Genetic Insights into Hereditary Cancer Risk in the Latin American Population

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Introduction

Current hereditary cancer risk data is mostly based on genetic testing performed in Caucasian and Ashkenazi Jewish populations. As a result, the distribution of mutated genes and their associated cancer risk in other ethnicities is not well understood. Previous studies of hereditary cancer in the Latin American population have focused on the BRCA1 and BRCA2 contribution to breast cancer. Interestingly, in some countries, more than 1 in 4 breast cancer patients were reported to have a BRCA mutation, indicating that the proportion of hereditary breast cancers in Latin America is even higher than in previously reported for high risk Caucasian (12.7%) and Ashkenazi Jewish cohorts (10.3%). However the utility of multi-gene panels for hereditary cancer risk have not been reported on. This study aims to provide insights into genetic cancer risk within the Latin American population, for breast cancer as well as ovarian, colorectal, melanoma, pancreatic, prostate, uterine and stomach cancers.

Methods

We describe the demographics and genetic results of 988 Latin American hereditary cancer high risk individuals from 6 countries (Argentina, Brazil, Colombia, Mexico, Peru, and Uruguay) who were referred by a physician to receive the Color Hereditary Cancer Test. The Color Hereditary Cancer Test assess 30 genes associated with increased risk for hereditary cancer including breast, ovarian, colorectal, melanoma, pancreatic, prostate, uterine and stomach cancers, and includes the following genes: APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIPI, CDH1, CDK4, CDKN2A, CHEK2, EPCAM, GREN1, MGMT, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, POLE, PTEF1, RAD50, RAD51, SMAD4, STK11, and TPS3. Ethnicity assignments and health history were based on self-reported information. The relatedness of individuals was not assessed in this study.

Conclusions

- Here, we present the results of testing high-risk individuals from six Latin American countries with a 30-gene panel for hereditary cancer risk. The overall pathogenic mutation carrier rate was 18.7%.
- Pathogenic variants were identified in 16 different genes on the panel, highlighting the utility of broader panel testing in Latin American populations.
- Nearly half of this high-risk cohort reported a personal history of breast cancer. The BRCA1 and BRCA2 mutation carrier rate for breast cancer patients in this cohort was 14.0%, which is similar to previously reported rates in Caucasian and Ashkenazi Jewish populations.

Results

Figure 1: Number of individuals from each country, stratified by reported ethnicity. Overall positive rate in the cohort was 18.7%, and the percent positive by ethnicity was 19.6% for Hispanics, 19.8% for Caucasians, 12.0% for other ethnicities (including Ashkenazi Jewish, African, Asian, Native American, and Multiple Ethnicity) and 15.7% for unknown ethnicities.

Figure 2: Just under half (46.6%) of the individuals in this high risk cohort reported a personal history of breast cancer, and 40.2% did not report a history of cancer.

Figure 3: Genes in which pathogenic or likely pathogenic variants were identified. The BRCA1 and BRCA2 carrier rate in the cohort was 11.0%. Importantly, approximately half (51.1%) of the pathogenic variants were identified in genes other than BRCA1 or BRCA2. Two individuals were found to carry two different MUTYH pathogenic variants. Bars are colored by the the hereditary cancer(s) that are most closely associated with the gene: breast/ovarian gene (blue), colorectal gene (orange) and other gene (yellow).

Figure 4: Individuals that reported a personal history of breast cancer had a mutation carrier rate of 20.7%. Two-thirds (67.7%) of the mutations found in breast cancer patients were BRCA1 or BRCA2, for a BRCA1 and BRCA2 mutation carrier rate of 14.0%.

Figure 5: Genes in which pathogenic or likely pathogenic variants were identified, stratified by country. The most frequently observed variants in each country are: MUTYH c.1187G>A and BRCA2 c.2806_2809delA/AAC in Argentina; MUTYH c.1187G>A in Brazil; MLH1 c.1459C>T and BRCA1 c.4484+977_4986+708del in Colombia; BRCA1 c.4327C>T and BRCA2 c.3759_3760delTA in Mexico; MUTYH c.934-2A>G in Peru and BRCA1 c.3526dupC and MUTYH c.536A>G in Uruguay.