURNER (MTS)Syndrom) sollte nicht nur auf „Stenosierung“ in MRT/CTA focussieren sondern die zugrunde liegende Hypermobilität(HSD) bzw. hypermobiles EHLERS-DANLOS Syndrom (hEDS) berücksichtigen(1)
MATERIAL und METHODE:Vom 01.07.2019 bis 19.07.2022 wurden 80 Pat. (w 70 ;87,5%, m 10; 12,5 %; mittleres Alter 29,98 Jahre) mit HSD/hEDS mit extravenöser ringverstärkter PTFE Prothese (ERPP) wegen NKS (n=2) oder MTS (n=1) oder beider Venen (n=15) operiert. Bei sechzig Pat.(75%) wurden ausser VKS auch abdom. Kompressionssyndrome (AKS) operiert. Fünfzehn Pat.(19,2 %) waren wegen VKS bereits ausserhalb i.v. gestentet worden (LRV n= 5,LBV n=5, LRV und LBV n=1, mit coils n=4), fünfzehn (19,2%) Fälle mit AKS ebenfalls:(DUNBAR nach Lap. n= 11, DUNBAR offen n=3, WILKIE nach DDJ n=2.) Die Revisionder AKS erfolgte in gleicher Sitzung.
ERGEBNISSE:WHS=0, Letalität n=0. Erfolg (Symptome; USD-DUPLEX), CTA : 93,7% (75 Pat) Drei Monate postop. bei 5 (6,3%) Pat. Indikation zum Wechsel der ERPP wegen Stenosierung distal. Sodann o.B.
DISKUSSION: Strategie :alle VKS ,auch mit AKS in einer Op. zu beseitigen, da HSD/ hEDS vermehrt Verwachsungen erzeugen. Die ERPP von R.BARNES et. al. (1988) (2) zur Therapie von NKS hatte wenig Echo,ist heute zur Behandlung des NKS aber positiv. Unsere Modifikation in Bezug auf MTS sowie NKS zeigte sehr gute,stabile Resultate. Im Gegensatz zum i.v. Stenting, welches nur den Venendurchmesser berücksichtigt, bewirkt ERPP eine Protektion der Venen und spreizt den anatomischen Raum , auch für das Duodenum!(WILKIE., wichtig für diese jungen HSD/hEDS Patienten.. Die Probleme des iv Stentings (Migration, Stenosierung, Penetration Thrombosierung) sowie Gerinnungshemmung werden vermieden.
SCHLUSSFOLGERUNG:ERPP ist erfolgreich bei VKS, auch in Kombination mit AKS und berücksichtigt Besonderheiten von HSD/hEDS. Die causale Beziehung zwischen VKS/AKS und HSD/hEDS wurde von uns erstmalig beschrieben.

ID: 142
Topics: Viszeralchirurgie, Basic+Translational

Low postoperative carbon dioxide levels are associated with impaired healing of intestinal anastomoses

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Background: Anastomotic leakage (AL) occurs in up to 10% of patients undergoing colorectal surgery. Macrophage polarization is critical for sufficient healing of intestinal anastomoses. Elevated carbon dioxide levels (CO2) mitigate pro-inflammatory signaling. The clinical significance of pro-inflammatory signaling and CO2 levels during AL was investigated.
Methods: A prospective database recording clinical data and surgical outcome of 360 patients undergoing colorectal surgery was established. Pro-inflammatory signaling markers within patient-derived mucosal biopsies were detected. Mucosal infiltration of macrophages was analyzed by immunohistochemistry. Inflammatory markers and perioperative blood gas values were correlated with surgical outcome. Primary murine macrophages (BMDMs) were treated with different CO2 levels during polarization. Cell culture medium was buffered and intracellular pH (pHi) was monitored to determine pH-dependent effects of CO2.
Results: Elevated mucosal protein levels of pro-inflammatory makers, such as the chemoattractant CCL2, and a pro-inflammatory gene signature were associated with AL. Patients with AL showed significantly enhanced CO2 kinetics during surgery and lower postoperative CO2 levels. Subgroup analysis suggested, that high CO2 levels and low pH were associated with lower mucosal CCL2 levels and macrophage infiltration. In vitro, high CO2 decreased pro-inflammatory signaling and migration in macrophages in a pH- and carbonic anhydrase (CA) 2-dependent manner. Patients with high mucosal CA2 protein expression showed a stronger correlation between CO2 levels and macrophage infiltration than patients with low CA2, suggesting enhanced CO2-sensitivity in patients with high CA2 levels.
Conclusion: Carbon dioxide is highly immuno-modulatory and a stricter control of perioperative CO2 levels might be beneficial for healing of intestinal anastomoses. In M1 (but not M2) macrophages, CO2 is sensed by CA2-driven changes in pHi.

ID: 143
Topics: Andere, Basic+Translational

The protein kinase CK2: A novel regulator of glucagon expression in α-cells

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We have already shown that the inhibition of the protein kinase CK2 enhances insulin expression by increasing the transcriptional activity of pancreatic and duodenal homeobox (PDX)1. Of note, this transcription factor is also involved in the regulation of glucagon gene expression in α-cells. Therefore, we hypothesized that CK2 inhibition decreases glucagon expression in a PDX1-dependent manner.
For this, αTC1 cells were treated with the CK2 inhibitors CX-4945 and SGC-CK2-1 as well as DMSO as control. In addition, we generated a CK2-deficient αTC1 cell line by CRISPR/Cas9 system. The viability of the cells was analyzed by lactate dehydrogenase (LDH) assays and growth curves. The glucagon expression and secretion was determined by Western blot analyses and enzyme-linked immunosorbent assays (ELISA). Quantitative real-time (qRT)-PCRs, reporter gene and streptavidin bead pulldown assays were used to study the regulatory mechanisms of glucagon gene expression. Isolated murine islets were treated with the CK2 inhibitors and glucagon expression as well as secretion were examined by immunohistochemistry and ELISA.
We found that the loss and the inhibition of CK2 significantly decrease glucagon secretion without affecting the viability of αTC1 cells. Additional experiments revealed that this is due to a reduced glucagon gene and protein expression. The analysis of the regulatory mechanism demonstrated that the loss of CK2 activity results in a rearranged binding of the transcription factors PDX1, paired box protein (Pax)6 and NKX6.1 to the glucagon promoter. Additional ex vivo experiments showed that the inhibition of CK2 in murine islets reduces glucagon expression and secretion.
In the present study, we found that CK2 regulates glucagon secretion by affecting the transcriptional control of its gene expression. These findings underline the crucial role of CK2 in the glucose metabolism.

ID: 144

Topics: Viszeralchirurgie, Basic+Translational

ECM-receptor signature is associated with basal-like subtype and immune exclusion in pancreatic ductal adenocarcinoma

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) is a devastating disease with extreme heterogeneity at both genetic and phenotypic level. Extensive desmoplasia is the prominent feature of PDAC, which mainly consists of cancer-associated fibroblasts (CAF), extracellular matrix (ECM), and immune cells. It is unknown whether ECM-receptor signature associated with the PDAC molecular subtypes and immune infiltration. Recently, we demonstrated that aberrant activation of CAFs and ECM deposition occur in early pancreatic tumorigenesis.

Materials and methods

The disease course of caerulein-induced acute pancreatitis in wild-type (WT) mice was compared to the early carcinogenic process of p48Cre/+; LSL-KrasG12D/+ (referred to as 'KrasG12D') mice with high temporal resolution. In clinical translation, we constructed a risk-score model based on each transcript's multivariate Cox regression coefficient, calculated from its expression level in the ICGC dataset (n=269). To further confirm the association mentioned above, we analyzed the published spatial transcriptomics (ST) dataset of human PDAC slides.

Result

ECM-receptor interaction is the only pathway enriched in KrasG12D pancreata across different stages of early pancreatic carcinogenesis. Notably, we observed that ECM-receptor and myCAFs signature is negatively correlated with NK and CD8+ cell infiltration but positively correlated with macrophage and neutrophil infiltration. Based on an integrated analysis of ST and sc-RNA-seq data, we observed that basal-like cancer cells, myofibroblast (myCAFs), and macrophages at the tumor-stromal interface collectively contribute to the molecular signature. Notably, the same ECM-receptor signature is associated with immune exclusion and basal-like subtype in human PDACs.

Conclusion

ECM-receptor signature associated with basal-like subtype and immune exclusion. The relevant clinical translation would have an impact on health care.

ID: 145
Topics: Viszeralchirurgie, Basic+Translational

Arp2/3 complex-mediated fibroblast migration signature is associated with poor prognosis of pancreatic cancer

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Introduction
Previously, we defined the critical role of Arp2/3 complex (actin-related protein 2/3 complex) in early pancreatic carcinogenesis, and its actin nucleator activity is essential for promoting profound cytoskeletal rearrangements in various biological contexts. Here, we investigated the function of Arp2/3 complex in mediating migration of cancer-associated fibroblasts (CAFs) by pancreatic ductal adenocarcinoma (PDAC).
Materials and methods
Caerulein-induced pancreatitis was used to generate early pancreatic carcinogenesis from p48Cre; LSL-KrasG12D mice. Human immortalized pancreatic stellate cells (hPSCs), and patients-derived primary CAFs are used for in vitro assays. Bioinformatic analysis of publically available data is used to identify molecular signatures.
Result
Based on transcriptional profiles with high temporal resolution (GSE65146), we performed a time-dependent Gene Set Enrichment Analysis (GSEA) analysis and found that fibroblast migration signature is associated with the early transformation process. In TCGA and ICGC datasets, we demonstrated that such fibroblast migration signature is related to poor clinical outcomes in humans. Further analysis uncovered that Rac1/Arp2/3 complex is mainly responsible for increased fibroblast migration capacity. Exploration of single-cell sequencing data revealed that Rac1/Arp2/3 complex activity is particularly increased in myofibroblast (myCAFs) compared to inflammatory CAFs (iCAFs). In vitro, application of Arp2/3 complex inhibitor dramatically reduced basal CAFs migration and TGFβ1-mediated CAFs migration.
Conclusion
Arp 2/3 complex-mediated myCAFs migration has an oncogenic function in both early carcinogenesis and overt PDAC. Further studies are required to explore the potential molecular mechanism underlying such function.

ID: 146

Topics: Viszeralchirurgie, Basic+Translational

mTORC1 promotes the formation of immunosuppressive microenvironment in pancreatic ductal adenocarcinoma

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Background
Implementation of immunotherapy against pancreatic ductal adenocarcinoma (PDAC) poses a clinical challenge due to its immunosuppressive tumor microenvironment. It is mainly due to desmoplastic stroma that constitutes a mechanical barrier around tumor and prevents immune cell infiltration.
Methodology
LSL-KrasG12D; p53-/-; Ptf1αCreER/+; R26RtdTomato (KPCERT) and mTORC1-inactive KPCERT; Rptor-/- mice were generated, and caerulein was used to accelerate the formation of PDAC. Primary cancer cells were isolated from tumor tissue. Transcriptional profiles were obtained by RNA-sequencing (RNA-seq).
Results
Compared to KPCERT mice, KPCERT; Rptor-/- mice had more prolonged survival with less desmoplastic stroma formation and more immune cell infiltration. The co-culture of murine PDAC organoid and pancreatic stellate cell (PSC) cells demonstrated that mTORC1 promoted the differentiation of inflammatory cancer-associated fibroblasts (iCAFs). Besides, RNA-seq data from PDAC tumor tissue displayed decreased expression of iCAF markers in the KPCERT; Rptor-/- tumors compared to KPCERT tumors
Conclusion
In murine PDACs, mTORC1 pathway contributes to the formation of desmoplastic stroma and immunosuppressive microenvironment potentially by promoting iCAFs differentiation.

ID: 147

Topics: Viszeralchirurgie, Basic+Translational

Phenotypic and molecular characterization of duct- and acinar-derived pancreatic ductal adenocarcinoma

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Background

Previous studies have illustrated that pancreatic ductal adenocarcinoma (PDAC) can originate from both pancreatic and acinar compartments. Caerulein- and ductal obstruction-induced pancreatitis specify the formation of pre-neoplastic lesions from acinar and duct compartments, respectively. It is unknown whether the cell of origin contributes to the phenotypic and molecular heterogeneity of overt PDAC.

Materials and methods

Caerulein-induced pancreatitis was used to generate acinar-derived PDAC from p48CreERTM/+; LSL-KrasG12D; p53flox/flox; R26RtdTomato mice. Ductal ligation was applied to accelerate duct-derived PDAC from Sox9-creERT2; LSL-KrasG12D; p53flox/flox; R26RtdTomato mice. Primary cancer cells were isolated from mouse tumors. The oncogenic signalling pathway was assessed in vitro. Transcriptional profiles were obtained by RNA-sequencing (RNA-seq) technique.

Results

Mice suffered from duct-derived PDAC had slightly longer survival than those having acinar-derived tumors. Histological characterization revealed that duct-derived PDAC contained less pronounced desmoplastic stroma than acinar-derived ones. This difference was also reflected in transcriptional profiles in that lower stroma and immune indexes were detected in duct-derived PDACs, compared to acinar-derived tumors. Further analysis uncovered that duct-derived PDAC is molecularly reminiscent of basal-like subtype of human PDACs. Moreover, duct-derived cancer cells are more responsive to TGFβ-mediated MAPK activation.

Conclusion

Duct- and acinar-derived PDACs are two cancer entities with different stroma components and tumor biology. Further studies are still required to explore the molecular mechanism underlying this difference.

ID: 148
Topics: Viszeralchirurgie, Basic+Translational

Metabolic profiling of the rat liver after portal vein ligation

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Background Portal vein ligation (PVL) is a surgical procedure enabling extended liver resection and leads to atrophy of the ligated and compensatory hypertrophy of the non-ligated liver lobes. Knowledge about metabolism in ligated and non-ligated liver lobes is essential, since volume increase of the non-ligated lobes does not necessarily reflect functional increase.
Methods Male Sprague-Dawley rats were subjected to 60% PVL. Tissue samples from the non-ligated right median (RML) and the ligated left median (LML) liver lobe were obtained during 5 days post-operatively (POD). Tissue damage was visualized by the HE stain. ADP/ATP, NAD/NADH, glucose/glycogen, and free fatty acids/triglycerides were determined biochemically. Changes in metabolic gene expression were estimated by sqRT-PCR.
Results In the LML, damage progressed until POD 3 and recovered again until POD 5. The RML remained unaffected. At POD 3, triglycerides in the LML were only half of that in the RML, in which triglycerides increased until POD 5. In both lobes, glucose and glycogen decreased at POD 3 and recovered again until day 5. NAD/NADH transiently increased in the LML at POD 3 and thereafter declined to levels comparable to those in the RML. ADP and ATP increased in both lobes. Yet, at POD 3, ADP was twice higher in the LML than in the RML. ATP behaved the opposite. Lipid metabolism gene expression decreased over time. After an initial increase in the expression of the gluconeogenic phosphoenolpyruvate carboxykinase in the LML, it declined thereafter. Expression of the key glycolytic transcription factor ChREBP was increased in the LML.
Conclusion Initially after PVL, liver carbohydrates and lipids serve as energy substrates for liver regeneration. While the RML is supported by portal vein substrates, the LML likely uses circulatory glucose via glycolysis as the main energy substrate. The decreased ATP levels as well as the high NAD/NADH ratio in the LML support this assumption.

