Summary
In Switzerland and the Western world cancer disorders remain a major cause of death. Early detection of cancer is an important prerequisite for reduction of mortality and may also improve quality of life by permitting effective therapy with fewer side-effects. Accordingly, some cantons introduced systematic screening programs, e. g. by offering mammography screening for all women 50 years of age or older aiming for early detection of breast cancer. Population benefit of these broad programs, however, is currently under debate giving its limited specificity, which may cause harm by false positive results and over-diagnosis. On the other hand, such general screening programs are not sensitive enough for high-risk individuals with genetic predisposition for cancers, who need intensified and early-onset preventive care. Moreover, recent data indicate, that individuals with genetic predisposition for cancer may also benefit from novel preventive drug therapies specifically targeting the pathway that is disturbed by their individual inheritable mutation. However, current clinical standards limit genetic testing for cancer predisposition to a small number of genes in a small number of patients with a very strong clinical suspicion of inherited cancer syndromes. Despite the evidence from recent broader genetic studies showing that genetic cancer predisposition is much more common than previously thought, translation of large scale genetic testing into the broader population is hampered by the large amount of genetic variants of unknown significance detected by such approaches and by the limited knowledge of natural history and insufficient preventive strategies in many conditions.
While many researchers in Switzerland address basic mechanisms of tumor pathogenesis or genetic alterations in tumor samples or are involved in clinical trials for cancer therapy in general, research on tailored prevention and gene specific pathogenesis through genetic germline testing of individuals, not tumor samples, is scarce. The aim of this project is therefore to comprehensively study genetic cancer predisposition by individual genome sequencing in patients. Next to identification of novel disease causing genes and mutations, the project will functionally characterize such novel mutations as prerequisite for future translation of this approach into medical practice. In order to improve prevention in individuals
with high cancer risk the project also aims for identification and verification of clinically actionable biomarkers and imaging with enhanced sensitivity and specificity. In order to address ethical issues, the project will evaluate patients' perception of risk and their attitudes towards incidental findings, as well as their attitudes towards implications of such findings for their relatives.