Main Project: Next Generation Sequencing analysis of bacterial and viral infectious agents in regular human CSF samples of patients with meningitis or meningo-encephalitis; a retrospective and prospective metagenomic study.

Meningitis and meningo-encephalitis may be caused by infection with viruses and bacteria, less commonly by parasites or certain drugs. In Western Europe viral infections with an incidence of 11/100’000 p are more common compared to bacterial infections causing 3-5 infections per 100’000 p. Neurofunctional sequelae after a bacterial meningitis appear in twenty per cent of the patients and the worldwide mortality ranges from 10 to 50 per cent\(^1\). Lethal viral infections are mainly (95 %) caused by Herpes simplex type 1 viruses and mortality ranges from twenty to eighty per cent for untreated cases.

Often the aetiology of meningitis or meningo-encephalitis may not be identified. Patients being generally in a severe state of health and conscious, the sampling of the cerebrospinal fluid (CSF) for diagnostic purposes cannot be done immediately. Moreover, as the administration of broad spectrum antibiotics is mostly performed prior to the CSF-sampling, bacteria flora is killed and the gold standard for the diagnosis of bacterial infection, the liquor cultivation, becomes impossible. However, for non-bacterial infection the causative agent has to be assumed, detected by polymerase chain reaction (PCR) and indirectly verified by serology. Consequently, a specific treatment for non-bacterial infections is seldom. These classical diagnostics often fail due to low pathogen load and strong methodological selectivity. The emergence of Next Generation Sequencing (NGS) technologies in recent years, allowing fast sequencing of total nucleic acids of a sample (metagenomics), could become a method of choice for the detection of previously undetected or even unknown aetiologies in CSF samples of patients with meningitis and meningo-encephalitis.

The project includes the evaluation and development of different sample preparation methods for subsequent NGS-analysis of CSF-samples. Furthermore, the workflow of a bench top NGS system will be optimized for the analysis of bacterial and viral DNA. Finally, available bioinformatics tools for metagenomic analysis will be adapted for the subsequent analysis of obtained NGS date.