ID: 149
Topics: Viszeralchirurgie, Klinische Studien

The safety and validity of an App-based prehabilitation program (Patronus Prehab App) in patients undergoing elective major surgery: The prospective, interventional PROTEGO MAXIMA Trial

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Background: Prehabilitation, including aerobic exercise training, aims to improve patients' physical fitness before major surgery and reduce postoperative complications. The validity and safety of an app-based prehabilitation program in acoordance with the Medical Drug Regulation (MDR) were tested with a risk-based endurance exercise software using wrist-worn wearables to measure heart rate (HR) and distance.
Methods: Patients undergoing major surgery performed a 37-min interval training on a treadmill based on heart rate reserve, wearing standard electrocardiographic (ECG) and two smartwatches, which were driven by the test software, assessing four different devices: iPhone 13, iPhone SE, Samsung A52 and Google Pixel 6. The hypothesis was that smartwatch measurements will not exceed a mean difference of ≤ 10 bpm and an acceptable range of variation of ≤ 50 bpM. Usability and lab testing were performed.
Results: Bland-Altman analysis from 49 patients revealed a mean HR difference of ≤ 10 bpm compared to standard ECG with the lowest variation for Pixel 6 (-0.6 [95% CI -5.7;4.4]), iPhone 13 (6.1 [95% CI 3.0;9.2]), iPhone SE (1.4 [95% CI -0.9;3.7]), Samsung (2.5 [95% CI -0.3;5.2])). More than 90% of all HR measurements fell into the predefined range of variation. Mean difference of distance compared to treadmill was lowest for iPhone SE with -4m (-4 [95% CI -502;495]). Laboratory values showed no significant increase for clinically relevant parameters. Usability data for alarm awareness of the devices was realized within a mean of 12.2s (2-45s). To date, no serious adverse event occurred.
Discussion: The devices provided an acceptable HR accuracy. Regarding safety, there were no critical lab detections, and usability testing revealed prompt and adequate reactions.
Conclusion: The findings provide preliminary support that the app-based prehabilitation program can be applied safely to patients before major surgery. Trial registration number CIV-21-07-037311.

ID: 150

Topics: Viszeralchirurgie, Basic+Translational

Mesenchymal stromal cells attenuate liver damage after partial hepatectomy in the mouse by mitigating thrombospondin-1, TGF-□, and epithelial-mesenchymal transition (EMT)

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Background Extended liver resection is a risk factor for post-hepatectomy acute liver failure (PHLF). Thrombospondin-1 (THBS1) might be involved by activation of latent TGF-b mediating sustained epithelial-mesenchymal transition (EMT) and subsequent liver damage. Mesenchymal stromal cells (MSC) prevented the THBS1- and TGF-b-mediated liver damage. To identify the increase of hepatic THBS1 after liver resection, we investigated in the mouse liver after two third hepatectomy, which cellular mechanisms were involved in the post-hepatectomy increase in THBS1.

Methods Two third partial hepatectomy (PH) was performed in male C57-Bl6J mice. Human bone marrow-derived MSC, differentiated into hepatocytic cells, were applied to the liver via intra-splenic injection. Liver damage and regeneration was assessed biochemically and histologically.

Results PH elevated serum transaminases indicating resection-induced liver damage, which was confirmed by HE staining. The epithelial markers E-Cadherin and ZO-1 were significantly down-regulated as shown by Western blotting. MSC treatment did not impact on these effects. Yet, MSC treatment augmented the proliferation rate of liver cells compared to untreated animals as shown by Ki67 immunohistochemistry suggesting that MSC supported liver regeneration. PH increased THBS1 in serum and liver accompanied by an elevation of hepatic TGF-b. Both the increase in THBS1 and TGF-b was attenuated by MSC treatment. By using CD42b and CD11b as markers, immunohistochemistry revealed that partial hepatectomy increased thrombocytes short-term (6 hours) and granulocytes long-term (48 hours) after surgery in the liver. This increase was attenuated by MSC treatment.

Conclusion Modulating recruitment of THBS1-secreting inflammatory cells like thrombocytes and granulocytes in the liver by MSC treatment may attenuate availability of active TGF-b and subsequent EMT. Thus, MSC support epithelial integrity and regeneration after PH.

ID: 151
Topics: Viszeralchirurgie, Basic+Translational

Non-canonical Wnt pathway member Frizzled 5 is downregulated in gastric cancer

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Gastric cancer is the third leading cause of cancer-related death with a 5-year overall survival of less than 30%. Surgical resection in combination with neoadjuvant chemotherapy represents the only curative treatment approach, however, response to treatment greatly varies between patients. A possible reason for the varying treatment responses are gastric epithelial tumor stem cells. The Wingless (Wnt) signaling cascade is involved in gastric carcinogenesis arising from gastric cancer stem cells, however, the underlying mechanisms are poorly understood. Especially the Wnt-receptor Frizzled 5 (FZD5), transducing non-canonical Wnt5a activity, seems to play a crucial role. Increased expression implicates potential tumor suppressing effects and is corelated with longer survival. This study therefore aims to analyze the expression and clinical significance of FZD5 in human gastric carcinoma.
We analyzed a cohort of 50 patients that underwent surgical resection of gastric carcinoma. Both intestinal and diffuse type of primary resected and neoadjuvant treated patients with pathologically confirmed R0 resection were included. The expression of FZD5 and the proliferation marker Ki67 was assessed by immunohistochemistry.
We show that FZD5 is expressed in the gastric epithelium. In both diffuse and intestinal gastric cancer tissue, the expression of FZD5 was significantly reduced compared to adjacent normal tissue ($p<0{,}001$), whereas proliferation within the tumor was increased according to Ki67 staining.
FZD5 expression is reduced in gastric cancer. The specific mechanisms underlying the downregulation of FZD5 in tumor tissue needs further investigation. Hence, in vitro and in vivo studies are required to fully understand the role of the Wnt5a-FZD5 axis in the development and progression of gastric cancer.

ID: 152
Topics: Orthopädie/Unfallchirurgie, Klinische Studien

Evaluation of IL-33R and Galectin-3 as new Biomarkers of Cardiac Damage after Polytrauma – Association with Cardiac Comorbidities and Risk Factors

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Introduction: Polytrauma is still one of the disorders with the greatest economic impact on healthcare in society. One of the predictors for poor trauma outcomes is cardiac damage. The present study investigates two new potential biomarkers in the diagnosis of cardiac trauma: Interleukin 33 receptor (IL-33R) and galectin-3. Next to the evaluation of these two cardiac biomarkers, this study assesses pre-existing cardiac damage or risk factors as potential predictors of cardiac damage after polytrauma.
Material and Methods: A retrospective study including 107 polytraumatized patients with an injury severity score (ISS) ≥16 admitted from 2017-2020 in a Level 1 Trauma Centre. Plasma samples were taken at admission in the emergency department. Furthermore, the pre-existing cardiac risk factors as well as pre-existing cardiac diseases were recorded. The patient collective was subdivided in 3 groups according to the initial troponin T value. Human galectin-3 and ST2/IL-33 receptor concentrations were detected in plasma samples by ELISA.
Results: Troponin T concentrations were significantly increased in non-survivors, patients with a need of catecholamines and in patients with pre-existing cardiac comorbidities. The analysis of cardiac risk factors showed that the initial blood sugar levels were associated with cardiac damage measured by troponin, while the Body mass index (BMI) or the triglyceride (TAGs) concentration was not associated with cardiac damage. Both, galectin-3 and IL-33R did not correlate with the cardiac damage measured by troponin concentration. But galectin-3 showed a weak correlation with the general injury severity and the IL-6 concentration in patients with pre-existing cardiac comorbidities.
Conclusion: Both, galectin-3 and IL-33R did not correlate with the cardiac damage measured by troponin concentration. Patients with cardiac comorbidities or high blood sugar levels showed significant higher concentrations of troponin T compared to patients without.

ID: 153
Topics: Viszeralchirurgie, Klinische Studien

Gender-specific differences in the perioperative management, early postoperative and long-term oncosurgical outcome in gastric cancer (Ca) - results of a prospective multicenter observational study

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Aim: To investigate gender-specific differences of the periop. management & outcome by gastric Ca resection based on data obtained in a prospective multicenter observational study.
Results: From 2007 to 2009, 2,897 patients were documented: male/female, 59.7/40.3% (mean age, 67.4/70.3 yr in men/women; p<0.001). Significantly more often, men complained on dysphagia as 1st symptom (p<0.009), had an intestinal type (Laurén's classification) in preop. & def. histol. finding (p<0.001) as well as showed ASA scoring III (p<0.017). As risk factors, a significantly higher alcohol consumption & nicotine abuse (p<0.001 each) was found in men as the esophagogastric junction was significantly more often diagnosed as Tu site (p<0.001). Duration of surgery (202 vs. 184 min; p<0.001) as well as hospital stay (21.0 vs. 20.7 d; p<0.024) were significantly longer in men in addition to significantly more frequent pulm. events postoperatively (p<0.001).
In contrast, women had significantly more often pain in the upper abdomen & vomiting as 1st symptoms as well as a diffuse/mixed type (Laurén) in the pre-/postop. histol. finding (p<0.001). Risk profile: women were more obese & less susceptible for general complications postoperatively (p<0.001).
Multivariable analysis revealed higher ASA scoring, M1 status, longer duration of surgery & hospital stay as signif. infl. factors for morbidity. W/ regard to mortality, men with mixed type (Laurén), R1/2 status, higher ASA scoring as well as complication in higher age induced a significantly higher risk to die. In addition, male gender need to be considered a significantly neg. infl. factor w/ regard to 5-yr overall & disease-free survival (no gender-based impact onto 5-yr local recurrence rate).
Conclusion: Taking into account the gender aspect, signif. differences of gastric Ca resection were found in periop. risk profile, Tu characteristics & early postop., operation-associated but also in long-term, i.e., tumor- or malignancy-related outcome.

ID: 154
Topics: Viszeralchirurgie, Klinische Studien

Impact of basic disease (chronic pancreatitis [Pan.] vs. pancreatic head cancer [Ca]) and perioperative immune status onto early postoperative outcome in pylorus-preserving pancreatic head resection by Traverso-Longmire (PPPD)

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Aim: To investigate the impact of various diagnoses (Pan. vs. Ca, both of which are treated with PPPD) and perioperative immune status onto the early postoperative outcome after PPPD through a defined time period
Methods: All consecutive patients, who had undergone PPPD for Ca or Pan. (inclusion criterion) through a 15-years time period, were documented in a computer-based registry as part of a clinical systematic retrospective observational study (design) for surgical quality assurance and reflexion of daily abdominosurgical practice (“real-world data“). The early postoperative outcome was characterized by postoperative morbidity (in detail, with general/special complication rate) and 30-d mortality. As marker of immune response, parameter of the SOFA score plus C-reactive protein (CRP), white blood cell count (L) and procalcitonin (PCT) among others.
Results: From 10/01/2002 to 09/30/2017, n=238 patients were documented in total (Ca patients, significantly older and with longer hospital stay). General and special complications with 21.6% (Ca) vs. 15.6% (Pan.) and 39.7% (Ca) vs. 42.7% (Pan.; p=0.224/p=0.623) but also 30-d mortality were only partly different by trend: 2.6% (Ca) vs. 2.1% (Pan.; p=0.796).
CRP was significantly increased (Ca/Pan.: 181.74/229.32 µg/l [d2]; p=0.026 and 180.69/240.65 µg/l [d3]; p=0.041), d1 vs. d0 with no significant difference (81.65/88.01 µg/l), which can also be found in CRP rise (“d2-d1“: 92.8/131.7 µg/l; p=0.034 - “d2-d0“ not shown).
In addition, CRP rises were significantly greater in early complications (yes/no: 122.69/83.1 µg/l; p=0.044 [d2-d1] and p=0.001 [d2-d0; data not shown]).
Conclusion: Cancer seems to cause no significant impact onto morbidity and mortality in standardized pancreatic head resection despite higher age and longer postoperative hospital stay in Ca patients. As marker for the occurrence of early complications, only CRP indicated a significant correlation.

ID: 155
Topics: Andere, Andere

3D PRINTING OF MINIPORTS FOR MICROLAPAROSCOPIC SURGERY USED IN NEWBORNS AND PREMATURE INFANTS

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Introduction
The industrial scale production of consumable medical supplies such as mini-instruments designated for minimally invasive pediatric surgery (MIS), explicitly for use in neonates and premature infants, has been constantly discontinued due to high manufacturing costs and very low demand, most probably.
The aim of our technical investigation was to create “miniports” of 1.4 mm in diameter using 3D printing technologies.
Method
The technical pilot study was performed as a joint collaboration between the Department of Pediatric Surgery at the University Medical Centre and the Department of Manufacturing Technology with Focus Machining at the Otto von Guericke University Magdeburg. We evaluated the feasibility and effectiveness of 3D printing technologies used for the production of mini-trocars and trocar valves. Different 3D printing techniques and 3D print ingredients.
Results
Four locally available 3D printing techniques were explored and evaluated for usability. In next step, three different printing materials (“White V5”, “Surgical Guide”, “Elastic 50A”) were considered for prototype production.
In three prototype models the gradually reduction of trocar diameter from 4 mm to 1,4 mm was attained. Two of three substances showed a high rate of material breakage and instability of the prototypes. The first two valves prototypes were not suitable for appropriate use. The next two valve generation obtain the functionality level as required. There were ten different trocar prototypes produced. Eight trocar prototypes were not suitable for use, two trocars were functioning properly.
Conclusions
The production of miniports for microlaparoscopy using 3D printing technologies is feasible. To obtain the optimum efficacy in terms of printing-material-stability in very-small-diameter instruments and their technical practicality are subjects of further ongoing studies.

ID: 156

Topics: Viszeralchirurgie, Basic+Translational

Molekulare Veränderungen nach Resektion von kolorektalen Lebermetastasen

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1. Hintergrund

Das kolorektale Karzinom (CRC) ist die zweit- bzw. dritthäufigste Todesursache aller Tumorerkrankungen von Männern und Frauen in Europa. Während frühe Tumorstadien mit einer sehr guten Prognose einhergehen, stellt das metastasierte CRC eine multidisziplinäre Herausforderung dar. Ein elementarer Bestandteil der Therapie ist die chirurgische Resektion von Lebermetastasen, die zwar eine potentielle Heilung verspricht, jedoch sind Rezidive häufig. Die immunologischen, zellulären und molekularen Veränderungen in Leber und Metastase nach Leberresektion von kolorektalen Lebermetastasen sind dabei nur unzureichend verstanden.

2. Methodik

Wir haben ein immunkompetentes Mausmodell entwickelt, in dem nach Implantation von CRC-Tumororganoiden mit definiertem Mutationsstatus in das Coecum eine orthograde Lebermetastasierung entsteht. Nach 4 Wochen wurde eine operative Leberteilresektion/SHAM-OP durchgeführt und die Tumorprogression im MRT verfolgt. Nach Euthanasie der Tiere wurden die molekularen und zellulären Veränderungen in Leber, Lebermetastase und Primarius durch FACS, RNA- und Proteinanalysen untersucht.

