Project openings in the Molecular Cancer Genetics group at IGP, Rudbeck Laboratory

We are looking for students with an interest in functional studies or genetics of cancer, or in development of computer tools for large sequence data analysis.

Our research: Mutations that cause normal cells to lose control over cell division and maintenance are important contributors to cancer development. Our main research topics are: (1) identification of cancer-causing mutations, (2) investigation of how specific mutations contribute to tumor development or metastasis, (3) strategies to utilize the specific genetic properties of cancer cells for targeted treatment, and (4) development of methods and procedures to aid or improve diagnosis.

We currently have openings for students in these projects:

1. Hundreds of genes have been proposed as cancer drivers following the introduction of next generation sequencing technologies in cancer genomics. Functional validation of candidate genes is essential to understand and utilize this information clinically. In a series of projects we have used rAAV gene targeting constructs to knock out or in function of candidate cancer genes in human cells to investigate their contribution to cancer associated phenotypes. We are currently have a project for extensive characterization of the oncogene *KRAS* where a student is welcome to join. Techniques that may be used during the project include widely used methods such as cell culturing, PCR, RT-qPCR and western blot.
2. Targeted cancer therapy is based on finding conditions resulting in selective killing of cancer cells while sparing the normal tissues of the patient. We propose a concept based on exploitation of the natural genetic variation in the human population and the cancer specific phenomenon loss of heterozygosity (LOH) to identify tumors that are sensitized to certain drugs relative to the normal tissues. We have identified and ranked human enzymes according to the prevalence of (1) functional variants as result of genetic variation (SNPs, STOPs or indels) and (2) LOH in common human cancers. For the candidate NAT2 we constructed and validated CRC cell model systems which in drug discovery efforts uncovered a compound with 3-fold increased cytotoxicity in cells lacking NAT2 *in vitro* and *in vivo*. Worldwide >50 000 colorectal cancer patients with NAT2 LOH could benefit from such treatment each year. In a similar effort we are now developing cell models for a promising candidate target enzyme that will be studied during the course of this project. Techniques used in the project may include cell culturing, transfection, functional cell analysis assays, western blot and PCR.
3. We have developed software tools for rapid and accurate mutational analysis of deep sequencing data from solid tumors with significant content of normal cells. These tools have superior indel calling capabilities, a major challenge in mutational analysis, as compared to state of the art. For this application, novel statistical mathematics has been developed and patented (Swaminathan et al, *Pattern Recognition* 2016). The current challenge is to perform a quality control over the raw data and implement the necessary data pre-processing steps to assure high accuracy of the analysis. We are looking for a highly motivated student with basic bioinformatics skills, but knowledge of Python is a benefit. The technical side of the project includes the manipulation of data from several next-generation sequencing platforms and programming tasks aiming at data quality control.

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