

CPH Seminar in Precision Medicine

“Dissecting novel genetic elements in cancer from The Cancer Genome Atlas”

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The Cancer Genome Atlas (TCGA) is a comprehensive effort to understand the molecular basis of cancer. We generated pseudogene expression profiles in patient samples of seven cancer types from TCGA RNA-seq data using a newly developed computational pipeline. Supervised analysis revealed a significant number of pseudogenes that were differentially expressed among established tumor subtypes and that pseudogene expression alone can accurately classify the major histological subtypes of endometrial cancer. Across cancer types, the tumor subtypes revealed by pseudogene expression showed extensive and strong concordance with the subtypes defined by other molecular data. In kidney cancer, the pseudogene expression subtypes not only significantly correlated with patient survival, but also helped stratify patients in combination with clinical variables. We further characterized the global A-to-I RNA editing profiles of 17 cancer types from TCGA and revealed a striking diversity of RNA-editing patterns in tumors relative to normal tissues. We identified an appreciable number of clinically relevant RNA editing events that are particularly enriched in non-silent coding regions. We experimentally demonstrated the effects of several cross-tumor recoding RNA editing events on cell viability and provided the first evidence that RNA editing could selectively affect drug sensitivity. These results highlighted pseudogene expression and RNA editing as exciting paradigms for investigating cancer mechanisms, biomarkers and treatments.

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