Hereditary Pancreatic Cancer Multi-Gene Test: Preliminary Results

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Background

Pancreatic cancer (PC) is recognized as a component tumor in many well-described hereditary cancer syndromes. Despite this, there are limited guidelines to direct clinicians in ordering genetic testing for sporadic and familial PC. The increased availability of cost-effective multi-gene testing presents an opportunity to better define criteria for hereditary PC testing.

Methods

DNA from 156 individuals with a personal and/or family history of PC was analyzed with PancNext™, a multi-gene test including sequencing and deletion/duplication analyses of the following genes: *APC, ATM, BRCA1, BRCA2, CDKN2A, MLH1, MSH2, MSH6, PALB2, PMS2, STK11,* and *TP53*; and deletion/duplication analysis of *EPCAM*. Clinical information was submitted by ordering healthcare providers.

Results

18 pathogenic mutations were identified among 16/156 participants (10.3%) with positive results, including 6 *ATM* (33.3%), 2 *MSH6*, 4 *BRCA*, 3 *APC* (I1307K), 2 *CDKN2A*, and 1 *PALB2*. Neither of the *MSH6* mutation carriers met Amsterdam II criteria for Lynch syndrome, and one of the *BRCA* mutation carriers did not meet National Comprehensive Cancer Network testing criteria for hereditary breast and ovarian cancer syndrome.

Of individuals with pathogenic mutations, 75% (n=12) had PC, diagnosed at a mean age of 54.2, compared to individuals without pathogenic mutations, where 42.9% had a diagnosis of PC diagnosed at a mean age of 60.5. Seventy-five percent of patients with pathogenic mutations (n=12) had a family history of PC, averaging 2 affected relatives.

Variants of unknown significance were identified in 23.7% of individuals (n= 37), including two individuals with pathogenic mutations and 6 individuals (16.2%) with more than one VUS.

Conclusion

Similar to other cancers, a genetic predisposition to PC will be identified in about 10% of individuals undergoing genetic testing. Interestingly, a third of the mutations identified were in the *ATM* gene, supporting findings from previous studies on the association of *ATM* mutations with hereditary PC. Additionally, the average age of diagnosis in our positive patients was younger than in patients with negative results, suggesting that a younger age at diagnosis may be correlated with hereditary predisposition.

This abstract will be presented as a poster at the National Society of Genetic Counselors Meeting in September 2014

Conflict of Interest: All of the authors are full-time employees of Ambry Genetics