CHARACTERIZATION OF TP53 MUTATIONS BY DNA AND RNA SEQUENCING OF HIGH GRADE SEROUS OVARIAN CANCER (HGSOC) FFPE SECTIONS

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INTRODUCTION

TP53 is the most frequently mutated gene across all cancers at approximately 50%, and in cancers such as HGSOC, up to 96%. In addition to the high incidence of DNA mutations at the gene locus, the TP53 pathway is also dysregulated through alternative mechanisms which involve other members of the regulatory cascade, such as overexpression of MDM2. Asuragen has developed sensitive NGS assays and algorithms to characterize DNA mutations and RNA expression profiles from the most challenging clinical samples, such as archival FFPE samples. In order to enable a more complete understanding of the functional consequences of TP53 mutations (or lack thereof), we present an application of these approaches to characterize TP53 function in FFPE sections from HGSOC through an integrated analysis of DNA and RNA sequencing.

METHODS

Primary debulking surgery FFPE tumor sections were collected from a cohort of 235 HGSOC patients. DNA from macro-dissected tumor and matched normal blood specimens were profiled by the QuantideX® NGS TP53 Coding Exon Assay (Asuragen, Inc.), and library analysis was performed using the QuantideX® NGS Reporter. TP53 mutation status of the tumor specimens was independently assessed by the AmpliSeq Cancer Hotspot Panel v1 (Thermo Fisher Scientific, Inc.). Whole transriptome RNA-Seq was performed using ribosomal RNA-depleted total RNA, strand-specific libraries, and 50 bp paired-end sequencing. Gene and isoform expression was assessed using the AmpliSeq® Coding Exon Panel and the AmpliSeq® Coding Exon Panel based on a FDR corrected p-value < 0.05. The graph shows boxplots of the median log2 CPM for a subset of genes (indicated along the X-axis) directly or indirectly regulated by p53.