Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Why mutations in the *BRCA1* or *BRCA2* genes increase the risk for breast and ovarian cancer?

Synopsis:
Women who inherit heterozygous mutations in the *BRCA1* or *BRCA2* genes have an increased risk of developing cancer, predominantly in the breast and ovary. Assuming the prevailing view that it is the adult progenitor/stem-like cells that give rise to cancer, we reason that in order to understand BRCA-associated oncogenesis and to contribute for improved risk assessment and prevention strategies, it is critical to study the transformation of the progenitor cells that originate breast and ovarian cancers. Our lab focuses on the founder c.156_157insAlu mutation (i.e. an Alu insertion in BRCA2 exon3), which represents 55% of all BRCA2 germinal mutation carriers in Portugal. How this founder mutation interferes with the normal function of the BRCA2 protein and increases susceptibility for breast and ovarian cancers is not known.

We are developing an innovative disease model that consists of mammary and Fallopian tube epithelial progenitors differentiated in vitro from induced pluripotent stem cells (iPSCs) derived from women who are mutation carriers. Moreover, our group has longstanding expertise in genome-wide methodologies to study nascent transcripts. Thus, we are in a unique position to address the hypothesis that cancer-associated BRCA mutations interfere with transcriptional programs and alter tissue stem cell identity.

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Webpage of the group

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