3. Ergebnisse

Die Leberesektion führt zu einer deutlichen Hypertrophie in der Restleber und zur Heraufregulation von verschiedenen Genen und Proteinen der sogenannten prämetastatischen Nische. Auf zellulärer Ebene findet sich eine vermehrte Infiltration von neutrophilen Granulozyten und Monozyten in Leber und Metastase. Zudem zeigt sich eine deutliche Überexpression von Tight-junctions in Leber, Primärtumor und Darm. Trotz der transkriptionellen Veränderungen zeigt sich in dem Modell keine vermehrte Metastasierung in der Restleber nach Leberresektion.

4. Konklusion

Die Resektion von kolorektalen Lebermetastasen versursacht in diesem Tiermodell eine Akkumulation von Zellen der angeborenen Immunität in der gesunden Leber und Metastase sowie die Entstehung einer prämetastatischen Nische, ohne jedoch die Metastasierung in der verbliebenen Leber zu beschleunigen.

ID: 157
Topics: Viszeralchirurgie, Klinische Studien

Outcome der Pankreatoduodenektomie nach chirurgischer T-Drainagen-Anlage versus ERCP und Stenteinlage bei Verschlussikterus

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Hintergrund: Bei Verschlussikterus mit hohem Serumbilirubin kann vor einer partiellen oder totalen Pankreatoduodenektomie (PD/TP) eine chirurgische T-Drainagenanlage oder ERCP mit Stenteinlage zur Gallengangsdrainage notwendig sein. Ziel dieser Studie war es, das postoperative Outcome zwischen beiden Verfahren zu vergleichen.
Methodik: Alle Patienten, die von 01/2016 bis 05/2021 eine PD oder TP mit vorhergehender T-Drainagenanlage erhielten, wurden aus unserer prospektiv geführten Pankreasdatenbank identifiziert. Mittels 1:2 Propensity-Score-Matching wurde eine Vergleichskohorte mit Z. n. ERCP und Stenteinlage ergänzt.
Ergebnisse: 43 Patienten nach T-Drainagenanlage wurden mit 86 Patienten nach ERCP und Stenteinlage verglichen. Die häufigste Diagnose war ein Pankreaskarzinom (75,2%). Der initiale Serumbilirubinwert war in der T-Drainagen-Gruppe höher als in der ERCP-Gruppe (17,4 mg/dl vs. 12,4 mg/dl, p<0,0001). Auch ASA-Status und CA 19-9 lagen bei den T-Drainagen- höher als bei den ERCP-Patienten. In 4,7% und 16,3% der Fälle kam es nach T-Drainagen-Anlage bzw. nach ERCP und Stenteinlage zu postoperativen/-interventionellen Komplikationen (p=0,0873). Nach der T-Drainagenanlage war der Gallengang entsprechend des intraoperativen Gallengangabstrichs zum Zeitpunkt der PD/TP signifikant seltener bakteriell besiedelt als nach der ERCP (6,7% versus 97,6%, p<0,0001). Es ergab sich hinsichtlich der postoperativen Komplikationen kein signifikanter Unterschied. Wundinfekte traten bei 4 Patienten (9,3%) nach T-Drainage und 13 Patienten (15,1%) nach ERCP auf (p=0,4205). Eine Relaparotomie war nach 5 Patienten (11,6%) und 14 Patienten (16,3%) erforderlich (T-Drainage vs. ERCP, p=0,6026).
Konklusion: Nach ERCP und Stent-Einlage liegt zum Zeitpunkt der Pankreasresektion bei 95,4% der Patienten eine bakterielle Besiedelung des Gallengangs vor. Ob diese Besiedelung zu mehr postoperativen Komplikationen führt, kann anhand dieser kleinen, monozentrischen, Studie nicht belegt werden.

ID: 158
Topics: Viszeralchirurgie, Basic+Translational

The significance of metabolic reprogramming during hepatic fibrosis

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Background: Patients with liver fibrosis have a higher risk for postoperative hepatic dysfunction after hepato-biliary surgery. Hepatic stellate cells (HSCs) activation and hypoxia play a central role during the development and progression of liver fibrosis. Loss of the HIF prolyl hydroxylase 1 (PHD1-/-) mitigates liver fibrosis in mice. The cellular mechanism mediating anti-fibrotic effects of PHD1-/- remains unclear. Upon activation, HSCs upregulate pyruvate dehydrogenase kinases (PDKs) and utilize anaerobic glycolysis, driving fibrotic remodeling. Since PHD1 deficiency is critically involved in metabolic reprogramming of hepatocytes, we investigated the significance of PDKs during activation of HSCs.
Methods: HSC activation was investigated utilizing human HSC cell lines (LX2 cells). Gene and protein expression of myofibroblast markers were analyzed applying RT-PCR and western blotting, respectively. Metabolic reprogramming of HSCs was determined by gene expression analysis, ATP-content-assay, and seahorse assay. Enzyme function of PHD1 or PDKs was attenuated by siRNA or treatment with pharmacologic PHD or PDK inhibitors. In patient-derived liver biopsies, PHD1 and PDK1-4 expression levels were detected by immunohistochemistry and correlated with different stages of liver fibrosis and cirrhosis.
Results: Upon TGF-β-inflicted HSC activation, PDK1 (but not PDK2-4) mRNA levels were upregulated. Additionally, siRNA-mediated PDK1 knockdown decreased expression of profibrotic genes and proteins, such as COL1A1 and ACTA2. In contrast, downregulation of other PDK2-4 did not affect fibrogenesis of HSCs. In liver biopsies, PDK4 was inversely correlated with higher stages of liver fibrosis compared to patients with lower stages or no fibrosis at all, while PDK1 showed proportional expression.
Conclusion: Targeting metabolic reprogramming of HSCs using selective PDK inhibition or stimulation could represent a promising treatment option in patients with liver fibrosis.

ID: 159

Topics: Viszeralchirurgie, Basic+Translational

Proteinkinase-inhibition augments the response against multidrug chemotherapy in pancreatic cancer

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Background
Pancreatic ductal adenocarcinoma (PDAC) is worldwide the 7th common cause of cancer related deaths [1]. Pancreatoduodenectomy is whenever possible combined with an adjuvant chemotherapy; in palliative situation chemotherapy is the only treatment route. However, there are commonly patients which show only little to non-response to the different chemotherapy-schemes [2]. The dysregulation of protein kinases is associated with numerous carcinogenic processes and furthermore chemoresistance [3]. Thus, there is a huge need to explore the molecular mechanisms which cause chemotherapy-resistance and find strategies to implement these findings in clinical practice.

Methods
Pancreatic cancer cells were transduced with a protein kinase library followed by continuous exposure to vehicle control or oxaliplatin (IC 90) chemotherapy for 21 days. Based on CISPR Cas9 knockout screening and next-generation sequencing as well as MAGeCK-VISPR analysis we identified candidate genes. We used CRISPR-Cas9 to knock out the target gene, and verified the screening hits for overcoming chemoresistance through in vivo and in vitro experiments.

Results
We identified several cell cycle checkpoint kinases and DNA damage-related kinases as targets for overcoming chemoresistance, including MAP3K7. We state, that loss of function of MAP3K7 makes PDAC cells sensitive to chemotherapy with oxaliplatin.

Conclusion
Our results suggest a new therapeutic combination for PDAC, and support the application of CRISPR-Cas9-based functional screening in identifying novel therapeutic targets to potentiate existing cancer therapies.

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ID: 160

Topics: Viszeralchirurgie, Klinische Studien

Clinical characteristics and oncological outcomes of surgically treated early onset gastric adenocarcinoma

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Introduction: The incidence of early onset gastric adenocarcinoma (patients <50 years at time of diagnosis, EOGA is rising. Tumors in younger patients are associated with prognostically unfavorable features as more advanced stages and diffuse histology. The impact of EOGA on prognosis, however, remains unclear. The aim of this study is to evaluate early onset age as a prognostic factor in a surgical cohort and assess treatment options.
Methods: We analyzed 738 patients (129 early onset/609 late onset) operated in curative intent from 2002 to 2021. Data was extracted from a prospectively managed database of an academic tertiary referral hospital. Differences in perioperative as well as oncological outcomes were calculated by chi-square test. Cox regression analysis was performed to assess disease-free survival (DFS) and overall survival (OS).
Results: There were more female patients (51.9% vs. 38.4%, p=0.005) in the EOAG compared to the late onset cohort. Patients were more likely to be treated with neoadjuvant therapy (62.8% vs. 43.7%, p<0.001) and radical surgical resections (non-partial gastrectomy 68.2% vs. 55.5%%, p=0.006). EOAG was found to be more likely metastasized into lymph nodes (pN+ 67.0% vs. 52.9%, p=0.005) and to distant sites (pM+: 18.8% vs. 8.7%, p=0.001) as well as to be poorly differentiated (G3/4: 91.5% vs. 67.1%, p<0.001). EOGA was more likely to show signet ring cells in the pathohistological workup (75.6% vs. 45.8%, p<0.001). There was no difference in perioperative outcomes. Survival analysis showed worse DFS (median DFS 42.5 vs. >60 months, p=0.049) but equal OS groups (median OS 88.0 vs. 74.6 months, p=0.84) in the EOAG.
Conclusions: This analysis confirmed that early onset gastric adenocarcinoma is associated with more aggressive tumor characteristics (more advanced stages, tumor grades) and diffuse histology. Those factors contribute to worse DFS. However, equal overall survival rates are achieved with aggressive multimodal therapy including neoadjuvant therapy and radical surgery.

ID: 161
Topics: Orthopädie/Unfallchirurgie, Klinische Studien

Stoma placement and quality of life in paraplegic patients with extensive sacral pressure ulcers: a retrospective case series

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Introduction
Decubitus ulcers are caused by pressure on tissues, which leads to reduced blood flow to the affected region. Pressure ulcers in patients with spinal cord injuries significantly affect independence and quality of life. The aim of this study is to evaluate the contribution of stoma formation in the treatment of III°/IV° sacral pressure ulcers in patients with spinal cord injuries.
Patients and methods
25 spinal cord injury patients with large sacral pressure ulcers underwent intestinal stoma formation and plastic surgeries to cover wounds between 2015 and 2020. All subjects were enrolled retrospectively and were sent a follow-up questionnaire in March 2022. Among the 25 contacted cases, 12 were lost to follow-up. Definitive wound closure was achieved in all cases.
Results
The rate of surgical complications (haematoma, infection, suture dehiscence) was 40% (10/25). Following a stoma, patients reported having reduced fatigue, lower fear of not finding a bathroom, decreased bowel function embarrassment and perceived diminished lack of understanding about their bowel function from others. Overall, 69.2% were highly satisfied, and 30.8% were very highly satisfied with their stoma. The quality of life (QoL) was improved, the time spent on bowel care was reduced after stoma formation compared to before, and all patients stated they would have a stoma implanted again and would suggest its formation to friends with similar wounds and spinal injuries.
Discussion
Pressure ulcers in the anal region represent a possible indication for the creation of a stoma, since the risk of wound contamination and flap loss is otherwise significantly increased. The present results are in line with the current literature.
An intestinal stoma, usually considered a last resort therapy, could be a helpful tool, especially for spinal cord injury patients with large anal area bedsores, to enhance the healing of bedsores. To achieve optimal patient care, individual decision-making is needed.

ID: 162
Topics: Plastische Chirurgie, Basic+Translational

Etablierung der Hautbank Hannover: Sterile Abnahme- und Prüfprotokolle zur Generierung vitaler, kryokonservierter allogener Hauttransplantate von lebenden Spendern

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Konservierte allogene Spenderhaut ist nach wie vor eine der Standardtherapien zur vorübergehenden Wundabdeckung bei Schwerbrandverletzte. Allogene Hauttransplantate sind derzeit als kryo- oder glycerolkonservierte Allografts über Hautgewebebanken in der ganzen Welt erhältlich. Die meisten dieser Hautgewebebanken sind auf Hautspenden von verstorbenen Körperspendern angewiesen. Aufgrund des chronischen Mangels an humanen allogenen Transplantaten und steigender Kosten bei der Beschaffung, hat die Medizinische Hochschule Hannover eine eigene Hautgewebebank aufgebaut. Die etablierte Hautgewebebank basiert dabei auf der Gewinnung allogener Hauttransplantate von lebenden Spenderinnen und Spendern, die sich einer chirurgischen Behandlung in der Abteilung unterziehen. Dabei werden die Hautspenden von den Resektaten, insbesondere nach postbariatrischen Eingriffen, wie beispielsweise Abdominoplastiken oder Oberschenkel- und Oberarmstraffungen, gewonnen. Über den Zeitraum von mehreren Jahren wurden Verfahren und Protokolle für die Entnahme und Prozessierung von allogenen Hauttransplantaten etabliert, die sich streng an den nationalen und europäischen Vorschriften und Richtlinien orientieren. Im Rahmen der Etablierung der Hautbank Hannover wurden umfassende Protokolle zur Prozessierung der vitalen Spenderhaut etabliert, die umfassende mikrobiologische Untersuchungen beinhalten. Dabei konnten lediglich vereinzelt Erreger der physiologischen humanen Hautflora nachgewiesen werden. Die Ergebnisse bilden derzeit die Grundlage für weiterführende Untersuchungen sowie für die Etablierung der klinischen Anwendung der prozessierten Spenderhaut und auch die behördliche Zulassung dieser Gewebe.
Zusammenfassend wird ein Prüf- und Abnahmeverfahren vorgestellt, das umfassende mikrobiologischen Screenings, eine penible Patientensicherheit sowie eine Sterilität und langfristige Vitalität der Spenderhaut in der Hautbank Hannover gewährleistet.

ID: 163
Topics: Viszeralchirurgie, Basic+Translational

Anzahl und Funktion von myeloiden Suppressorzellen (MDSCs) bei Patienten nach Lebertransplantation

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Einführung
MDSCs sind myeloide Zellen mit suppressiver Aktivität gegenüber anderen Immunzellen, insbesondere T-Zellen. In der klinischen Forschung zu Organtransplantationen sind in den vergangenen Jahren erste spannende Daten über den begünstigenden Einfluss von MDSCs auf die Immunantwort und das Organüberleben veröffentlicht worden. Daten im klinischen Kontext der Lebertransplantation (LTx) fehlen jedoch bisher gänzlich.
Methoden
Für die hier vorgestellte Studie werden über unsere Transplantations-Ambulanz Patienten mit chronischer Lebererkrankung auf der Warteliste zur Transplantation und Patienten nach bereits erfolgter LTx rekrutiert und einer Immun-Analyse unterzogen. Gesunde Erwachsenen dienen als Kontrollen. Die Studie wurde durch die lokale Ethik-Kommission bewilligt (467/2021B02).
Ergebnisse
Es wurden bisher Blutproben von insgesamt 17 Patienten nach erfolgter LTx und 11 gesunde Probanden analysiert und miteinander verglichen. Hierbei zeigte sich ein signifikant erhöhter Anteil von granulozytären MDSCs und monozytären MDSCs in der Gruppe nach LTx verglichen zu den gesunden Probanden (jeweils $p<0,001$). Im Gegensatz hierzu zeigte sich kein signifikanter Unterschied für regulatorische T-Zellen (Tregs). Bei der anschließenden Funktionsanalyse mittels Hemmtest der CD4+ T Zell-Proliferation konnten MDSCs von Patienten nach LTx die T-Zellproliferation in gleicher Weise wie bei gesunden Kontrollen hemmen.
Schlussfolgerung
Unsere Ergebnisse belegen erstmalig einen signifikanten Anstieg und deutliche suppressive Aktivität von MDSCs bei Patienten nach LTx im Vergleich zu gesunden Kontrollprobanden, während sich kein Unterschied für Tregs zeigte. Die weitere longitudinale Korrelation dieser Zellen mit dem individuellen klinischen Verlauf und die Ausweitung der Analyse auf Patienten mit chronischer Lebererkrankung könnten weitere wichtige Schritte zu einem besseren Verständnis der dynamischen immunologischen Prozesse im Kontext der klinischen Organtransplantation darstellen.

