

## GERMLINE GENETIC OF RARE CANCERS

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Thanks to panel sequencing, large amounts of data on constitutional variation have recently become available. In the last meetings I have sought to compare these results with population-based family history data. Family studies are able to describe aggregation of any defined cancers in families. The Swedish Family-Cancer Database is the largest of its kind in the world, covering the Swedish families through nearly a century with all cancers in family members since the start of national cancer registration in 1958. The database allows estimation of familial risks, ages of cancer onset and the proportion of familial cancer in different family constellations. However, the focus of comparisons between family and genetic studies has been biased towards the most common cancers for which large volumes of sequencing data has accrued.

Here, I want review, through interactive discussion, rarer solid cancers for which familial risks are often higher than those for common cancers. I want to go through the list of cancers with comments and maybe conclusion if we reach an agreement. Familial risk for lip cancer is 2.0 and it is a rare cancer so familial genetics would not be easy. Small intestinal cancer is also rare but the familial risk is 5.6, higher for the carcinoid component than for adenocarcinoma. Genes for carcinoids have been elusive. Non-medullary thyroid cancer has familial risk of 4.3 and main low-risk genes are known. Thyroid cancer manifests in some rare cancer syndromes including Gardner syndrome (papillary thyroid cancer), familial adenomatous colorectal polyposis (100-fold risk for papillary cancer) and Turcot syndrome (papillary and follicular cancer). Thyroid anaplastic cancer is an exquisitely aggressive tumor for which genetic basis remains unknown. Familial bone cancer is extremely rare, familial risk is 6.9. International collaborative efforts would be beneficial to boost germline genetics of rare cancers.