Hongyao Yu Dr. sc. hum. **Discordant Familial Risks for Lung and Colorectal Cancers** Fach/Einrichtung: Molecular Genetic Epidemiology Doktorvater: Prof. Dr. Kari Hemminki

Lung cancer and CRC are common cancers which have high incidence and mortality rates worldwide. The concordant familial risks of lung cancer and CRC have been investigated in a number of previous studies. However, the studies on discordant familial risks of these two cancers are rare. Since different cancers could be caused by the same susceptibility gene or the shared environment, data of associations of discordant cancers may provide useful information for identifying common risk factors. The aim of this study was to investigate the discordant familial risks for lung cancer and CRC.

People in the offspring generation and their FDRs in the FCD, a total of 15.7 million people, were taken into the study. ICD-7 was used to identify cancers and PAD and SNOMED were used to identify histological types.

In lung cancer analyses, 28 most common cancers (12 smoking related cancers, 14 cancers smoking relation not established and 2 cancers not related to smoking) were taken as cancer X. RRs for cancer X were estimated in families with increasing numbers of probands with lung cancer, and in the reverse analyses, RRs for lung cancer were estimated in families with increasing numbers of probands with cancers X. The cancer risks were also estimated by sex and histological types of lung cancer respectively.

In CRC analyses, 34 most common cancers were cancer X. RRs for cancer X were estimated in families with increasing numbers of probands with CRC, and in the reverse analyses, RRs for CRC were estimated in families with increasing numbers of probands with cancers X. After that, HNPCC families were excluded from the study to see whether the RRs changed. In addition, CRC was categorized into colon cancer and rectal cancer to investigate whether there were distinct associations of colon and rectal cancers with discordant cancers.

Poisson regression model was employed to estimate RRs and their corresponding CIs for 95%, 99% and 99.9%. Age group, calendar period, sex, socioeconomic status and residential area were covariates and person-years were the offset. Trend tests were performed to assess whether RRs increased by the number of probands with cancers

Nine smoking related cancers and CUP were associated with lung cancer. Among cancers without established to smoking only anal and connective tissue cancers and Hodgkin lymphoma could be associated with lung adenocarcinoma. Negative associations of lung cancer were observed with endometrial and prostate cancers. The study of CRC found that at least the associations of melanoma, myeloma, CUP, thyroid and eye cancers with CRC were unrevealed before. In addition, colon cancer was a stronger risk factor for CRC and colon cancer than rectal cancer. Nervous system cancer is only associated with colon cancer and lung cancer only with rectal cancer.

The complete coverage of cancer registry and the Multigeneration Register in Sweden allowed us to investigate the discordant familial risks of lung cancer and CRC. Our study may provide information on identifying cancer susceptibility genes and on genetic counseling.