ID: 164
Topics: Viszeralchirurgie, Basic+Translational

Verbesserung der intestinalen Anastomosenheilung im murinen Kolitis-Modell durch niedrigdosierte Prednisolon-Therapie

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Hintergrund: Die hochdosierte Therapie mit Glukokortikoiden ist ein etablierter Risikofaktor für Anastomoseninsuffizienzen nach Darmresektionen bei Patienten mit chronisch-entzündlichen Darmerkrankungen. Es ist jedoch weiterhin unklar, ob eine niedrigdosierte Glukokortikoid-Therapie möglicherweise einen positiven Einfluss auf das postoperative Outcome bringt. Wir präsentieren hier die erste Studie, die die dosis-abhängige Wirkung einer perioperativen Prednisolon-Therapie in einem murinen Kolitis-Modell in Kombination mit der chirurgischen Anlage einer intestinalen Anastomose untersucht.
Methoden: Bei 84 BALB/c wild-typ Mäusen erfolgte die Anlage einer kolorektalen Anastomose in mikrochirurgischer Technik. Bei der Hälfte der Tiere erfolgte die Induktion einer Dextran-Natrium-Sulfat (DSS) Kolitis. In jeder Gruppe erhielt jeweils ein Drittel der Mäuse eine niedrigdosierte (0,13mg/kg; ND) und eine hochdosierte (0,53mg/kg; HD) Prednisolon-Therapie für 7 Tage präoperativ bis zur finalen Evaluation am postoperativen Tag 3 bzw. 7.
Ergebnisse: Die hochdosierte Prednisolon-Therapie führte zu einer Verdopplung der Anastomoseninsuffizienz-Rate in Mäusen mit DSS-Kolitis (14,3% vs. 28,6%), die niedrigdosierte Therapie zu einer reduzierten Krankheitsaktivität und keiner Erhöhung der Insuffizienzrate (14,3%). In der histologischen Untersuchung zeigte sich eine vorteilhafte Wirkung der niedrigdosierten Prednisolon-Therapie auf die Rate von mikroskopischer Abszessbildung im Bereich der Anastomose (28,6% vs. 50,0%) und den histologischen Heilungsscore. Die Prednisolon-Therapie führte bei Kontroll-Mäusen zu einer dosis-abhängigen Erhöhung der mikroskopischen Abszessrate (15.38% vs. ND: 28.57% vs. HD: 53.85%), jedoch ohne erhöhte Insuffizienzrate.
Konklusionen: Unsere Daten zeigen einen positiven Effekt einer niedrigdosierten Prednisolon-Therapie auf die intestinale Anastomosenheilung bei Mäusen mit DSS-Kolitis, der mit einer Verringerung der präoperativen Krankheitsaktivität korreliert.

ID: 165
Topics: Plastische Chirurgie, Basic+Translational

Non-invasive monitoring of soft-tissue sarcoma response to neoadjuvant radiotherapy through quantification of circulating tumor DNA and multiparametric MRI

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Background:
Soft-tissue sarcomas (STS) are a heterogeneous group of rare, yet malignant tumors. Surgery remains the cornerstone of treatment for localized STS. Neoadjuvant radiotherapy (NRT) may decrease the risk of local recurrence. However, NRT might come at the cost of metastatic spread due to delayed resection, and intra-/ post-operative complications. Therefore, the effectiveness of NRT for different histological STS subtypes has to be scrutinized. This prospective study evaluates the response of various STS during the course of NRT using innovative, non-invasive methods.
Methods:
Liquid biopsies: Detection of circulating tumor DNA (ctDNA) in patient blood samples through targeted next-generation sequencing (NGS). Patient-specific exome sequencing allows the detection of individual structural variants (SVs). Circulating free DNA (cfDNA) is isolated from peritherapeutically collected patient plasma samples and ctDNA quantified therein.
Multiparametric MRI (mpMRI): Combination of conventional MRI sequences with diffusion-weighted imaging (DWI) and dynamic contrast enhancement (DCE). Multiparametric MRI is performed before, during, and after neoadjuvant radiotherapy. Accurate co-registration of mpMRI with the macroscopic, histologic, and immunohistochemical resected specimen allow an analysis of morphological changes during NRT.
Results:
Quantification of ctDNA mirrors the clinical course and tumor activity. We present imaging markers that allow the characterization of tumor masses for heterogeneous STS and the evaluation of therapy response.
Conclusion:
In a prospective study, we aim to evaluate the response of STS during the course of NRT using non-invasive methods and targeted NGS. Through quantification of ctDNA, tumor activity is correlated with multiparametric imaging data and immunohistology to assess therapy response. This will lead to the future development of tumor- and patient-specific therapy concepts, to minimize recurrence and surgical complications.

ID: 166
Topics: Andere, Basic+Translational

Carvacrol exerts anti-angiogenic effects against triple-negative breast cancer

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Background
Carvacrol, a monoterpene phenol enriched in the essential oils of various aromatic plants, is widely used as a fragrance in cosmetics and also as a food additive. Its anti-cancer potential has been extensively reported. However, the effects of carvacrol on angiogenesis, which is essential for tumor growth and metastasis, remains elusive so far. In the present study, we aimed to explore the anti-angiogenic activity of carvacrol in triple-negative breast cancer (TNBC).
Methods
In vitro proliferation, migration, tube formation and spheroid sprouting assays were performed to assess the angiogenic activities of vehicle- or carvacrol-treated human umbilical vein endothelial cells (HUVECs). A mouse dorsal skinfold chamber model was further established to evaluate the effects of carvacrol on TNBC angiogenesis and growth. Finally, Western blotting was performed to clarify the molecular mechanism of carvacrol action. All values were expressed as means ± SEM. Statistical significance was accepted for a value of $P < 0.05$.
Results
Carvacrol at non-cytotoxic doses significantly suppressed the proliferation, migration, tube formation and spheroid sprouting of HUVECs. In addition, daily intraperitoneal injection of carvacrol (50 mg/kg) significantly reduced the tumor size (day 14: 14.2 ± 2.2 mm2 vs. 8.3 ± 1.5 mm2), functional microvessel density (day 14: 243.4 ± 19.3 cm/cm2 vs. 131.0± 8.9 cm/cm2) as well as perfusion of tumor microvessels when compared to controls. Mechanistically, carvacrol down-regulated the expression of vascular endothelial growth factor receptor-2 (VEGFR2), fibroblast growth factor receptor-1 (FGFR1) and Tie2 in endothelial cells.
Conclusions
Our study shows a potent anti-angiogenic action of carvacrol, which may largely contribute to its anti-cancer activity. This natural product may therefore represent a potential candidate or lead compound for TNBC therapy.

ID: 167
Topics: Viszeralchirurgie, Basic+Translational

Pharmacologic inhibition of the IRE1α-XBP1s pathway impairs PDAC cell growth in vitro

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Introduction and purpose: Cancer cells rely on the unfolded protein response (UPR) to overcome endoplasmic reticulum (ER) stress caused by changes in cellular demand for protein folding. The ER-transmembrane protein IRE1α plays a crucial role in orchestrating the UPR: Upon ER stress IRE1α deploys its cytoplasmic kinase-endoribonuclease modules to activate the transcription factor XBP1s. XBP1s promotes ER expansion and proteosomal degradation of ER misfolded proteins. Although studies have implicated the importance of the IRE1α-XBP1s pathway for tumor cell survival in various cancer malignancies, so far, the validity of IRE1α as a potential therapeutic target in Pancreatic Ductal Adenocarcinoma (PDAC) is still unknown. Here, we aimed to assess IRE1α's therapeutic potential in PDAC by investigating the biological relevance of IRE1α for PDAC cell viability in vitro.
Methods: The activation of the IRE1α-XBP1 pathway was analysed by qPCR and immunoblotting in several different human PDAC and human pancreatic epithelial (HPDE, HPNE) cells as well as patient-derived organoids (PDOs). The IRE1α-XBP1 pathway was inhibited using IRE1α kinase (Compound 18) or RNase inhibitors (STF-083010 and 4μ8C). Cell viability was assessed using ATP-consumption and colorimetric assays as well as cell proliferation by the use of an Incucyte.
Results: The baseline expression of phospho-IRE1α and XBP1s/XBP1u mRNA Ratio was increased in PDAC compared to HPDE cells. While Thapsigarin, an ER stress inducer, significantly activated the pathway, IRE1α kinase and RNase inhibition dose-dependently reduced the levels of XBP1s and subsequently impaired tumor cell viability and proliferation of PDAC cell lines. Intriguingly, survival of PDOs was also significantly impaired.
Conclusion: Pharmacological IRE1α inhibition significantly reduces PDAC cell growth in vitro. This strongly supports a rationale for therapeutic targeting of IRE1α in PDAC.

ID: 168
Topics: Viszeralchirurgie, Basic+Translational

Cancer-specific differences of cellular and humoral immune responses against tumor associated antigens

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Objectives Tumor associated antigens (TAAs) are frequently expressed in various cancer types and represent important targets for cancer immunotherapy. Differential antigen occurrence may contribute to heterogeneity in tumor immune infiltration and patient outcome. In this study, we combine analyses of expression levels of 10 TAAs with functional assessment of cellular and humoral responses to these antigens.
Design 53 treatment-naïve patients with a diagnosis of 5 different cancer types (NSCLC, CRC, RCC, HCC and BCA) were included. The expression of 26 TAAs in tumor samples was determined using NanoString. Peptide pools for the 10 TAAs with the largest cross-cancer overlap were selected for 2-color Fluorospot (IFN-γ and IL-2) and protein bound bead assays to assess the frequency of tumor-specific cellular and humoral immune responses in peripheral blood samples.
Results TAAs are frequently co-expressed and show cancer-type specific expression patterns. Especially strongly expressed antigens also show a tumor-specific expression. A cellular-anti-TAA response was detected in 69.8% of patients, while 43.4% showed a humoral anti-TAA response. Survivin was the TAA and CRC the cancer type that most frequently showed T cell responses (45.3% and 85.7%, respectively). Although TAA expression and cellular or humoral immune responses to one or multiple antigens are common, co-occurrence of response and expression of the same antigen is rare.
Conclusion The presented data support cancer immunoediting rather than a lack of endogenous immune response as mechanism underlying immune tolerance. The cancer type dependent differences regarding TAA-specific immune responses should be considered in immune monitoring and design of immunotherapeutic trials.

ID: 169
Topics: Thoraxchirurgie, Klinische Studien

Prognostic factors for long-term survival following complete resection by lobectomy in stage I non-small cell lung cancer

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Background: The aim of this study was to evaluate predictors for long-term overall survival (OS) in patients with stage I non-small cell lung cancer (NSCLC).
Methods: All patients undergoing complete resection by lobectomy for stage I NSCLC between October 2012 and December 2015 at a single center were included. Univariable and multivariable Cox regression analyses were performed to identify prognostic factors.
Results: A total of 92 patients were included. Univariable and multivariable Cox regression analyses revealed preoperative neutrophil to lymphocyte ratio (NLR, $p = 0.005$), preoperative diffusion capacity of the lungs for carbon monoxide (DLCO, $p = 0.010$) and forced expiratory volume in 1 second (FEV1, $p = 0.041$) as well as male gender ($p = 0.026$) as independent prognostic factors for OS. Combining the calculated cutoff values for FEV1 (<73.0%) and NLR (>3.49) into one parameter resulted in a highly significant difference in survival times when stratified by this variable.
Conclusions: Recently, much emphasis has been put on the prognostic importance of blood biomarkers in NSCLC. In our study, NLR was an independent factor for OS, as were baseline characteristics such as DLCO, FEV1, and gender. Further studies on the association of biomarkers for systemic inflammation and lung function parameters with respect to patient survival are warranted.

ID: 170
Topics: Andere, Basic+Translational

Extracellular vesicles derived from activated-pancreatic stellate cells enhance the chemoresistance and plasticity of pancreatic adenocarcinoma in the tumor microenvironment

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Background
Pancreatic ductal adenocarcinoma (PDAC) possesses the identity of a high-aggression but insensitive chemotherapy reaction. PDAC benefits from the tumor microenvironment (TME) mainly composed of pancreatic stellate cells (PSCs) and cancer-associated fibroblast. Quiescent PSCs may transform into activated PSCs (aPSC) during tumorigenesis, and aPSCs have been confirmed the promotion of cancer chemoresistance. Extracellular vehicles (EVs) from activated PSCs (aPSCs) have shown the potential in modulating cancer biology. Our study aims to explore the PSC-EVs' effect on chemoresistance and tumor plasticity of PDAC.
Methods
PSCs were isolated from PDAC-adjacent normal tissues and representative markers were checked. Different culture systems were applied to PSCs and aPSCs. EVs were isolated from PSCs by ultracentrifugation and proved the quality. MTT assay was carried out to detect the chemoresistance of cancer. The tumor's metastatic and metabolic capacity was evaluated by Transwell invasion and seahorse XF assay. Liquid chromatography-mass spectrometry was used to verify the biological function of PDAC after EVs' intervention.
Results
With the impact of the PSC-EVs, PDAC cell lines displayed increased survival in gemcitabine treatment and enhanced invasion. We also found that PSC-EVs also caused the metabolic alteration of the Warburg effect in PDAC cells. In addition, aPSC-EVs revealed relatively stronger effects on PDAC cells compared with PSC-EVs on tumor chemoresistance and the Warburg effect. PDAC proteomic analysis explored interesting markers, including epithelial-mesenchymal transition (EMT) markers (FN1), metabolism markers (CD36) and Wnt signaling (Wnt5a).
Conclusion:
Our data suggested a significant role of PSCs-EV on chemoresistance and metastasis of PDAC, which might link to the EMT-like process and metabolic alteration. The effect of EVs could be boosted due to the activation of PSCs in the TME, which may explain mutualism between the PSCs and PDAC.

