

NOVEL RNA-SEQ PLATFORM ENABLES REPURPOSING OF APPROVED DRUGS IN RARE CANCERS, IMPROVING OUTCOMES

Gitte Pedersen*. *Genomic Expression Inc, Beverly, MA, USA*

Background Rare cancers are those that affect fewer than 40,000 people per year in the U.S. As a group, they make up just over 25% of all cancers and are responsible for 25% of all cancer deaths each year. There are few effective drug treatment options for rare cancers, whereas over 300 drugs have been approved by the FDA for treating non-rare cancers. Repurposing already approved cancer drugs to treat rare cancers is much faster and cost-effective than developing new drugs, but success depends on matching these drugs to rare cancers with the corresponding drug targets.

RNA sequencing has the potential to identify many clinically actionable molecular changes, whereas DNA sequencing is limited to some targeted drugs and typically misses the identification of aberrantly expressed checkpoint inhibitors, tumor antigens, and fusion events.

To enable RNA-sequencing in clinical samples, we had to overcome two issues: 1) tissue samples are typically embedded in FFPE, which results in highly fragmented RNA, making sequencing of samples difficult; 2) how best to interpret aberrant gene expression events and translate these results into clinical action.

Methods We address this issue through the implementation of our CLIA-validated *quantitative* OneRNA[®]-sequencing platform for treatment navigation. The OneRNA platform is an end-to-end integration of 1) CLIA-validated quantitative mRNA sequencing chemistry optimized for FFPE tumor specimens and low input liquid biopsy samples, such as blood, saliva, or urine, and 2) a validated bioinformatics pipeline, normalization methods, and an interpretative database that matches aberrant gene expression events to already approved drugs. Actionable genes are defined as genes that code proteins or nucleic acids that (1) are direct targets of drugs, (2) are ligands for the drug targets, or (3) are treatment selection biomarkers listed on the FDA label.

Results This study demonstrates the potential clinical utility of OneRNA[®] in detecting aberrant gene expression events and connecting them through a drug target and biomarker database to already approved drugs. Examples of improved outcomes in rare cancers are presented. The potential impact includes truly individualized treatment options in rare cancers. OneRNA[®] typically identifies 5 or more already approved drugs in all patients, whereas DNA sequencing only identifies 1 drug in 80% of the patients.

Conclusions The OneRNA[®] Platform can be used to expand treatment options for patients with rare cancers and with refractory cancers by matching tumors to existing drug targets, and by identifying high penetrance gene expression variants that may serve as targets for future drugs.

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