Title: An Urgent Need for Policy Change: the Cancer Susceptibility Mutation R337H with a Founder Effect in South and Southeastern Brazil

Author: Mell Aguiar

Principal Investigator: Danielle Braun, PhD

Scientific Advisor: Theo Huang, PhD

Dana-Farber Cancer Institute

Abstract:

An increase in the incidence of and mortality from breast cancer (BC) has been observed in females between 20 and 49 years in all parts of Brazil, with the South and Southeastern regions experiencing the highest incidence rates. The TP53 gene R337H germline mutation occurs at an unusually high frequency in these regions because of a founder effect, and is thought to increase BC risk in women. Despite R337H's elevated prevalence and role in the proliferation of hereditary BC cases in this part of Brazil, there is still widespread disagreement over what constitutes an appropriate manner of identifying carriers, particularly for patients between the ages of 36 and 46. All points considered, establishing region-specific testing criteria for this at-risk group of young, female BC patients is of utmost importance. In this context, the aim of this review was to investigate different testing recommendations for this population, to explore the accessibility of testing, and to consider disease management options for Brazilian BC patients. Qualitative analysis revealed that TP53 variant testing could be justified for all female BC patients meeting hereditary breast and ovarian cancer criteria in South Brazil who were diagnosed before the age of 45. But, any such protocol, regardless of efficacy, will not impact the population until major public policies are changed. Genetic testing is not available under Brazil's public healthcare system which covers approximately 75% of the population, and only BC patients diagnosed below the age of 35 are eligible for TP53 mutation testing under the private system which covers the remaining 25% of the population. Based on these findings, it is clear that TP53 variant testing criteria should be adapted to the specifics of South and Southeastern Brazil and that Brazilian healthcare policies must change alongside them for the proper implementation of hereditary BC management in the country.