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Master Thesis

Allele-specific Transcription in Human Cancer

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In recent years, our view of gene expression has changed profoundly, revealing pervasive transcription of the genome and we now appreciate the complexity of its regulation. Although we now know that regulation can take place at any level of the gene expression process, only certain layers of control such as transcriptional regulation and chromatin modifications have been extensively studied. However, researchers have not paid much attention to others such as antisense and allele-specific expression despite their widespread occurrence. This was largely due to underestimation of their importance and technical limitations. Antisense transcripts are at least partially complementary to a corresponding (mainly protein-coding) sense transcript and can have diverse functional roles in gene regulation (e.g., modifying epigenetic marks). This genomic arrangement also clearly suggests that antisense transcripts are mainly involved in allele-specific gene regulation/silencing.

We aim to construct a comprehensive picture of these processes in a large panel of cancer samples and healthy controls by making use of the current wealth of transcriptomics and (epi)genomics data provided in the constantly growing public repositories. In order to investigate the two processes, we plan to analyse these datasets in a high-throughput and highly optimised manner to obtain transcriptional resolution on all four DNA strands (both alleles) - this is not routinely performed in expression studies and will resolve confounding results for numerous transcripts, which otherwise would remain undetected.

Hence, the **overall goal** of this thesis is to establish an RNA-seq analysis pipeline to enable the **analysis of allele-specific processes** in available RNA-seq datasets.

Specifically, the following **aims** should be pursued:

1. Literature research on public repositories and RNA-seq analysis.
2. Data collection and curation: download of publicly available suitable RNA-seq datasets for experiments comparing cancer and healthy tissue samples.
3. Development of a pipeline in R to process and analyse RNA-seq datasets, resulting in **allele-specific differential expression.**
4. Validation/testing, computation of summary statistics & visualisation of the analysis results.

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References

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