Biomarkers and epigenetic drivers across multiple cancer types

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Despite decades of research there are few cancer biomarkers being used in clinics. While most common cancer types are intensively studied for biomarkers, the less common and rare cancers are understudied. This is further complicated by the fact that there are more than 100 cancer types, thus the outlook to find biomarkers for each cancer type remains distant.

Here we aim to find pan cancer biomarkers, which are differentially expressed across multiple cancer types and thus will be clinically usable for both common and rare cancer types.

In our previous work (1), we used the Cap Analysis of Gene Expression (CAGE) profiles of 225 cancer cell lines and 339 normal primary cell samples from FANTOM5 project. CAGE is a 5' sequence tag technology that globally determines transcription start (sites TSS) in the genome and their expression levels. As a complementary data set, we used RNA-seq data from 4,055 tumors and 563 normal tissues profiled by The Cancer Genome Atlas (TCGA). In both data sets (FANTOM5 and TCGA), we performed cancer vs. normal differential expression analysis across all available cancer types.

We identified a core set of pan-cancer biomarkers (of both coding and non-coding transcripts) that are recurrently perturbed in both the cancer cell lines from FANTOM5 and clinical tumors from TCGA.

In our current work, we aim to find epigenetically regulated pan cancer biomarkers (epi-biomarkers) (2). Epi-biomarkers are up- or down- regulated because underlying epigenetic aberrations. Here, we focus specifically on DNA methylation data from TCGA to identify to hypo- and hyper-methylation events that are linked to aberrant gene expression in cancer. Our preliminary results conform that some of the most stable pan cancer biomarkers are driven by aberrations of DNA methylation.

References:

1. Kaczkowski, B. et al. Transcriptome Analysis of Recurrently Deregulated Genes across Multiple Cancers Identifies New Pan-Cancer Biomarkers. Cancer Research. 76, 216–226 (2016).

2. Kaczkowski, B., Hashimoto, K. & Carninci, P. Epi-drivers and cancer-testis genes. Translational Cancer Research 5, (2016).