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Familial aggregation of cancer in Swedish families with special reference to colorectal adenoma, gastro-intestinal carcinoid tumours and pancreatic cancer

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Understanding the familial clustering of cancer improves our knowledge of cancer etiology and provides information for cancer risk assessment in genetic counselling. The population based Swedish Family-Cancer Database offers unique possibility for investigating the familial aggregation of cancers because data on family relationships and cancer diagnoses were obtained from registered sources. This thesis utilized the 2006 update of the Database that includes over 11.5 million individuals. Familial relative risks were used to compare the incidence of cancer among those whose family was affected by cancer with the incidence of cancer among those without a family history of cancer. The results are organized around three major points:

1. Since there is limited information on the risk of colorectal adenoma for individuals with parents or siblings affected by extracolorectal malignancies, familial relative risks of colorectal adenoma for the offspring and siblings of patients with extracolorectal cancer were estimated utilizing the Swedish Family-Cancer Database. Associations of colorectal adenoma with HNPCC cancer sites - the endometrium, stomach and pancreas - were identified. In addition, there was a higher risk of colorectal adenoma for the offspring and siblings of patients with prostate cancer. The siblings of patients with multiple myeloma and the offspring of patients with leukaemia were at an increased risk of colorectal adenoma. These results indicate that certain extracolorectal cancers unrelated to colorectal cancer syndromes are associated with colorectal adenoma.

2. Using the 2006 update of the Swedish Family-Cancer Database it was possible to investigate the familial aggregation of gastrointestinal carcinoids. The results confirm that individuals with a parental history of carcinoids are at a higher risk of developing carcinoids compared to those whose family was not affected by carcinoid tumours. Carcinoids were associated with a parental history of breast and liver cancers. An excess of carcinoid tumours was found among the offspring of patients with non-Hodgkin lymphoma. The risk of carcinoid tumours was elevated among siblings of patients with colon and rectal cancers. Parental cancers of the brain, endometrium and kidney, as well as squamous cell skin cancer associated with small intestinal carcinoids in the offspring. The risk of appendiceal carcinoid tumours was increased among the offspring of women with breast cancer. Parental history of small intestinal carcinoid tumours associated with cancers of the breast and kidney in the offspring. The translation of these data into screening programs needs further research. However, the relatively high familial risks should stimulate efforts for gene identification.

3. The aim of the third part of the thesis was to characterize the familial association of pancreatic cancer with other malignancies using the 2006 update of the Swedish Family-Cancer Database. Since early age of onset has been a reported characteristic of hereditary cancer, relative risks of cancer were calculated according to parental / sibling age of cancer diagnosis. Pancreatic cancer risk was increased among individuals with a sibling history of early onset lung and breast cancer. The risk of pancreatic cancer was elevated in individuals with a parental history of cancers of the liver, kidney and larynx. Associations were also found between parental history of pancreatic cancer and cancers of the small intestine, colon, breast, lung, testis and cervix in the offspring. The risk of breast cancer was higher among individuals whose parents were diagnosed with pancreatic cancer before age 72. These results suggest that pancreatic cancer aggregates in families with several types of cancer. Smoking may contribute to the familial aggregation of pancreatic and lung tumours, and the familial clustering of pancreatic and breast cancer could be partially explained by inherited mutations in the BRCA2 gene.