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Student: Krappinger Julian

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Non-coding Natural Antisense Transcripts: Large-Scale Analysis of Expression Patterns in Human Cancers

Julian Krappinger; Julia Feichtinger

Although a large part of the transcriptome does not encode proteins, research on long non-coding cis natural antisense transcripts (ncNATs) lags far behind the investigation of their protein-coding counterparts. These transcripts are overlapping with their partner transcripts but are transcribed in opposite orientation to their partners. They are involved in gene regulation through multiple functional processes, and it has been suggested that many could affect the expression of their sense partners. In an effort to present a detailed overview of ncNATs and their expression patterns, we investigated a large collection of human RNA-seq samples in cancerous and normal conditions by making use of public repositories as an immense resource.

Strand-specific RNA-seq samples of cancerous and healthy tissues were curated (>4000 samples). Subsequently, we applied our high-throughput RNA-seq analysis pipeline on the curated data. After rigorous quality assessment, we mapped the data to the human reference genome and further determined new transcript models using a reference-guided assembly approach. Novel transcripts were refined by a custom transcript selection approach, which combined novel transcripts with known lncRNA resources and filtered artifacts. Finally, transcripts were filtered depending on their coding potential assessment and classified based on their genomic location. After computing the expression levels, we determined the differential gene expression of ncNATs in large patient cohorts and conducted diverse statistical analyses.

We explored our large collection of normal and cancerous tissue samples in an effort to establish a detailed overview of ncNAT expression, including the evaluation of ncNAT dysregulation, expression heterogeneity in cancerous conditions and their tissue/cancer-specificity. Furthermore, our analyses shed light on correlations of ncNATs with their partners and focused further on immune-related and germline-specific ncNATs.