Genomic screening for hereditary cancer syndromes in 22,033 individuals
Christin Collins1, Alka Chaubey1, Taraka Donti1, C.A. Valencia1, Stephanie Ross1, Suresh Shenoy1, Zhili Lin1, Zeqiang Ma1, Abhinav Mathur1, Akanchha Kesari1, B.R. Nallamilli1, Yang Wang1, Jing Xie1, Alice Tanner1, Madhuri Hegde1,2
1PerkinElmer Genomics, 2Emory University

INTRODUCTION

• Given recent increases in the amount of elective genomic testing ordered, clinical laboratories will need to address the unique challenges inherent in this testing
• Identification of variants of uncertain significance in elective genomic testing is of minimal clinical utility, and therefore not reported by our laboratory
• Only pathogenic and likely pathogenic variants were reported due to the demonstrable clinical utility for this population

• CHALLENGE: Understand the clinical utility and diagnostic yield of genomic screening for hereditary cancer in an “allcomers” population, the majority of which have no reported personal or family history of cancer
• APPROACH: Multi-gene panel sequencing of an unselected population for genes associated with hereditary cancer

METHODS AND RESULTS

NGS sequencing workflow

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<th>Sample</th>
<th>Whole Blood</th>
<th>DNA Extraction</th>
<th>Sample QC</th>
<th>Automated Library Prep</th>
<th>Library QC</th>
<th>NGS</th>
<th>Result</th>
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DISCUSSION/CONCLUSIONS

• Of the 22,033 samples tested, 905 (4.1%) had a pathogenic and/or likely pathogenic variant detected.
• Data strongly supports screening and reimbursement for inherited cancer panels for early identification and intervention.
• For genes with low or reduced penetrance, multiple pathogenic variants may be detected in a reportedly unaffected individual.
• Data help identify highly penetrant and low penetrance genes and variants.
• Modalities for VUS (variant of uncertain significance) reporting still need to be assessed carefully (PMID 30453057). Resources to evaluate VUS on periodic basis require significant effort.
• Careful return of result strategies need to be established for post-testing follow-up and education.
• Population based screening should be considered for other common inherited conditions.