Informed consent for whole exome sequencing (WES) and explanations about the methodology

UNIVERSITÄTS KLINIKUM FREIBURG
ZKJ ZENTRUM FÜR KINDER- UND JUGENDMEDIZIN

Institution / Referring clinician	Patient (Name, date of birth, clinical information)

The purpose of whole exome sequencing (WES) is to identify genetic causes associated with the disease.
The consent is voluntary and can be withdrawn at any time during the process.

What is WES?
Traditional genetic testing involves the sequencing of genes that are disease causing. Standard methodology used for "single gene" sequencing is mostly labor-intensive. For any kind of genetic testing, DNA from patient is required. DNA can be isolated from blood or other tissues such as skin or hair follicles. The latter ones are used for the distinction of somatic (in certain cells only, for example leukemia cells in blood) or germline (in all cells, i.e. found also in skin tissue) DNA changes.
Using WES all coding DNA regions (approximately 1.5%) of the genome, the so called "whole exome" can be analyzed at once. It is estimated that the majority of disease-causing DNA changes are contained within the whole exome.
The changes in patient´s DNA will be compared to databases with known DNA changes that are not disease to exclude these variants in further analysis. The remaining DNA changes will be compared to DNA sequence of other family members (if applicable) which can help to understand the disease-causing value of certain genetic changes.
The clinical information from the referring physician will be helpful to decide which of the many genetic changes identified are likely to be responsible for patient´s disease. These genetic changes will be reported to the referring physician. DNA changes not related to the disease will be reported only at patient´s request (see below "secondary findings")

What are the limitations and risks of WES?
Using current methodology only the maximum 90-93% of the whole exome can be sequenced, thus some mutations that are disease-causing might be missed. Large genomic deletions cannot be identified using this method.
The patient might not receive certain results (if no disease-causing mutation was found) and the true diagnosis may not be discovered by this method.

Secondary findings
WES may identify DNA changes that are not related to the investigated disease, however might have implications to the patients. According to the American College of Medical Genetics and Genomics (ACMG), approximately 1% of sequencing reports will include mutations in genes involved in various medical conditions that can be monitored or effectively treated. The mutations in 57 genes causing such conditions (including some cancer syndromes, certain types of heart disease or high cholesterol, but also genetic diseases that do not have any effective treatment) were suggested to be reported to the referring physician: ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med. 2013 Jul;15(7):565-74.
We will not seek and report these DNA changes, unless the patient requests us to do this. Please sign one of the following two options regarding the secondary findings (adult patient, or patients 'guardian)

☐ I choose to receive results about secondary findings .....
☐ I choose NOT to receive any results about secondary findings .....

Confidentiality and data handling
All laboratory analyses will be performed after anonymization, so that any patient-specific information cannot be retrieved from the generated data. The results will be reported only to the referring physician and will not be given to any individuals (including health insurance companies) without additional written permission of the patient. The data and results are stored on password-secured clinic computers (accessible only by trained specified personnel) and not on internet clouds or other internet-based solutions including email.

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Date	Patient, parent or patient´s guardian	Referring Clinician