ID: 171
Topics: Viszeralchirurgie, Basic+Translational

Translational Research Approach to Improve Individualized Pancreatic Tumor Therapy

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Objective: Primary pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancer types in Germany with a 5-year survival rate below 10% and expected mortality increase. Despite vast research efforts, prognosis has not improved. Translational research is needed to provide a deeper comprehension of PDAC to improve predictability of disease progression, treatment options and prognosis.
Methods: 15 ml EDTA blood of pancreatic tumor patients were collected pre-, intra- (portal vein) and 5 days postoperatively. Circulating epithelial tumor cells (CETCs) expressing epithelial cell adhesion molecule (EpCAM) were labeled and detected using the Maintrac method. Circulating tumor stem cells were grown into spheres. The number of CETCs and spheres of each blood sampling were compared to the patients' outcome. PDAC biopsies were grafted onto the Chorioallantoic Membrane (CAM), a 3D in-vivo model, for one week and treated with Cisplatin and NaCl 0,9% as control. Tumor angiogenesis was measured using Laser speckle contrast analysis (LASCA). The focus laid on histological analysis of primary tissue and explanted CAM tumors utilizing H.E. staining. Engraftment rate and therapeutic effects are monitored immunohistochemically by Ki67 staining.
Results: Biopsy engrafting was mostly successful, with 91% survival of inoculated eggs. First histological analysis suggested main histopathological characteristics remained similar to primary tissue. Ki67 evaluation showed ongoing proliferation. Correlation of CETCs and sphere growth with clinical outcome is ongoing.
Conclusion: The CAM model might bridge the gap between cell culture and animal testing leading to a more precise understanding of PDAC. There might be a correlation between the aggressiveness of the tumor and the response to surgery/chemotherapy and the number of growing spheres. It may be a tool for personalized medicine helping identify the most effective therapy not least through the inoculation of the spheres on CAM.

ID: 172
Topics: Andere, Klinische Studien

LAMS (lumen-apposing metal stent) dislocation as complication of EUS-GE (Endoscopic Ultrasound-guided GastroEnteroanastomosis) - representative case report on the complication management by interventional re-endoscopy

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EUS-GE using LAMS is a new promising method for the treatment of tumorous duodenal stenosis.
Method: Case report on an EUS-GE with AXIOSTM stent dislocation into the colon and formation of a colojejunal fistula - here, the endoscopic solution by transcolonic insertion of an intestinal stent with recreation of the gastroenteroanastomosis is described.
Results (case description): A 78-years-old patient (pat.) developed tumor stenosis at the “flexura duodenojejunalis” with retention stomach as a result of a locally advanced & metastasized pancreatic cancer. This prompted for the creation of an EUS-GE.
A 7-Fr. nasojejunal tube was placed over the stenosis & the small bowel was filled with water & contrast medium. Subsequently, a jejunal loop was transgastrically detected by endoscopic ultrasound & a LAMS (20 mm Hot AXIOSTM stent) was directly placed. The ultrasound control showed a properly deployed stent. The diet was well tolerated & the pat. could be discharged on the 4th postinterventional day.
Fourteen d later, he presented with malodorous vomiting & watery diarrhoea.
Gastroscopy surprisingly revealed AXIOSTM stent dislocation into the colon with gastro-colostomy & wide fistula from the colon to the jejunum.
Due to the palliative situation, a 6-cm fully covered intestinal stent was inserted through the AXIOSTM & via the colon into the jejunum. This created a functional gastrojejunostomy through a transcolonic stent interposition. The pat. was discharged 2 d later with a stable oral intake.
After 1 week, a laparotomy was performed due to accident-related injuries, which, like the CT scan, did not reveal any evidence of peritonitis. The patient died later from the complications of the accident.
Conclusion: EUS-GE is a challenging procedure that should only be performed in tertiary centres with high expertise in interventional EUS incl. adequate abdominal surgery "back-up". In experienced hands, a re-endoscopic approach may solve complications such as stent dislocation.

ID: 173
Topics: Andere, Klinische Studien

Atypical site of the papilla of Vater is challenging with regard to the endoscopic management of cholangiolithiasis and cholangitis

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Atypical location of the papilla of Vater (papilla) is a rare anatomical variant & requires special attention plus expertise in papilla-associated pathological lesions as well as therapeutic manipulations, which are illustrated in this case.
Method: Report on a case w/ intrapyloric location of the papilla, choledocholithiasis & cholangitis in an 89-years-old female patient as well as occlusive jaundice.
Results (case description): The patient presented repeatedly for upper abdominal pain & fever, w/ clinical signs of cholangitis in cholestasis. An MRCP revealed a 19x6 mm prepapillary concrement w/ cholestasis. On abdominal ultrasound, the common bile duct (CBD) was difficult to find, only in the left lateral position. The initial passage of the duodenoscope for ERCP via the pylorus failed due to ulcer stenosis angulation. The passage became possible under wire-guidance & fluoroscopic control.
Surprisingly, the papilla could not be identified in the standard position.
Re-ERCP w/ diagnostic gastroscope & an attachment cap was performed, assuming an atypical localisation of the papilla. A tiny intrapyloric ostium at the junction of gastric & intestinal epithelium was found, which was confirmed fluoroscopically as the papilla.
After the initial dilatation to 10 mm, the extraction of the biliary stone was not successful. Then, it was decided to dilate the papilla up to 15 mm. This allowed a direct oral cholangioscopy w/ stone extraction. At the dilatation site, a covered, almost circular lesion was visible w/o signs of perforation (conservative therapeutic approach). On the following days, the inflammation & cholestasis decreased.
Conclusion: If the papilla can not be found in the standard position, a rare atypical position should be considered. A gastroscope offers a much better setting for the latter. A papillotomy should be avoided, balloon dilatation should be preferred. The size of the balloon should be chosen appropriately to the size of the stone to avoid a CBD lesion.

ID: 174

Topics: Viszeralchirurgie, Basic+Translational

Glial cell line-derived neurotrophic factor improves intestinal wound healing by upregulation of proliferative pathways

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Introduction: Inflammatory Bowel Diseases (IBD) encompassing Crohn's disease and Ulcerative colitis are chronic relapsing disorders. The etiology is multifactorial and remains incompletely understood. However, mucosal healing is known as a predictor for remission and clinical improvement of IBD patients. The enteric nervous system might play a crucial role in intestinal epithelial barrier (IEB) regulation and seems to be involved in IBD pathogenesis. The soluble factor Glial cell line-derived neurotrophic factor (GDNF) has been shown to be critically involved in IEB maturation. The aim of this study was to decipher the role of GDNF in mucosal healing and to characterize potential molecular pathways.

Methods: Intestinal wound healing was analyzed in colonoscopy biopsy-based wound assay and dextran sodium sulphate (DSS)-induced colitis. C57BL/6 mice were treated either with GDNF or sodium chloride intraperitoneally. Tissue samples were used for RNA and protein analyses. To decipher potential signaling pathways wound scratch assay and proliferation assay were performed in CaCo2 cells and murine enteroids.

Results: GDNF application resulted in an improved intestinal would healing with an increased wound closure rate as revealed in biopsy-based wound assay. In the DSS-induced colitis model, GDNF treated mice showed improved recovery after DSS application indicating an enhanced intestinal healing. These observations were confirmed in vitro by performing wound scratch assays in Caco2 cells and enteroids. Further molecular analyses reveal that the improved wound healing after GDNF application was caused by an upregulation of LGR5-positive cells and activation of src-signalling resulting in enhanced cell proliferation.

Conclusion: GDNF promotes intestinal wound healing under inflammatory conditions by upregulation of proliferation pathways. Thus, GDNF application could be a new therapeutic strategy that aim to limit mucosal inflammation and improve intestinal barrier function.

ID: 175
Topics: Andere, Basic+Translational

High hydrostatic pressure enables head and neck cancer devitalization and induction of immunogenic cell death

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Immune checkpoint inhibition is a milestone in the therapy of advanced head and neck cancer (HNSCC). Nevertheless, many patients do not benefit from immune therapy. One promising approach to reactivate immunosurveillance and extend immunotherapy is the development of therapeutic anti-tumor vaccines. However, head and neck cancer vaccines have not yet presented their true potential in clinical trials.
Present study introduce high hydrostatic pressure (HHP) for safe HNSCC devitalization and induction of immunogenic cell death. HHP specifically devitalizes cells without major changes in molecular structures. Therefore, HHP may enhance the development of whole-cell anti-tumor vaccines, which represent tumor heterogeneity and thus antigen-diversity.
Four HNSCC cell lines were treated with 150, 300, 450, and 600 MPa HHP for 10 min. Cell death was analyzed by photometry, fluorescence quantification and spectral flow cytometry. Autofluorescence quantification after implantation on the chicken CAM was used to confirm safe devitalization in vivo: Present study found that the presence and type of cell death depend on the HHP amplitude: 150 and 300 MPa were insufficient for comprehensive HNSCC cell death. HHP above 450 MPa induced complete and predominantly necrotic cell death. DNA double strand breaks may play a major role in HHP-related tumor cell death.
The present study results show that 450 MPa of high hydrostatic pressure lead to safe and reproducible head and neck cancer devitalization with immunogenic cell death. HHP-based autologous whole-cell anti-tumor vaccines may complement future immunotherapy combinations for high mutational burden cancer.

ID: 177

Topics: Thoraxchirurgie, Basic+Translational

Blutungsmanagement nach Verletzung des linken Vorhofes durch Ballonokklusion – eine experimentelle Studie

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Hintergrund: Bei der Resektion von zentralen Lungenkarzinomen kann es durch die Präparation zu Verletzungen des linken Vorhofes kommen. Die Folgen sind mangels verfügbarer Herz – Lungenmaschine meist deletär. Es sollen an einem ex - vivo Modell drei initiale Versorgungsstrategien nach Vorhofverletzung miteinander verglichen werden.
Methodik: Es wurde an einem frisch geschlachteten Schwein ein unverletztes Herz – Lungenpaket entnommen. Zur Simulation eines Kreislaufes erfolgte eine venöse Kanülierung über die Arteria pulmonalis und die arterielle über den linken Vorhof, die Aorta wurde geklemmt. Es wurde somit ein kardiopulmonaler Bypass etabliert (Mittlerer HLM - Fluss: ca. 2 Liter /Minute). Am linken Vorhof wurde durch einen Aortic Punch eine konstante Läsion von 4 mm gesetzt. Es wurden drei Gruppen (jeweils n =8) untersucht: Gruppe 1: Fingerkompression und Naht, 2. Ballonokklusion und Naht und 3. Ausklemmen und Naht. Der Volumenverlust (ml) bis zum definitiven Verschluss der Läsion wurde gemessen.
Ergebnisse: Ein Kruskal-Wallis-Test zeigt, dass die Volumenverluste durch unterschiedliche Verschlussarten beeinflusst werden (Chi-Quadrat = 15,716, p = .000). Post-hoc-Tests (Dunn-Bonferroni-Tests) zeigen, dass sich nur die Gruppen "Ballonkathether" und "Ausklemmen chirurgisch" (z = 3,668, p = .000) und die Gruppen "Ballonkathether" und "Finger" signifikant unterscheiden (z = -3,136, p = .002). Die Ballonkathether-Anwendung bewirkt den gewünschten Effekt zur Minderung der Volumenverlusten. Es handelt sich um einen starken Effekt nach Cohen mit r = .917.
Konklusion: Wird im Rahmen von Operationen an der Lunge der linke Vorhof verletzt, so erscheint die initiale Ballonokklusion der Läsion die erfolgversprechendste Strategie des Blutungsmanagements.

ID: 178
Topics: Andere, Basic+Translational

Einschätzung der lateralen Wärmeausbreitung während der bipolaren Gefäßversiegelung an einem ex vivo Modell

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Hintergrund: Bei jeder bipolaren Versiegelung von Gefäßen tritt als Nebeneffekt eine laterale Wärmeausbreitung auf, die umliegendes Gewebe irreversibel schädigen kann. Durch eine thermographische Untersuchung an einem ex vivo Modell soll diese eingeschätzt werden.
Material und Methode: Unsere Untersuchungen mit zwei verschiedenen Versiegelungsinstrumenten wurden an einem ex vivo Modell der Schweinecarotiden durchgeführt. Zur Einschätzung der lateralen Wärmeausdehnung wurde ein Index zur Einschätzung des Schädigungsrisikos basierend auf der thermographischen Messung und histologischen Untersuchung gebildet.
Ergebnisse: Bei Instrument 1 zeigte sich eine Ausdehnung der kritischen Zone > 50°C von 2315±509µm oberhalb und 1700±331.3µm unterhalb der Branchen. Die Ausdehnung der Nekrosezone war 412.5±79.0µm oberhalb und 426.7±100.7µm unterhalb der Branchen. Bei Instrument 2 lag die kritische Zone > 50°C bei 2032±592.4µm oberhalb und 1182±386.9µm unterhalb der Branchen. Die Ausdehnung der Nekrosezone war 642.6±158.2µm oberhalb und 645.3±11.9µm unterhalb der Branchen. Unser Risikoindex ergab ein niedriges Risiko für Instrument 1 und ein moderates Risiko für Instrument 2 hinsichtlich des Auftretens von Kollateralschäden.
Konklusion: Die Thermographie ist eine brauchbare Methode zur Bestimmung der lateralen Wärmeausdehnung bei der bipolaren Versiegelung. Der Index schätzt das Risiko für die Schädigung des umliegenden Gewebes ab.

ID: 179
Topics: Viszeralchirurgie, Basic+Translational

Aldo-Keto Reductase 1C3 enhances radioresistance in esophageal adenocarcinoma cells via inhibiting ferroptosis

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Background: Esophageal adenocarcinoma (EAC) is the 7th most commonly diagnosed malignancy worldwide. Aldo-keto reductase 1C3 (AKR1C3), an enzyme involved in prostaglandins metabolism, has been reported the involvement in radioresistance in many types of cancers. However, the role of AKR1C3 mediating the radioresistance of EAC has not yet been explored.
Methods: In our study, we first established a radioresistant variant of EAC cell line OE33 (OE33R) by consistently exposing ionizing radiation with a total dose of 50Gy. Clonogenic cell survival assay confirmed enhanced survival of OE33R. The oxidative phosphorylation and glycolysis were detected by Seahorse real time metabolic analysis. SLC7A11 expression level was validated by Western blotting. Cell ferroptosis was validated by flow cytometry with C11 Bodipy staining.
Results: OE33R has a higher expression level of AKR1C3 than OE33. Silencing ARK1C3 could restore the radiosensitivity of EAC cells. AKR1C3 overexpression rewired the EAC metabolism by modifying oxidative consumption rate (OCR) and extracellular acidification rate (ECAR). Solute carrier family 7 member 11 (SLC7A11) expression was related to AKR1C3 level. C11 Bodipy level had a significant difference after irradiation between OE33 control and AKR1C3 overexpressed cell line (36.07 ±3.19 % vs 26.83±1.01 %). AKR1C3 dysregulation modified the irradiation induced ferroptosis of EAC cells.
Conclusions: Our preliminary data indicated that AKR1C3 might regulate the radioresistance of EAC via inhibiting ferroptosis and may function as a promising target to restore the radiosensitivity of EAC.

