Experimental validation of RNA sequencing data in small intestinal neuroendocrine tumors

Master project (30 hp) – available for 2 students
Department of Surgical Sciences, Endocrine Surgery
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Background:
Small intestinal neuroendocrine tumors (SI-NETs) are the most common malignancy of the small intestine and arise from enterochromaffin cells scattered in the intestinal mucosa. These tumors are slow growing (Ki-67 proliferation index < 2%), however the majority of patients are diagnosed at metastatic stage with 5-year overall survival rate of around 60%. To date, the genetic and epigenetic drivers of SI-NETs remain elusive. The most common genetic aberration in SI-NETs is loss of one copy of chromosome 18 in > 60% of tumors, and pathogenic mutations were found in CDKN1B gene, which encodes the cyclin-dependent kinase inhibitor p27 (8.5%). Loss of chromosomes 9, 11 and 16, as well as gain of chromosomes 4, 5 and 20, are other common chromosomal aberrations in these tumors. Despite major efforts to improve prognostic variables, there is still a lack of reliable biomarkers for clinical use. In order to identify new molecular prognostic factors, we have studied gene expression variation in SI-NETs and identified differentially expressed genes related to specific copy number alterations.

Aim
The aim of this project is to validate and functionally characterize the candidate genes found by expression analysis to develop potential biomarkers of poor prognosis, and to identify driver genes in SI-NET tumorigenesis. The specific aims are:

1. Investigating the expression level of the target genes in SI-NET cell lines
2. Investigating a possible role of the target genes in tumorigenesis

Methods
The student will determine the expression level of the candidate genes in the SI-NET cell lines, CNDT2.5 and GOT1 using q-PCR and western blotting analysis. According to this result, the student will transfect the cell lines with silencing or expression plasmids, and will perform proliferation, apoptosis and migration assays to elucidate the role of the target genes in SI-NET tumorigenesis.

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