Project openings in Tobias Sjöblom's research group group at IGP, Rudbeck Laboratory

Our research spans several topics and provides opportunities for students to explore many different types of molecular laboratory and data analysis approaches. Our main focus is in improving treatment and diagnostics for cancer, but some of our studies are also centered on other diseases or conditions.

We are looking for motivated students that want to develop their skills in bioinformatics analyses, laboratory work centered on cell signaling or drug screening in cell and organoid models, or data science and machine learning. Current project proposals are listed below.

1. **Genomic analysis of a large cohort of colorectal cancer cases**
   This project aims to increase the knowledge of colorectal cancer development through detailed characterization of the somatic genomic and transcriptomic landscapes of a large number of primary colorectal tumors from Swedish patients. This study is the largest single combined whole genome and transcriptome sequencing effort in colorectal cancer to date through collaboration between the U-CAN colorectal cancer investigators at Uppsala University, Umeå University, and KTH.

   We are looking for students specializing in bioinformatics to participate in the data analyses. Basic knowledge of Linux and programming and scripting in Python or R is required. Previous experience with genomic data analysis or next-generation sequencing knowledge is an advantage.

2. **Development of novel precision cancer therapy based on collateral lethality**
   Tumors with loss of heterozygosity (LOH) may be sensitized to certain anticancer drugs due to loss of enzyme catalytic activities that exist in normal cells. Through bioinformatic analysis of genomic variants, we have identified an enzyme important for metabolizing and eliminating a large proportion of clinically used drugs as a candidate target for novel cancer drug discovery and development. In the project we will 1) perform drug library screening to select drug candidates that show greater potency on cells with low enzymatic activity, 2) carry out extended studies of potential hits, and 3) develop effective therapeutic strategies by combining conventional medicines with identified novel hit compounds.

   We are looking for students who want to work with wet-lab techniques, such as immunoblotting, cell and organoid culture, and drug screening. There are also opportunities to work with identification of new potential targets for this novel therapy concept in adult and pediatric cancers through bioinformatic approaches.

3. **Characterization of a novel EPHB2 mutant with respect to its proteolytic cleavage**
   The Eph receptors constitute the largest subgroup of tyrosine kinase receptors. They are part of a bi-directional signaling pathway where their ephrin ligands, which either are transmembrane proteins or attached to the cell membrane with a GPI anchor, are also capable of signaling. These receptors and ligands are best known for their roles in axon guidance and cell migration. EphB receptors are paradoxical receptors in that they promote proliferation in normal intestinal epithelium but also act as tumor suppressors in colon cancer development. In a recent study, we found a mutation (p.R155C) at the cleavage site in the ligand-binding domain of the EPHB2 in metastatic human colon cancer samples. The affected arginine residue is conserved in 11 of 14 human ephrin receptors. Furthermore, there were 12 reported mutations in the residue when looking

into all cancers of the TCGA dataset. Hence, we are now studying how this particular EPHB2 mutation affects human CRC progression, particularly at the metastatic phase.

We are looking for students who want to study cell signaling in cancer through study of EPHB2 wild type and mutant overexpressing cell lines. Techniques used in the project include qPCR, western blot, cell culture and growth curve analysis, confocal microscopy, and specific receptor cleavage assays.

4. **Machine learning for automated analysis of radiology examinations**
Machine learning and computer vision is being used more and more extensively for solving various radiology tasks. Several large data sets of X-ray and CT images from e.g. lungs and knees have been annotated by our collaborating radiologists. In this project we are developing machine learning models and pipelines for automatic grading of common conditions, such as knee osteoarthritis and pulmonary embolism.

   We are looking for students to participate in model development and building of different automated pipelines for clinical radiology tasks. Knowledge of the basics of machine learning and some basic programming skills are required. Experience of using Python for data science and/or machine learning is an advantage.

Further information and application: Professor Tobias Sjöblom (tobias.sjoblom@igp.uu.se), https://www.igp.uu.se/forskning/cancerprecisionsmedicin/tobias-sjoblom/.