Possible founder mutation in CDKN2A in the Latino population

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Background: Pathogenic mutations in *CDKN2A* cause an autosomal dominant condition known as Familial Atypical Multiple Malignant Melanoma (Pancreatic Cancer) (FAMMM (PC)). This condition is characterized by a significant lifetime risk of developing a single/multiple melanoma(s) as well as pancreatic cancer. The present work reports the case of a 50-year-old Hispanic patient with pancreatic cancer who carries a *CDKN2A* variant, which is primarily found in individuals of Hispanic descent. **Methods:** Extensive clinical data from the patient and her family were obtained; informed consent and a DNA sample from peripheral blood were taken. A multi-gene panel test (MGPT) for hereditary cancer risk was performed at multiple laboratories. Variant data was reviewed with respect to classification evidence in light of discrepant classifications among labs (ClinVar accessed 7/2/2019). **Results**: At age 50y, the proband was diagnosed with a pancreatic adenocarcinoma with a personal medical history (PMH) of breast cancer at age 30y. Patient's family medical history (FMH) was remarkable for cancer, specifically: male breast, brain, encapsulated unspecified primary, and an unspecified abdominal. There was no known PMH/FMH of melanoma. *CDKN2A* c.146T>C (p.I49T) was identified in the proband and is classified as a moderate-risk, likely pathogenic variant by one clinical diagnostic lab (VLP) based on intermediate functional defects and identification in families affected with melanoma and/or pancreatic cancer. The proband also carries a variant of unknown significance in each *MSH6* and *XRCC2*. At one diagnostic lab, 123 probands carried this variant. 8 had a pancreatic cancer-targeted MGPT 114 of whom had a comprehensive cancer MGPT. >80% of individuals who carry *CDKN2A* c.146T>C self-identify as being of Hispanic descent. Among the carrier population 52% reported a PMH and/or FMH of PC and/or melanoma although, among the probands, PC was approximately twice as prevalent as melanoma. A case-control study would contribute to the classification and risks associated with this alteration. **Conclusions:** The *CDKN2A* c.146C>T (p.I49T) moderate-risk VLP was identified in a proband with a PMH consistent with FAMMM (PC). This alteration may be a Latino founder mutation conferring reduced risk for FAMMM (PC) and may be more inclined to be associated with PC relative to melanoma.