ID: 180
Topics: Viszeralchirurgie, Klinische Studien

The validity of an App-based risk scoring defining an aerobic endurance prehabilitation program (Patronus Prehab App) in patients undergoing elective major surgery: The prospective, interventional PROTEGO MAXIMA Trial

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Background: Prehabilitation aims at improving patients' abilities prior to surgery to positively impact perioperative outcomes. To understand the improvement of a prehabilitation intervention, a set of well-measurable risk data is required. This study aims for risk score cut-offs correlated to postoperative outcomes. The hypothesis was that the (Calculated Risk analysis index) RAI-C score, the Easter Cooperative Oncology Group (ECOG) score, and the Timed-Up and Go (TUG)-test are predictive of postoperative outcomes by day 90 after surgery.
Methods: Patients undergoing major surgery were risk-scored with a digital software tool (Patronus Prehab App) and the scores correlated with 90-day outcomes (ICD 10 diagnosis, surgical OPS codes, Clavien-Dindo (CD) classification and survival). ROC analyses were performed to obtain cut-off values for the Rai-C score and the TUG. $\chi 2$ tests were performed for ECOG scoring and univariate analysis.
Results: 104 patients were included (32.7% female and 67.3% male). The mean age was 60.79 ± 13.834 years. The mean RAI-C score was 21.68 ± 10.592 and the mean TUG was 7.8 ± 2.671. The ECOG score was 0 in 89.4% and 1 in 10.6% of patients. Cancer was the leading diagnosis in 71.2%. 90-day mortality was 4.8%. Complication rates at 90-days were 52%. Major complication rates CD>II were 24%. The mortality predictive cut-off value for the Rai-C score was 24 (sensitivity 80%; specificity 65%; AUC: 0.791; p=0.001), for the TUG 8 seconds (sensitivity 70%; specificity 70%; 0.797; p=0.002). Predictive markers for postoperative mortality were the activity of daily living items mobility (p=0.000), toilet use (p=0.000) and ECOG (p=0,028).
Conclusion: The risk assessment within the software is a viable method to reliably identify risk factors before major surgeries. Risk scores (RAI-C, ECOG, TUG) correlate with postoperative mortality.

ID: 181
Topics: Viszeralchirurgie, Basic+Translational

Lipidomic Characterization of Liver Regeneration after Portal Vein Ligation using Rapid Evaporation Ionisation Mass Spectrometry (REIMS)

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Background: A severe risk of liver resection is posthepatectomy liver failure due to insufficient remaining liver function. To increase the liver remnant volume and consequently liver function, a portal vein embolization (PVE) can be performed. PVE leads to tissue hyperplasia by activation of cellular regeneration. It is known that liver regeneration is accompanied by considerable lipid accumulation in hepatocytes. Aim of the present study was the lipidomic characterization of liver regeneration using REIMS.
Methods: Tissue characterization (regeneration and control) was performed in rat and human tissues. Regeneration was induced in rat using portal vein ligation for 5 d (n=5) and in human (n=7) by PVE leading to samples from embolized (emb) and regenerated (reg) liver tissues. Tissues were analyzed for their lipidomic profiles by REIMS using a TOF mass spectrometer. Bioinformatic data analysis was performed using Progenesis Qi and EZinfo.
Results: Principal component analysis (PCA) revealed that differences between emb and reg rat liver tissues were observed on days 2-3. In these tissues, glycerophospholipids (GPL) were reduced compared to other time points. Contrary, fatty acids (FA) had the strongest increase on day 2-3 in emb tissues, still elevated on day 5 compared to control animals. After 5 days the lipid pattern in emb and reg tissue equalize and both accumulate in the same cluster. PCA of human PVE liver tissues showed a PVE time span-dependent clustering separating from control tissues. Further analysis revealed that, specific GPL and Triacylglycerides (TAG) increase time-dependently in their abundance in reg tissues with highest levels after 7 weeks PVE time.
Conclusion: The data indicate that human tissues obtained after PVE reflect late regeneration stages in rats. Therefore, we conclude that major regeneration steps in humans including lipid accumulation happen very early and are already reduced in their intensity after hemihepatectomy was performed.

ID: 182
Topics: Andere, Basic+Translational

Establishing esophageal adenocarcinoma organoids and paired cancer associated fibroblasts for in vitro tumor growth monitoring and drug screening

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Background
The lack of appropriate translational research models remains a major challenge in esophageal adenocarcinoma (EAC) research. Patient-derived organoid (PDO) features in vitro simulations of human development and organ regeneration. We aim to establish EAC PDOs and paired cancer-associated fibroblasts (CAFs) from patient-derived tumor tissue, and to explore the feasibility of using EAC PDOs for tumor growth monitoring and drug screening.
Methods
EAC patients' primary tumor tissues were collected, minced, and digested into single cells, which were further seeded into extracellular matrix (ECM) gel and cultured with EAC specific organoid medium. EAC PDOs were validated using immunohistochemistry (IHC) and immunofluorescence (IF) staining by comparing PDOs with paired tumor tissue. The drug sensitivity of PDOs was performed by exposing PDOs to gradient chemotherapeutical drug concentrations and then measured using an ATP-based luminescent cell viability assay. Transwell co-culture system was used to indirectly co-culture PDOs with paired CAFs. The growth rates of PDOs with and without CAFs co-culture were tracked under a phase contrast microscope by size measuring.
Results
Six EAC PDOs were initiated and two paired EAC PDOs and CAFs were further applied in functional assesment. PDOs exhibited similar expression patterns to paired tumor tissues in pan-ck, CK 7 and Ki67, displaying negative staining for fibroblast marker αSMA. Drug sensitivity assay indicates that the PDO model is feasible for drug screening where the two PDOs show different responses to cisplatin treatment (IC50: 62.9 μM and 106 μM , respectively). PDOs with paired CAF co-culture show higher tumor growth rates as compared to the PDOs alone.
Conclusion
EAC PDO is a feasible preclinical in vitro 3D model and can be widely applied in the translational research of EAC. With paired CAFs, EAC PDOs are promising tools in studying the interaction of EAC tumor cell and CAFs within the tumor microenvironment.

ID: 183

Topics: Orthopädie/Unfallchirurgie, Basic+Translational

Effect of combined C5/CD14 immunomodulators on the liver of polytrauma injured pigs after 72h

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Background: The individual dysfunction of the liver and other organs caused by liver injury involves complex pathophysiological mechanisms, which are still not well understood. A systematic understanding of the pathological changes and inflammatory response of the liver after trauma is necessary and beneficial for the prevention and resolution of various clinical problems resulting from liver injury.
Methods: A pig model of polytrauma (PT) and hemorrhagic shock (HS) was established at the University of Aachen. All groups except the sham group received blunt pulmonary contusion, hepatic dissection, bilateral lower limb femoral shaft fractures and hemorrhagic shock. Four groups were investigated: 1) sham animals; 2) polytraumatized pigs treated with an external fixation, 3) treated with a nail, 4) treated with a Nail+Immunomodulation (combined C5/CD14 inhibitor). Serum samples were obtained at 0 h, 1.5 h, 2.5 h, 24 h, 48 h and 72 h after completion of PT+HS, and liver samples were obtained after euthanasia of the pigs. Paraffin sections of liver tissue were stained for HE and scored for damage. We assessed the level of liver tissue damage and inflammation in each group using various methods including MPO staining, qPCR and ELISA.
Results: The liver injury score of the immunomodulated polytrauma/nail group was lower than in the nail-treated group alone. The levels of ALT and AST were significantly decreased in the immunomodulated group compared to the nail group after 72 hours ($p<0.05$).
Conclusion: In experimental polytrauma, the combined inhibition of C5/CD14 resulted in some reduction of polytrauma-induced liver damage and inflammation.

ID: 184

Topics: Viszeralchirurgie, Basic+Translational

Surgical Audio Guidance (SURAG) macht das Einbringen der Veress-Nadel sicherer.

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Hintergrund:
Das Einbringen der Veress-Nadel in der Laparoskopie führt in bis zu 4% zu Verletzungen der inneren Bauchorgane. Um das Einbringen der Veress Nadel noch sicherer zu machen, wurde ein Navigationssystem (Surgical Audio Guidance - SURAG) entwickelt. Dieses gibt eine akustische Rückmeldung, sobald die Nadelspitze den Bauchraum erreicht. Ziel dieser Studie war es, die Rückmeldung des SURAG-Systems mit der subjektiven Wahrnehmung des Chirurgen bzgl. des Erreichens der Bauchhöhle durch die Veress Nadel zu vergleichen.

Methodik:
Bei zwei Körperspendern (aus dem Institut für Anatomie) wurde die Veress Nadel jeweils 12-mal (5-mal infra-, 5-mal supraumbilikal und 2-mal direkt durch die Nabelmitte) eingebracht. Zur Sichtkontrolle wurde ein Laparoskop (5 mm, 30°) im rechten Mittelbauch eingebracht. Der Monitor war für den Chirurgen nicht einsehbar. Das Einbringen der Veress Nadel erfolgte durch jeweils einen in der Laparoskopie erfahrenen und einen nicht erfahrenen Chirurgen. Sobald der Chirurg das Erreichen des Bauchraumes wahrgenommen hat, hat er dies durch ein lautes „Ja“ signalisiert. Diese Angabe, sowie die akustische Rückmeldung des SURAG-Systems wurden auf Video dokumentiert um anschließend die Trefferquoten beider Angaben zu vergleichen.

Ergebnisse:
Das SURAG-System war in allen 24 Versuchen (100 %) mit dem gegebenen Signal korrekt. Das Einbringen der Veress-Nadel erfolgte durch den erfahrenen Chirurgen 18-mal und durch den weniger erfahrenen Chirurgen 6-mal. Der erfahrenere Chirurg hatte eine falsch-positive Quote von 11 % und der nicht erfahrene Chirurg von 33 % der versuche.

Konklusion:
Das SURAG-System ist als ein zusätzliches Sicherheitssystem zu empfehlen. Die Fehlerquote bei den Chirurgen entspricht in etwa dem aus dem klinischen Alltag bekannten Wert. Es sind weitere klinische und experimentelle Studien notwendig, um das SURAG-System für den klinischen Einsatz zu validieren.

ID: 185
Topics: Viszeralchirurgie, Klinische Studien

Composition of the oral and gastrointestinal microbiome in patients with Barrett's esophagus and esophageal adenocarcinoma

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Background
A growing body of evidence shows that human gastrointestinal bacteria play an important role in the etiology of gastrointestinal cancer. Due to the anatomically close location, oral microbiota can migrate into the esophagus. We hypothesized that the oral flora may affect the esophageal flora and thus influence the progression of esophageal disease. Nevertheless, the precursor to EAC(esophageal adenocarcinoma) is BE (Barrett‘s esophagus), we speculate that in the bacterial composition, healthy controls, BE and EAC even show a progressive trend.
Methods
In our retrospective study, BE patients (Barrett's esophagus) (n=1), EAC patients (esophageal adenocarcinoma) (n=3) and healthy subjects (n=2) were recruited. Both the saliva sample and the endoscopic mucosal biopsies of healthy tissues and lesion tissues were taken for microbiome analysis using 16S-based amplicon sequencing, which made a multidimensional comparison possible.
Results
Quantitatively, in the esophageal tumor tissues showed decreased species richness than in the healthy esophageal tissues, while esophageal lesion tissues and saliva samples showed the similar species richness. Compositionally, on the one hand, a significant decreased relative abundance of Bacillales, Enterobacteriales, Pseudomonadales and Sphingomonadales in the tumor tissues compared with normal esophageal tissues was observed at the order level. On the other hand, the bacterial composition of esophageal tumor tissues and saliva tissues showed great similarity.
Conclusion
The bacterial composition of normal esophagus should be very different from that of saliva tissue. When the bacterial composition of esophageal tissue approaches the bacterial composition of saliva tissue, it indicates the occurrence of esophageal lesions. Therefore, it can be speculated that the salivary bacteria migrate to the esophagus and participate in the pathological changes of the esophagus.

ID: 186

Topics: Andere, Basic+Translational

Infraschallexposition kann die Kraft-Frequenz-Beziehung am isolierten atrialen menschlichen Myocard ändern

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Hintergrund: Die Exposition des Menschen gegenüber technischem Infraschall nimmt stetig zu (z.B. durch Klimaanlagen, Straßenlärm, Windkraftanlagen). Es wurde bereits gezeigt, dass isoliertes Myocard bei konstanter Stimulation mit 60 bpm (beats per minute) mit einer Kontraktilitätsminderung reagiert, wenn die Lautstärke des Schallsignals 100 dB übersteigt. Wesentliche Determinante myocardialer Kontraktilität ist die Kraft-Frequenz Beziehung. Es wurde untersucht, ob Infraschallexposition die Kraft-Frequenz-Beziehung beeinflusst.
Methodik: als chirurgisches Resektionsmaterial anfallendes atriales Myocard von 6 Patienten wurde präpariert, so dass isolierte Trabekel (0.3x 6 mm) entstanden. Diese wurden zwischen Kraftaufnehmer und Längenadjustor fixiert, auf optimale Länge vorgedehnt und mit variablen Frequenzen stimuliert(30, 60, 90, 120, 150 bpm; Messbedingungen: 37°C, oxygenierte Krebs-Henseleit Lsg, supramaximale Stimulation). Die Kraftentwicklung wurde als Funktion der Stimulationsfrequenz gemessen a.) unter Kontrollbedingungen ohne Infraschallexposition, b) bei einem Präparat des gleichen Patienten unter permanenter Infraschallexposition (20 Hz sinus, 100 dB).
Ergebnisse: in Serie (a) steigt die Kraft von 2.4+ 0.4 mN bei 30 bpm auf 5.8 +0.6 bpm bei 120 mN und fällt dann bei 150 bpm auf 5.6 + 0.7 mN (n=6). In Serie (b) (Infraschall) liegt der initale Wert bei 30 bpm bei 2.0 + 0.3 mN, steigt bei 60 mN auf 4.4 + 0.5 mN ohne bei weiterer Frequenzerhöhung weiter zu steigen (bei 120 bpm: 4.0 +0.3 mN), $p<0.001$).
Konklusion: Die Daten zeigen, dass bei 100 dB Infraschallexposition nicht nur eine insgesamt niedrigere Kraft am isolierten Myocard generiert wird, sondern dass die regulatorische Kraft-Frequenz-Beziehung zur Modulation der Kontraktilität nicht mehr erhalten ist. Als Ursache kommen direkte Interaktionen mit der Aktin-Myosin-Interaktion in Betracht oder veränderte Eigenschaften mechanosensibler Ionenkanäle, die den intracellulären Calciummetabolismus steuern.

