Print this Page for Your Records Close Window

Control/Tracking Number: 2020-A-1634-ACMG
Activity: Abstract
Current Date/Time: 11/6/2019 9:28:47 AM

Exome Reanalysis Results In An 8% Reclassification Rate

Author Block: Kelly Farwell Hagman, MS, CGC[1], Meghan Towne[2], Kelly Radtke[1], Kirsten Blanco[3], Jennifer Huang[1].
[1]Ambry Genetics, Aliso Viejo, CA, USA, [2]Ambry Genetics, Dedham, MA, [3]Ambry Genetics, Aliso Viejo, CA.

Abstract:
Diagnostic exome sequencing (DES) has the potential to end expensive, invasive, time-consuming testing and lead to changes in patient care. Upon initial analysis, ~25% of patients with underlying Mendelian diseases receive a diagnosis via DES . A major benefit of exome sequencing is the ability to reanalyze the same set of data and benefit from new gene-disease discoveries, new variant information, as well as changes in the patient's medical and/or family history.
This study analyzes a cohort of patients who underwent DES at a commercial lab between January 2016 and August 2018, and for whom a client-initiated exome reanalysis was subsequently requested. During this time frame, a total of 436 patients had ≥1 client-initiated reanalysis request. A second request was received for some patients, bringing the total number of reanalysis/reclassification reports issued to 452. Overall, the rate of reclassification from client requested re-analysis was 8% (36/436). Client-initiated reanalysis requests resulted in 34 upgraded reports (7.54%), 2 downgraded reports (0.44%), and 415 unchanged reports (92.02%). 20 total reclassified reports in this cohort (46.5%) resulted in a change in clinical utility, meaning a negative or uncertain result was upgraded to a likely positive or positive result. Among the 36 reclassified reports, 8 (22.2%) were due to variant reclassification, 13 (36.1%) were due to gene reclassification, and 15 (41.7%) were due to new clinical information allowing for an upgrade in clinical overlap.
All reports with an initial positive/likely positive conclusion prior to the reanalysis request were unchanged after reanalysis. All the changes (both upgrades and downgrades) occurred in reports that had an initial conclusion of negative or uncertain, or a finding in a novel gene. No difference was seen in sex or age between the reanalysis requests that resulted in upgrades or those that remained unchanged. Approximately 64% (289/451) of client-driven reanalysis requests included updated clinical information. 9.34% of requests with new clinical information resulted in an upgrade, while this was the case for only 4.91% of requests without new clinical information. Among the 34 upgraded reports following client-initiated reanalysis, 77.14% included new clinical information. Reanalysis requests that included additional family history and/or updated testing results were significantly more likely to result in an upgrade ($p<0.05$). Examples of changed testing or family history included new biochemical test results and new information regarding affected status of a relative.
Overall, 8% of clients ordering a re-analysis received a reclassified report and most notably new test results or new family history details resulted in a significantly higher likelihood of a reclassification. These data highlight the utility of DES in providing a comprehensive and timely molecular diagnosis with the ability to continually assimilate new information. In addition to the potential to end the diagnostic odyssey for patients, the ability to continually reanalyze exome data adds to the economic value of the test compared to traditional testing methods. The data also emphasize the importance of counseling patients about the likelihood of a result reclassification in the future.
:

Encore Presentation (Complete):
Yes/No: No

Presentation Preference (Complete): Platform or Poster Presentation
Topic Category (Complete): Laboratory genetics and genomics
Keyword (Complete): Genome Sequencing ; Clinical History ; Identification of Disease Genes ; Mutation Detection ; Whole exome sequencing
Award Information (Complete):
Do you wish to be considered for the PerkinElmer Diagnostics Company Travel Award and meet all qualifications?: No, I am not interested.
Do you wish to be considered for the David L Rimoin Inspiring Excellence Award and meet all qualifications?: No, I am not interested.
Do you wish to be considered for the Carolyn Mills Lovell Genetic Counselors Award and meet all qualifications?: No, I am not interested.

Electronic Signature (Complete):
***Please agree below:** I Agree

Attached Files: No Files Attached
Status: Complete