World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:15, No:10, 2021

Analytical Validity Of A Tech Transfer Solution To Internalize Genetic Testing

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Abstract : ASPIRA Labs now offers an en-suit and ready-to-implement technology transfer solution to enable labs and hospitals that lack the resources to build it themselves to offer in-house genetic testing. This unique platform employs a patented Molecular Inversion Probe (MIP) technology that combines the specificity of a hybrid capture protocol with the ease of an amplicon-based protocol and utilizes an advanced bioinformatics analysis pipeline based on machine learning. To demonstrate its efficacy, two independent genetic tests were validated on this technology transfer platform: expanded carrier screening (ECS) and hereditary cancer testing (HC). The analytical performance of ECS and HC was validated separately in a blinded manner for calling three different types of variants: SNVs, short indels (typically, <50 bp), and large indels/CNVs defined as multi-exonic del/dup events. The reference set was constructed using samples from Coriell Institute, an external clinical genetic testing laboratory, Maine Molecular Quality Controls Inc. (MMQCI), SeraCare and GIAB Consortium. Overall, the analytical performance showed a sensitivity and specificity of >99.4% for both ECS and HC in detecting SNVs. For indels, both tests reported specificity of 100%, and ECS demonstrated a sensitivity of 100%, whereas HC exhibited a sensitivity of 96.5%. The bioinformatics pipeline also correctly called all reference CNV events resulting in a sensitivity of 100% for both tests. No additional calls were made in the HC panel, leading to a perfect performance (specificity and F-measure of 100%). In the carrier panel, however, three additional positive calls were made outside the reference set. Two of these calls were confirmed using an orthogonal method and were re-classified as true positives leaving only one false positive. The pipeline also correctly identified all challenging carrier statuses, such as positive cases for spinal muscular atrophy and alpha-thalassemia, resulting in 100% sensitivity. After confirmation of additional positive calls via long-range PCR and MLPA, specificity for such cases was estimated at 99%. These performance metrics demonstrate that this tech-transfer solution can be confidently internalized by clinical labs and hospitals to offer mainstream ECS and HC as part of their test catalog, substantially increasing access to quality germline genetic testing for labs of all sizes and resources levels.

Keywords : clinical genetics, genetic testing, molecular genetics, technology transfer
Conference Title : ICHGG 2021 : International Conference on Human Genetics and Genomics
Conference Location : Paris, France
Conference Dates : October 28-29, 2021

Open Science Index, Biomedical and Biological Engineering Vol:15, No:10, 2021 publications.waset.org/abstracts/139070.pdf