ID: 187
Topics: Herz-/Gefäßchirurgie, Basic+Translational

No Reduction of Contractile Isometric Performance in Human Atrial Myocardium at Infrasound Levels of 80 and 90 dB

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Background: Technical infrasound as present in the neighbourhoud of wind turbines can induce disturbances of myocardial force generation when more than 100 dB are applied. However, as the sound frequency is below 20 Hz it is not be heard by the human ear. The current study analyses, whether infrasound energy of 80dB and 90 dB applied to electrically driven isolated human myocardium has effects on the contractile performance, as near windparks (at 1000 m distance) noise levels between 80-90 dB are measured.
Methods: human atrial myocardial musce preparations, obtained from patients undergoing cardiac surgery (n= 8) , were prepared (0.3x6 mm), stretched to optimal length and electrically stimulated (75 bpm) for a period of almost 120 minutes (isometric conditions, 37°C, oxygenated Krebs-Henseleit solution). Two samples were obtained from each patient: one was subjected to infrasound and the other served as a control. The extent of isometric contraction force (CF), contraction duration (CD) und resting tension (RT) were measured before and after infrasound exposure. The changes in these values were compared to the control samples in each trial. Two different levels of infrasound were used: 80 dB und 90 dB.
Results: The extent of force generation (CF) did not correspond to the infrasound level, that was applied. Contraction duration and resting tension failed to be significant from the control group when infrasound was applied.
Conclusion: the data show, that under the given experimental conditions infrasound levels of 80 and 90 dB do not induce significant alterations of the contractile behaviour of isolated human atrial preparations. However, further research is required to repeat these experiments using more physiological experimental conditions: isotonic, temperature-variation, varying stimulation frequencies, altered preloads. It has to be considerd, that sinusoidal sound was applied that may not be comparable to the pulsed sound signals as emitted by windturbines.

ID: 188
Topics: Viszeralchirurgie, Basic+Translational

Phenotypic characterization of colorectal liver metastases: capsule versus no capsule and the potential role of epithelial mesenchymal transition

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Background: Colorectal liver metastases (CRLM) can be encased in a fibrous capsule separating cancer from normal liver tissue, which correlates with increased patient survival. This study elucidates cellular and molecular mechanisms of capsule formation and the possible role of epithelial mesenchymal transition (EMT).
Methods: 34 CRLM from 34 patients were analyzed by EMT-pathway-profiling- and custom-PCR-arrays to identify differences in gene expression between CRLM with (n=20) and without capsule (n=14). In parallel, those 34 CRLM were used to analyze 16 gene products at the metastasis margin viaimmunohistochemistry.
Results: Encapsulated CRLM show elevated expression of signal transduction pathways and effector molecules involved in EMT; E-Cadherin and Keratin-19 were more prevalent and transcription as well as translation (immunohistochemistry) of pGSK-3-β, SOX10, Tomoregulin-1 and Caldesmon were increased. By contrast, loss of E-cadherin and the prevalence of snail 1 were increased in CRLM without capsule. Collagen I, III and Versican were identified as capsule components with the extracellular matrix fibers running concentrically encircling the malignant tissue and parallel to the invasive front. Caldesmon was also demonstrated as capsule constituent.
Conclusions: The fibrous capsule of CRLM is produced by cells with mesenchymal characteristics; it functions as a protective border by both, features of fiber architecture and inhibition of invasive growth through EMT recruiting mesenchymal cells such as myofibroblasts by transformation of surrounding epithelial or even carcinoma cells. By contrast, EMT demonstrated in non-encapsulated CRLM may lead to a more mesenchymal, mobile and tissue destructive carcinoma cell phenotype and facilitate malignant spread.

ID: 189
Topics: Viszeralchirurgie, Klinische Studien

Endoskopische Vakuumtherapie versus Stentbehandlung von Ösophagusanastomosen (ESOLEAK): Studienprotokoll für eine prospektive randomisierte Phase-2-Studie

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Hintergrund:
Intrathorakale Anastomoseninsuffizienzen (AI) sind eine der Hauptkomplikationen nach der Ivor-Lewis-Ösophagektomie. Es gibt zwei vielversprechende endoskopische Behandlungsstrategien: die Platzierung von selbstexpandierenden Metallstents (SEMS) oder die endoskopische Vakuumtherapie (EVT). Bislang gibt es keine prospektiven Daten über die optimale endoskopische Behandlungsstrategie.
Methoden:
Diese randomisierte Phase-2-Studie wird an zwei deutschen Zentren für Ösophaguschirurgie durchgeführt und soll innerhalb von zwei Jahren insgesamt 40 Patienten einschliessen. Patienten die sich einer onkologischen Ivor-Lewis-Ösophagektomie unterzogen haben und endoskopisch eine ösophageale AI aufweisen, werden in diese Studie aufgenommen. Die Patienten werden im Verhältnis 1:1 in zwei Behandlungsgruppen randomisiert. Die Interventionsgruppe erhält eine EVT, während die Kontrollgruppe mit SEMS behandelt wird. Der primäre Endpunkt dieser Studie ist die subjektive Lebensqualität, die von den Patienten anhand eines systematischen und validierten Fragebogens (EORTC QLQ C30, EORTC QLQ - OES18-Fragebogen) beurteilt wird. Wichtige sekundäre Endpunkte sind die Heilungsrate, die Dauer des Krankenhausaufenthalts, behandlungsbedingte Komplikationen und die Gesamtsterblichkeit.
Diskussion:
Die jüngste Metaanalyse, in der die Implantation von SEMS mit der EVT bei der Behandlung von AI verglichen wurde, ergab eine höhere Erfolgsrate für die EVT. Die ESOLEAK-Studie ist die erste Studie, in der beide Behandlungsmethoden prospektiv verglichen werden. Ziel der Studie ist es, geeignete Endpunkte für die Behandlung von Anastomosenlecks zu finden sowie eine adäquate Berechnung der Stichprobengröße zu ermöglichen und die Durchführbarkeit künftiger Interventionsstudien zu bewerten. Aufgrund des explorativen Designs dieser Pilotstudie ist der Stichprobenumfang zu gering, um die Frage zu beantworten, ob die EVT oder die SEMS-Implantation die bessere Behandlungsstrategie darstellt.

ID: 190
Topics: Viszeralchirurgie, Basic+Translational

CytoskeletonAssociated Protein 4 (CKAP4) is critical for esophageal adenocarcinoma cells

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While the incidence of EAC is rapidly increasing, its prognosis remains poor, with a five-year survival rate of 20%. Consequently, the discovery of new molecular targets for an efficient characterization of EAC patients is necessary. CKAP4 has been attributed to be increased in various cancer entities and together with Dickkopk-1 (DKK1), CKAP4 has a role in tumorigenesis. However, its role in EAC development and progression is widely unknown.
In a Barrett's esophagus, in vitro cell culture model of BE and EAC, CKAP4 expression levels were analysis. In OE33 and OE19 cells a knockdown of CKAP4-expression was done by siRNA for 48h and 72h. A RNA-seq was done in siCKAP4 OE33 cells.
CKAP4 was present in all cell lines of the Barrett's sequence (squamous epithelium, metaplasia, dysplasia, and EAC). CKAP4 surface expression was significantly increased in OE33, OE19 and Flo-1 cells. Tumor-associated proliferation, phosphorylation of Akt and MAPK were decreased in siCKAP4 cells, while DKK1 mRNA-expression was increased in siCKAP4 OE33 cells. This was confirmed by decreased colonies in CFA in siCKAP4 cells. FACS analysis showed a significant increase in the amount of apoptotic cells after siCKAP4 transfection. SiCKAP4 led to an increased expression of adhesion molecules, suggesting an impact of CKAP4 in cell adhesion. RNA-seq in siCKAP4 OE33 cells had shown altered immune related pathways, cell-cell signaling, increased apoptosis and decreased proliferation-associated mediators.
The role of CKAP4 is barely investigated in EAC at this time. Acting as a Dickkopf-1 (DKK1) receptor, the DKK1-CKAP4-axis might promote cell proliferation independently to the Wnt-pathway. Based on our current results, it can be assumed, that CKAP4 is important for EAC cell growth, proliferation and cell adhesion. Nevertheless, further characterization of CKAP4 is necessary, particularly focusing on the CKAP4-DKK1-axis to provide more evidence for its contribution in EAC development.

ID: 191

Topics: Viszeralchirurgie, Basic+Translational

Identification and classification of tumor cells in specimens of patients with Barrett's carcinoma by Hyperspectral imaging (HSI)

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Hyperspectral imaging (HSI), as recently applied in medicine, is a novel technology combining imaging with spectroscopy. It might be used to identify, classify and discriminate malignant and non-malignant cells of histopathologic specimens. HSI allows the determination of a spectrum between the visual and near-infrared light (500-1000nm).
After surgical resection, specimens (n=96) of Barrett's cancer were fixed in 4% formaldehyde and slices were conducted (3µm), which were stained with hematoxylin and eosin (HE). Differences in the absorbance of squamous epithelium and esophageal adenocarcinoma (EAC) cells were determined at eosin's and hematoxylin's maximal absorption of 530 nm and 590 nm. A classification algorithm, which combines a multilayer perceptron (MLP) with a Gaussian filter and data reduction based on principal component analysis (PCA) was used for discrimination.
For the first time in literature, we were able to analyze esophageal adenocarcinoma, tumor stroma and squamous epithelium cells by HSI. For both, the squamous epithelium and the esophageal adenocarcinoma cells, the intragroup variances were quite low. A set of 20 specimens was used in a testing phase, which showed MLP by using reflectance data to provide the best results. Leave-one-patient-out-cross validation for all 96 specimens showed an accuracy of 77% with a sensitivity of 87% and a specificity of 72% for EAC determination and visualization.
Squamous epithelium and EAC cells show specific spectral alterations due to their HE-staining, when measured by HSI. However, the training algorithms need further validation to foster a semi-automatic decision-making process in histopathological tumor cell identification.

ID: 192
Topics: Viszeralchirurgie, Basic+Translational

Characterization of PD-L1 in an esophageal adenocarcinoma cell culture model

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While the incidence of EAC is rapidly increasing, its prognosis remains poor, with a five-year survival rate of 20%. Consequently, the discovery of new molecular targets for an efficient characterization of EAC patients is necessary. PD-L1, which is over expressed in many cancer entities, might also play a role in the treatment esophageal adenocarcinomas.
Cells of the Barrett's esophagus in vitro model were analyzed for their PD-L1 expression. The cells were treated by chemotherapeutics (5-FU, cisplatin and oxaliplatin) and inhibitors, addressing immune check points (Nivolumab and Atezolizumab). Proliferation and PD-L1 expression levels were analyzed.
While cells of the squamous epithelium, metaplasia, dysplasia displayed a weak PD-L1 expression, the EAC cells showed a heterogeneous expression. The highest PD-L1 expression was found in OE33 cells, while OE19 cells did not showed no PD-L1 expression. 5-FU, cisplatin and oxaliplatin treated OE33 cells showed a decreased PD-L1 expression. The proliferation was decreased by 10 to 20% in OE33 and OE19 cells after Nivolumab and Atezolizumab treatment.
Recent studies had shown, that PD-L1 is an important target molecule also in the esophageal adenocarcinomas. We could show an impairment by conventional chemotherapeutics to PD-L1 in EACs. As PD-L1 is often heterogeneously expressed, future studies also should pay attention to altered PD-L1 levels under therapy.

ID: 193
Topics: Andere, Basic+Translational

Cholinergic control of trauma-mediated cytokine release by innate immune cells involves endothelial NO synthase activation and P2X7 receptor modification

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Objective: The clinical interest in interleukin-1β (IL-1β) is outstanding, as IL-1β contributes to the pathogenesis of inflammatory diseases including trauma-associated sterile inflammation, where ATP originating from damaged cells is an important trigger. We identified a cholinergic mechanism that inhibits the ATP-mediated release of IL-1β by innate immune cells via nicotinic acetylcholine receptors (nAChRs). Here, we investigate the metabotropic signalling pathway that links nAChR activation to the inhibition of the ATP-sensitive P2X7 receptor (P2X7R).
Methods: Human monocytic cells, THP-1 cell-derived macrophages, primary human monocytes, peripheral blood mononuclear cells (PBMCs) from wild-type and endothelial nitric oxide synthase (eNOS) gene-deficient mice were used. Cells were stimulated with ATP and IL-1β was measured in cell culture supernatants. A panel of nAChR agonists, eNOS inhibitors, NO donors (SNAP, SIN-1) and the siRNA technique were used. Patch-clamp experiments were performed on HEK cells overexpressing human P2X7Rs or P2X7Rs with point mutations at cysteines in the C-terminal intracellular loop.
Results: In monocytic cells and macrophages, the inhibitory effect of nAChR agonists on the ATP-mediated IL-1β release was blunted by eNOS inhibitors and siRNA silencing eNOS expression. In PBMCs from eNOS gene-deficient mice the inhibitory effect of nAChR agonists was absent. The inhibitory effect of nAChR agonists was mimicked by NO donors. In HEK cells, ATP-induced P2X7R ion-current changes were abolished by SIN-1. This inhibitory effect was reversed by mutation at C377, suggesting that a modification at this cysteine inhibits the ionotropic P2X7R function.
Conclusion: We provide first evidence that metabotropic signalling of nAChRs involves eNOS activation and P2X7R modification, which results in inhibition of ATP-mediated IL-1β release. This signalling pathway might pave the way towards innovative therapies for trauma-induced sterile inflammation.

ID: 194
Topics: Viszeralchirurgie, Basic+Translational

Targeting the canonical WNT signaling pathway – a potential novel therapy in Crohn´s associated fibrosis

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Background. Crohn's disease (CD) is characterized by chronic recurrent intestinal inflammation that leads to progressive fibrotic remodeling of the intestinal wall. Despite advances in medical therapy for CD, 50% of patients still require surgical treatment 10 years after initial diagnosis mainly due to stenosis formation. At present, a specific anti-fibrotic therapy does not exist, underlining the medical need for further research in this area. The exact mechanism of fibrosis development in CD is not yet understood, but WNT signaling has been shown to play a critical role in fibrosis in other organs. However, the role of WNT-signaling in CD and its potential druggability is not well characterized.
Methods. Bulk RNA sequencing was performed to uncover important mechanistic pathways in strictures of CD patients. To elucidate the functional role of matrix producing fibroblasts, primary cells were isolated from CD patients, undergoing ileocecal resection. To test the potential of therapeutic application of an anti-WISP1 antibody, a mouse model was established combining DSS colitis and ileocecal resection.
Results. Gene set enrichment (GAGE) revealed highly upregulated WNT- (p adj < 0.0029) as well as integrin signaling (p adj < 0.16) in CD fibrosis compared to matched normal tissue. Functional and gene analysis showed upregulated migratory potential of fibrotic fibroblasts, as well as matrix production capabilities. RNA sequencing of resected specimens and fibroblasts has drawn our attention to WISP1, which is 2-fold upregulated in fibrotic cells validated by WNT-qPCR-array.
Conclusion. Aberrant WNT-signaling leads to the development of fibrosis in CD patients. One candidate for a druggable protein could be WISP1, a downstream target gene of WNT-signaling. This hypothesis will be further investigated in both our in vitro and in vivo models to propose a therapeutic target aimed at decreasing the number of surgical procedures in CD patients.

