GeNeXpreSS

Whole Genome Sequencing as a Diagnostic Tool: Utility and Challenges

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A whole new way to see!

(Ellingford et al, 2016)

With the recent technical developments in analyzing big data, whole genome sequencing has unlocked a whole new way in clinical genomics to evaluate various rare diseases, including the highly heterogenous group of inherited retinal diseases (IRD). Illumina Hiseq sequencing has given it a new direction through its high coverage and accuracy to identify and validate a particular variant more confidently than the ABI SOLiD platform. Whole Genome Sequencing (WGS) was performed in 46 individuals out of 562 patients with IRD for whom diagnostic Next Generation Sequencing (NGS) did not identify any mutation. The study also compared the sensitivity and specificity of WGS and diagnostic NGS in detecting Single Nucleotide Variations. By using WGS, it was possible to detect disease-causing variants in 11 individuals for whom a molecular diagnosis was not made previously. The authors concluded that WGS reported a higher rate of mutation detection as WGS had a more powerful pipeline to detect structural variants and variants in noncoding regions. The deletions identified with the pipeline ranged from <1.7 Kb to >520 Kb in size, including the identification of break points in noncoding regions. This study highlights the benefit of WGS as a superior tool compared to diagnostic NGS for evaluation of IRD patients if the cost factor can be minimized.

WGS about WGS: What General public Surmise about Whole Genome Sequencing (Roberts et al, 2017)

A randomized controlled trial was done to examine the use of WGS and family health information in cardiology and primary care settings compared to the use of family health information alone. A total of 202 patients were surveyed before and 6 months after the disclosure of the WGS results. Compared to patients for whom family health information alone was used, the patients for whom WGS results were combined with family health information were generally able to understand key facts about the sequencing trial, had less decisional regret and a good level of satisfaction about the utility of WGS findings. Due to the higher cost of the service, the patients had a preset expectation about the outcome of the service. Hence a decent communication between the physician and the patient to explain the utility of the WGS and its results in a clear and effective manner is very important. For better understanding of people with lower health literacy, it is suggested to have enhanced consent forms, informative videos and brochures and extended discussion schedules by physicians. A successful implementation of WGS in clinical settings is critical to guide future practice.

WGS unveils human faces

(Lippert et al, 2017)

Of the various promises of genome sequencing technology, this study challenged its ability to associate genotype to physical traits. The target was to utilize individual level of genotype obtained from WGS to match with the predictive model data created from the various physical features like facial structure, voice, eye color, skin color, height, weight and BMI. A model to estimate the age of a person was also generated. A sample size of 1061 individuals from African, European, Latino, East Asian, and South Asian ethnicity was considered for the study. R^2_{cv} value (R-squared evaluates how much of the variability in the actual

values is explained by the model, *cv* - coefficient of variation) was calculated between observed and predicted models to assess the influence of each covariate on predictive accuracy. Although the success rate was not uniform for all the models, the prediction accuracy for face, voice and age supported the efficiency of the model. Statistical significance will be higher if it can be applied on a larger sample size. In the long run, WGS could be helpful for genomic forensic sciences studies.

A Drop of Blood Suffices!

(Bassaganyas et al, 2017)

Dried Blood Spot (DBS) specimens represent an unparalleled resource to investigate rare genetic disorders in newborn, such as inborn errors of metabolism. The current work proposed a successful protocol to do WES and WGS from DBS samples without whole genome amplification prior to library preparation. The authors attributed the success of this method to factors such as preservation of the cards at -20°C under desiccation, keeping DNA intact, automated DNA extraction protocol yielding a good quantity of DNA, smaller amount of DNA needed for the newer exome capture kits and a shorter DNA shearing time. The study proved that even very low amounts of genomic DNA from DBS could generate acceptable exome coverage. The successful implementation of a protocol to produce high quality exome and genome sequences from newborn DBS offers an unparalleled opportunity to advance the understanding of rare disease associated and polymorphic variants in various populations.

References

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