Project Title: Epigenetics of Acute Lymphoblastic Leukemia

Background: Cancer is the second most common cause of death in children in the developed countries. Acute lymphoblastic leukemia (ALL) is the most common malignancy, with 200-250 newly diagnosed cases in the Nordic countries each year. Despite impressive improvements, 20% of ALL patients still die from relapse or treatment-related complications. Thus there is a need for identification of specific subgroups of ALL patients that would benefit from alternative treatment approaches.
DNA methylation occurs naturally on cytosine bases at CpG sequences in the human genome. Methylation of CpG sites is an epigenetic mark with an important role during cell differentiation and aberrant DNA methylation is well established as a hallmark of human disease. It has recently been suggested that loss of DNA methylation could lead to chromosomal instability, and consequently to the large scale translocations and rearrangements, which are characteristic of cancer cells, including ALL cells.

Aim: Our aim is to identify epigenetic signatures that predict the response to drug treatment and clinical outcome in patients with acute childhood leukemia. In the project we are using modern genomic technologies to analyze well characterized primary cell samples from children with acute leukemia. The specific aim for the 20-30 week degree project will be to establish a protocol for selecting methylated regions of the genome using methyl binding proteins in ALL cells and sequence the enriched regions on the Illumina Genome Analyzer.

Methods:

- PCR
- Quantitative PCR
- Enrichment of methylated DNA using methyl binding proteins
- "Massively parallel" sequencing with the Illumina Genome Analyzer (GA)

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Duration: 20-30 weeks, starting as soon as possible (Spring 2010)

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