ID: 195
Topics: Viszeralchirurgie, Basic+Translational

Der protoonkogene Effekt der Tyrosinkinasen Axl, Mer and Tyro 3 im kolorektalen Karzinom

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Hintergrund
Weltweit ist das kolorektale Karzinom das dritthäufigste Karzinom unter den soliden Tumoren. Trotz multimodaler Therapieansätze und deren stetiger Verbesserung weist es im metastasierten Zustand lediglich ein 5-Jahres Überleben von unter 30% in Europa auf. In Vorarbeiten konnten wir zeigen, dass von Makrophagen exprimierte Gas6 als Ligand für die Tyrosinkinasen Axl, Mer and Tyro3 zur Progression in Form von gesteigerter Proliferation, Invasion und Kolonieformation in kolorektalen Karzinomzellen führte. In humanen Kolonkarzinomen korrelierte eine hohe Expression auf mRNA Level der Rezeptoren von Mer und Tyro3 mit einem schlechteren Patientenüberleben.
Methodik
Um die protoonkogene Relevanz der Tyrosinkinasen Axl, Mer und Tyro3 zu charakterisieren, wurde unter Verwendung des CRISPR/CAS-9 Systems ein stabiler Knockout in CT26 Karzinomzellen in vitro etabliert. Mittels siRNA wurden transiente Knockdowns aller drei Tyrosinkinasen in CT26 sowie humanen HCT116 Zellen in vitro durchgeführt. In vivo wurde das Tumorwachstum in einem subkutanen Modell unter Knockout der Tyrosinkinasen evaluiert.
Ergebnisse
Inhibition durch Knockout bzw. Knockdown der drei Tyrosinkinasen in CT26 Zellen führte zu einer verringerten Proliferation, Migration und Invasion. Selbiger Effekt zeigte sich in den humanen HCT 116 Zellen, welches eine mögliche Relevanz in humanen kolorektalen Karzinomen suggeriert. In Proteinanalysen zeigte sich eine stimulierte Apoptose unter Inhibition der Tyrosinkinasen, welches auf aktive anti-tumorale Effekte hinweist. Im Mausmodell zeigte sich unter Knockout von Axl, Mer und Tyro3 ein signifikant reduziertes Tumorvolumen sowie damit einhergehend ein verringertes Tumorgewicht.

Konklusion
Der Knockout der Tyrosinkinasen Axl, Mer, Tyro3 in CT26 Zellen führt zu einer Reduktion protoonkogener Charakteristika wie Proliferation in vitro und in vivo. Zur Evaluation eines möglichen therapeutischen Nutzens ist eine Validierung in humanen Kohorten notwendig.

ID: 196
Topics: Viszeralchirurgie, Andere

Acquisition and Preprocessing of Robotic Assisted Minimal Invasive Esophagectomy Video Data at a High-volume Center

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At the University Hospital Cologne, a high-volume certified center of excellence for surgery of the upper gastrointestinal tract, over 300 upper GI cancer surgeries are performed annually. With over 70 Robotic Assisted Minimal Invasive Esophagectomy (RAMIE) cases each year, the obtained operative data present a great opportunity for clinical evaluation, surgical training and research. Specifically, the application of Artificial Intelligence (AI) to analyze the video data can lead to detection and prediction of clinically relevant target features. This project proposes a framework for the establishment of an infrastructure for data collection and utilization of RAMIE video data from a high-volume center.
We composed a team-based framework for recording and data collection of RAMIE cases. The framework entails a structured data acquisition pipeline, incorporating various contributors. We use the Stryker SDC3 to record the laparoscopic conduit preparation from the Stryker platform. The thoracic part is recorded by the Medicap USB300 from the Da Vinci Xi platform. Furthermore, we report on a concise preprocessing pipeline, including the video format conversion, data cropping and merging and de-identification to comply with privacy regulations. After preprocessing, the RAMIE video data is annotated with respect to the desired clinically-relevant target features to build the dataset for AI model training and validation.
The recording infrastructure has been implemented in the high-volume center from 01/2022. The RAMIE video acquisition, data preprocessing and annotation led to the generation of a successful data pipeline resulting in a concise RAMIE dataset. We report about various pitfalls throughout the implementation and how to overcome them. To date around 50 RAMIE cases video data were collected and preprocessed and are currently undergoing annotation.
This infrastructure and RAMIE dataset will support AI-based research for intraoperative risk mitigation in the future.

ID: 197

Topics: Viszeralchirurgie, Basic+Translational

Untersuchung und Abgrenzung des Energiestoffwechsel in proliferierenden Hepatozyten und Hepatozellulären Karzinomzellen

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Weltweit ist eine steigende Prävalenz des hepatozellulären Karzinoms (HCC) zu beobachten. Im HCC sind eine Reihe an metabolischen Veränderungen bekannt. Eine Anpassung der Energieversorgung findet auch in proliferierenden Hepatozyten während der Regeneration statt. Das Ziel der Arbeit ist der Vergleich der metabolischen Krebs- mit der Proliferationssignatur an in-vitro Zellmodellen.

Für proliferierende Hepatozyten wurden gentechnisch veränderte primäre humane Hepatozyten (PHH) (s.g. Upcyte®-Hepatozyten, HepaFH3-Klon) genutzt, wobei PHHs als Kontrolle dienten. Als HCC-Modell wurden die Hepatomazelllinien, HepG2 und Huh-7, sowie aus HCC-Gewebe isolierte primäre humane Hepatomazellen (PHC), verwendet. Mittels RT-qPCR und biochemischer Assays wurden die Zellen hinsichtlich hepatischer Differenzierungs-, Tumor- und metabolischer Marker charakterisiert.

Alle proliferierenden Zellmodelle (HepaFH3, HepG2, Huh-7, PHC) zeigten eine Abnahme der hepatischen Differenzierungsmarker (Albumin, CYP3A4). Die proliferierenden Hepatozyten (HepaFH3) exprimierten die Tumormarker (SPP1, SPINK1, KPNA2). Die verstärkte Expression von LDHA und HIF1A in HepaFH3, HepG2, Huh-7 weist auf eine starke anaerobe Stoffwechselaktivität hin, die mit der Proliferationsrate korrelierte. Parallel wurde in diesen Zellen verstärkt c-MYC, GLUT1, PKM und HK2 nachgewiesen, während in PHC und PHH hepatische Standardenzyme (GLUT2, PKL, HK1) exprimiert wurden. Die funktionellen Daten (Glucose, Laktat, Glykogen) stimmen mit den Transkriptdaten überein.

Die Mehrzahl der HCC-Marker sind bei proliferierenden Zellen nachweisbar. Die Anpassung des Energiestoffwechsels scheint durch die Proliferationsrate determiniert zu sein und führt zu einem Austausch der Stoffwechselenzyme. Die metabolischen Daten der PHC sowie deren klinischen Daten weisen auf ein langsames Tumorwachstum hin, sodass eine Differenzierung zwischen Proliferations- und Tumormarkern vorgenommen werden muss.

ID: 198
Topics: Andere, Basic+Translational

Herunterregulation der ADP-Ribosylierung und Deacylierung als Bindeglied zwischen genotoxischer Schädigung und akzelerierter Gewebsalterung

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1) Hintergrund/Fragestellung
Genotoxische Gewebsschädigung durch Behandlungen wie Chemotherapie und Bestrahlung führen zu einem seneszenten Gewebsphänotyp ähnlich einer vorzeitigen alterungs-ähnlichen Gewebe-degeneration. Dies führt zu der Hypothese, dass Proteine, die Alterungsvorgänge regulieren auch in diesen Prozessen eine Rolle spielen könnten.
Sirtuine sind NAD-Abhängige Deacylasen und ADP-Ribosylasen und zeigen eine lebensverlängernde Wirkung in verschiedenen Tiermodellen. Die Aktivität von PARPs (Poly-ADP-Ribose-Polymerasen) ist u.a. wichtig für DNA-Reparatur ist ebenfalls mit Langlebigkeit assoziiert. Ziel der Untersuchungen war es, die Expression von Sirtuinen und PARPs in strahlengeschädigtem Gewebe zu charakterisieren.
2) Methodik
Genotoxische Schädigung von Rattenlungen erfolgte durch externe oder interne Bestrahlung mit Dosen bis 20 Gy (extern) und ca. 55 Gy (intern mit radioaktiv markierten Microbeads). Quantifizierung der Proteinmengen und deren Phosphoylierung erfolgte mittels Western Blotting.
3) Ergebnisse
Die Expression von SIRT1 wird im strahlengeschädigten Gewebe 2 Monate nach externer Bestrahlung (ER, external radiation) leicht heraufreguliert. Demgegenüber kommt es zu einem zumindest zeitweisen Verlust von SIRT2, 3, 5, 6 und 7. Gleichartige Veränderungen finden sich auch nach Applikation hoher Dosen von interner Bestrahlung (IR, internal radiation). PARP-1 geht nach beiden Bestrahlungsmodalitäten komplett verloren während PARP-2 nach ER etwa auf die Hälfte herunterreguliert wird.
4) Konklusion
Die Reduktion sowie in einigen Fällen der Verlust von Sirtuinen und von PARP1 und -2 stellt einen schweren Eingriff in die zelluläre Homöostase dar, da Prozesse wie DNA-Reparatur stark behindert und Seneszenz gefördert sein muss. Diese Erkenntnisse bieten Ansatzpunkte zur Therapie genotoxischer Schäden und sollten beachtet werden bei zusätzlichen Eingriffen in deren Aktivität, wie z.B. bei Behandlung mit PARP-Inhibitoren.

ID: 199
Topics: Orthopädie/Unfallchirurgie, Basic+Translational

Serum levels of GFAP and NfL are related to the neurological impairment and spinal edema after traumatic spinal cord injury

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Background
Neurological examination in the acute phase after spinal cord injury (SCI) is often impossible and severely confounded by pharmacological sedation, or concomitant injuries. Therefore, diagnostic biomarkers that objectively characterize severity, or the presence of SCI are urgently needed to facilitate clinical decision-making.
This study aimed to determine if serum markers of neural origin are related to i) presence and severity of SCI, and ii) magnetic resonance imaging (MRI) parameters in the very acute post-injury phase.
Methods
We performed a secondary analysis of serological parameters, as well as MRI findings in patients with acute SCI (n=38). Blood samples were collected between days 1-4 post-injury. Serum protein levels of Glial Fibrillary Acidic Protein (GFAP), Neuron-Specific Enolase (NSE), and Neurofilament light protein (NfL) were determined. A group of 41 age- and sex-matched healthy individuals served as control group. In the group of individuals with SCI, pre-operative sagittal and axial T2-weighted and sagittal T1-weighted MRI scans were available for 21 patients.
Results
Serum markers of neural origin are different among individuals who sustained traumatic SCI depending on injury severity, and the extent of the lesion according to MRI in the acute injury phase. URP-CTREE produced preliminary cut-off values for NfL (75.217 pg/ml) and GFAP (73.121 pg/ml) allowing a differentiation between individuals with SCI and healthy controls within the first four days after SCI.
Conclusion
Serum proteins NfL and GFAP qualify as diagnostic biomarkers for the presence and severity of SCI in the acute post-injury phase, where the reliability of clinical exams is limited.

ID: 200
Topics: Orthopädie/Unfallchirurgie, Klinische Studien

An effective prehospital management after traumatic cervical spinal cord injury can positively influence the neurological as well as the functional outcome

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Introduction
Traumatic spinal cord injury (SCI) leads to a variety of deficits in affected individuals. There is accumulating evidence of a potential beneficial effect of early surgical intervention on the neurological and functional outcome after traumatic SCI. The emergency medical service (EMS) system in Central Europe is well developed allowing short transportation times between the injury site and the hospital. Also, early decompression surgery is the in-house standard at our level I trauma center with a specialized SCI unit.
This study aimed to investigate the relationship between prehospital management and neurological recovery after SCI.
Methods
We performed a retrospective analysis of data from patients who were treated at the Spinal Cord InjuryCenterin the level I trauma center. Follow-up data has been collected prospectively as part of the European Multicenter Study about Spinal Cord Injury (EMSCI) registry. We included data acquired over a 17-year period (2004 – 2021). Data from patients above the age of 18 years, who sustained traumatic SCI without severe concomitant injuries or traumatic brain injury have been included in our analysis.

Results
We identified data from a total of 241 patients (196 males), who met in- and exclusion criteria. The main predictor for the neurological outcome was the level of the lesion with significantly worse neurological recovery in individuals who sustained thoracic injuries. Patients with cervical trauma had significantly higher chances to regain function when they have been initially admitted to a specialized center compared to those who were admitted to a regional trauma center and relocated afterwards. The outcome was not associated with the distance between the site of injury and the hospital well established emergency medical service system.
Conclusion
In case of suspected cervical SCI, a direct transport to a specialized spinal cord injury center should be pursued.

ID: 248
Topics: Thoraxchirurgie, Basic+Translational

Zero Echo Time Lungen-MRT in der präoperativen Planung pädiatrischer Patienten mit Tracheobronchialer Stenose

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Hintergrund/Fragestellung
Der Goldstandard zur Diagnostik einer Einengung des Bronchialsystem bei pädiatrischen Patient*innen ist die Laryngotracheoskopie in Kombination mit einer Thorax-CT. Die Visualisierung der Lunge und des Tracheobronchialsystems mit konventionellen MRT-Sequenzen war bisher nur eingeschränkt möglich. Mit Zero Echo Time (ZTE)-Sequenzen können auch die lufthaltigen Strukturen des Thorax dargestellt werden. Ziel dieser Studie ist es, die diagnostische Genauigkeit und Reproduzierbarkeit von ZTE-Sequenzen in der präoperativen Planung pädiatrischer Patient*innen mit tracheobronchialer Stenose zu evaluieren.

Methodik
Alle zwischen dem 1.1.2019 und 10.10.2022 an einem 1.5 T GE Signa Artist Scanner am Universitäts-Kinderspital Zürich durchgeführten Lungen-MRT-Untersuchungen wurden retrospektiv evaluiert. In die Studie wurden nur Patient*innen mit per Laryngotracheoskopie gesicherter Stenose der Atemwege eingeschlossen, bei denen eine ZTE-Sequenz akquiriert wurde. Anhand multiplanarer Rekonstruktionen wurden die Diameter der Luftwege im Bereich der Stenosen, an der proximalen Trachea sowie am rechten und linken Hauptbronchus von zwei unabhängigen Radiologen gemessen und hieraus die Interraterreliabilität berechnet. Zusätzlich wurden bei 5 Patient*innen die in der Thorax-CT bestimmten Diameter mittels gepaartem T-test mit den Werten aus den ZTE-Sequenzen verglichen.

Ergebnisse
Von 191 Patient*innen, die im oben genannten Zeitraum eine Lungen-MRT-Untersuchung mit ZTE-Sequenzen erhielten, wurde bei 12 Patienten im Alter von 1-160 Monaten (Median 11.5, IQR = 43) eine Tracheobronchialstenose diagnostiziert. Hiervon hatten 7 eine pulsatile Kompression des Tracheobroncialsystems durch vaskuläre Strukturen, 2 eine Bronchialatresie, 1 ein Scimitar Syndrom, 1 eine Tracheomalazie nach Verschluss einer ösophagotrachealen Fistel und 1 eine endobronchiale Raumforderung. Die Messwerte der ZTE-Sequenzen wiesen keinen signifikanten Unterschied zu den CT-Daten auf ($p>0.05$). Es zeigte sich eine hohe Interraterreliabilität.

Konklusion
ZTE-Sequenzen weisen in der präoperativen Planung tracheobronchialer Stenosen eine mit der Thorax-CT vergleichbare hohe diagnostische Genauigkeit und Reproduzierbarkeit auf und eignen sich daher als Bildgebungsmodalität ohne Strahlenbelastung für eine präoperative Feindiagnostik insbesondere bei Kindern.