

## Current Projects

### 1) Molecular epidemiological host-pathogen interaction study of nontuberculous mycobacteria (NTM) infections

Severe infections with nontuberculous mycobacteria (NTM) are marker diseases for several defined immunodeficiency disorders. However, whether NTM infections in otherwise healthy people reflect more subtle immunological abnormalities has not been systematically addressed. In cooperation with Philipp Henneke and Dirk Wagner, we will initiate an epidemiological host-pathogen-interaction study in order to identify genetic, epigenetic, and environmental factors in the etiology and outcome of NTM infections. One obstacle to the interpretation of data generated in this context is the relative rarity of NTM infections. In cooperation with scientists at the Institute of Medical Biometry and Medical Informatics (IMBI) headed by Martin Schumacher, statistical tools will be developed for complex data analysis in the rare disease context. Molecular epidemiological research, which aims to identify risk factors and prognostic factors for NTM infections at the population level, has the potential to stimulate novel pathogenic and therapeutic approaches to immunodeficiency.

### 2) Molecular epidemiology of inter-individual differences in immune response and risk of recurrent infections

Well defined, in particular monogenetic immunodeficiency disorders have a very low incidence. However, they represent only the tip of the iceberg of clinical deviations from "immune competence". Within a prospective study design, we will explore inter-individual differences in immune response which underlie poorly understood "milder" phenotypes, such as recurrent or unusually severe infections with common bacteria or vaccine failure and their determinants. A further aim is the identification of modifiable factors that can be addressed to decrease risk of infection-related morbidity due to imbalanced immune responses, particularly in the elderly. In the planned cohort we will also document how ageing and environmental/dietary factors and other stressors modulates cellular and humoral immunity over time and what consequences this might have on the clinical immunocompetence against microorganisms. This project will be in collaboration with several CCI (affiliated) groups and Martin Schumacher (IMBI, Freiburg).

### 3) Interplay of genetic, epigenetic and environmental factors in the etiology of lymphomas

Lymphomas belong to a heterogeneous group of malignancies that are strongly associated with primary immunodeficiency. To identify risk factors for lymphomagenesis, a large international consortium with the acronym InterLymph has been founded. In collaboration with Nikolaus Becker (DKFZ, Heidelberg), Paolo Boffetta (IARC, Lyon), Silvia de Sanjosé (Catalan Institute of Oncology, Barcelona), Christine Skibola (UC Berkeley), Nathaniel Rothman (NCI, USA) and other scientists of the InterLymph consortium, we will continue to explore the association of genetic variants and environmental factors in the etiology of lymphomas. In a prospective study, the European Prospective Investigation into Cancer and Nutrition (EPIC) study, we cooperate with Christoph Plass and Rudolf Kaaks (DKFZ, Heidelberg) and Paolo Vineis (Imperial College, London) to identify epigenetic and lifestyle risk factors for lymphomas. These projects will provide pilot data for new model building exercises in the rare disease – multi-variable context in cooperation with Martin Schumacher and his team (IMBI, Freiburg).