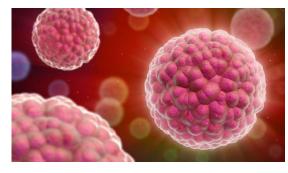


Optimizing Treatment of Pancreas Cancer Patients with BRCA Gene Mutations

The Breast Cancer Associated (BRCA) 1 and 2 genes were originally identified in women with a strong family history of breast cancer. These genes produce proteins that repair DNA damage. This function is impaired in individuals inheriting a mutated form of the gene from either parent, resulting in a greater risk of accumulating cancer-promoting DNA damage. Until recently it was thought that

BRCA mutations were rare in pancreas cancer patients. However, recent work being done here at Princess Margaret Cancer Centre suggests a much higher frequency. Importantly, although BRCA mutations promote the development of cancer, they also make the cancer sensitive to specific types of treatment, and we now treat BRCA positive pancreas cancer patients with the chemotherapy drug Cisplatin. Although this can be highly effective, it has significant side effects and we need to develop better treatments for these patients.



A priority is to examine the effects of BRCA mutation on the growth and treatment sensitivity of pancreatic cancers

As part of our comprehensive pancreatic cancer research program, we have successfully grown

cancer tissue obtained during surgery for pancreatic cancer in mice, and find that these tumours (called xenografts) closely resemble the features and growth patterns seen in the original patient. The total number of patient-derived xenografts is now more than 100 and 6 of these were derived from BRCA positive patients.

The purpose of this application for research funding is to support experiments that will:

- 1) Examine in detail the effects of BRCA mutation on the growth and treatment sensitivity of pancreatic cancers.
- 2) Test alternatives for treatment of these cancers. It is expected that the results of these studies will then be used for the design of next-generation treatments for patients. Initial experiments will be done using 3 BRCA positive xenografts, and results compared to 3 that were derived from patients with normal BRCA, and are expected to complete by the end of 2013.

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