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**MOLECULAR GENETICS OF BREAST CANCER**

Dr. Dutil's team focuses on the study of genetic susceptibility to disease in the population of Puerto Rico. The Hispanic population is the fastest growing minority in the United States. The total 7 million Puerto Ricans (living in the island and on the continent) make up 18% of the Hispanic population and comprise the second largest Hispanic subgroup in the country. However, little is known about the disease genetics make up of this population. The long term goal of our research program are 1) to understand how inter-individual and inter-population genetic variations regulate the onset, progression and response to treatment in human diseases, and 2) develop strategies and tools to translate these findings to the health care system serving minority populations.

**Hereditary Breast Cancer**

It is estimated that 5-10% of all breast cancer are hereditary and caused by mutations in the *BRCA1* and *BRCA2* genes. Knowledge of the incidence and prevalence of BRCA mutations in a specific population or ethnic group is necessary to provide accurate genetic counseling for breast cancer patients and their families. Our long term objective is to provide the population of Puerto Rico with accurate and efficient tools for the clinical management of hereditary breast cancer. More specifically, we aim to identify the prevalent BRCA mutations in Puerto Rico and evaluate available models of carrier risk assessment in this minority population. This objective will be achieved by pursuing the following specific aims: 1) assessment for *BRCA1* and *BRCA2* mutations in a sample of breast cancer patients from Puerto Rico, 2) evaluation of the BRCAPRO and Myriad II carrier risk calculation models in a sample of breast cancer patients from Puerto Rico.

**Familial Breast Cancer**

For most cases of breast cancer, familial aggregation is not explained by mutations in the *BRCA* genes. It is believed that common alleles or combination of alleles interacting with environment and lifestyle factors impact on breast cancer risk in those families. First, we are evaluating the association of single nucleotide polymorphisms (SNPs) and copy number variants (CNVs) in the genes involved in DNA repair for their association with breast cancer susceptibility. The rationale for the choice of the DNA repair pathway genes as candidates relies on the observation that the DNA repair capacity is lower in women that have had a breast than in controls. Second, we are using admixture mapping to determine the role of genetic ancestry in determining breast cancer risk. The incidence of breast cancer shows marked variations among different ethnic groups in the United States, with the highest rates in Caucasian women. Because the Puerto Rico population has a mixed genetic ancestry, we can use ancestry informative markers (AIMs) to localize the breast cancer causing genetic factors that are underlying the prevalence variations among the different ethnic groups that make up the Puerto Rican population.

Unlike lifestyle risk factors, inherited predisposition genotypes cannot be modified. By characterizing the role of genetic factors in cancer risk, we can act on modifiable risk factors. Research has shown that those who are educated about their increased risk of

breast cancer are more likely to engage in risk-reducing behaviors and early detection strategies. Furthermore, a better understanding of the etiology of breast cancer predisposition is expected to allow the development of new preventive strategy specifically targeted to individual needs.