Report NCU grant

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Main applicant: Fredrik Wiklund

Project title: Genetic epidemiology of prostate cancer prognosis

NCU grant received (€): 60.000

Project commencement and completion dates: 2012-01-01--2012-12-31

Please e-mail report to: ncu@kreftforeningen.no

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1. **Brief description of the project, written in a language understandable to non-scientists (Maximum length: 100 words)**

   The overall aim of this project is to improve our understanding of genetic causes for the survival of prostate cancer patients. To achieve this we intend to perform large-scale genomic assessments in several population-based prostate cancer cohorts from the Nordic countries. Already performed genome-wide assessments of prostate cancer survival will set the basis for our study from which targeted explorations of indicated genomic regions will be performed.

2. **Summarize the major findings of the project (Maximum length: 400 words)**

   We have performed an inventory of available prostate cancer study populations among the participating groups. To date we have access to genomic DNA from a total of 12,000 prostate patients in Sweden and Finland. Through national registries we have complete information regarding clinical characteristics and disease prognosis. As of latest follow-up a total of 1,200 patients had died due to prostate cancer. High priority is currently given to increase available sample size and this will be achieved through retrieval of DNA samples from Norwegian prostate cancer patients through the national CONOR bank.

   A first replication study of genetic variants implicated as associated with prostate cancer survival has been performed. In total 10 genomic regions showing strongest association with prostate cancer survival in a prostate cancer GWAS study was taken forward for replication. Replication was performed in the CAPS population comprising 3,000 patients among whom 600 have a lethal outcome. Overall the results from this replication study were negative. None of the 10 genetic variants were observed to be associated with prostate cancer survival in

the CAPS population. This highlights the importance of independent validation of initial screening discoveries to exclude false positive findings.

We have initiated a whole exome sequencing project of lethal prostate cancer patients. In total 100 patients that have died due to there disease at a very young age (below 65 years) have been selected for sequencing. Exonic sequences will be enriched using a Nimblegen capture kit. The enriched DNA will be fragmented, tagged and sequenced using Illumina sequencing allowing for high diploid coverage of the individual exomes. As reference population to contrast individual variants observed among the lethal prostate cancer patients a set of 1,200 populations control ascertained in a Swedish Schizophrenia study will be used. Whole exome sequencing of these 1,200 controls has already been performed and aligned variants are available to be used in our study. DNA preparation and library building has been completed for all our cases and we plan to start the exome sequencing early fall 2012.

3. Describe how the project has increased our knowledge of the prevention, cause and/or cure for cancer (Maximum length: 150 words)

So far the current project has not increased our knowledge regarding genetic determinants for prostate cancer prognosis. Epidemiological studies support existence of inherited genetic variants that are of importance for the outcome of prostate cancer patients. It is evident that our efforts so far to identify these variants have been limited by small study populations (low statistical power). Therefore we are currently working intensively with ascertaining additional prostate cancer study populations from the Nordic countries to increase our possibility to succeed with our overall aim.

4. Outline how Nordic cooperation has added value to this project (Maximum length 100 words)

Existence of national population and disease registries coupled to large biological banks make the Nordic countries uniquely positioned for performing population-based genetic epidemiological studies of prostate cancer prognosis. Through pooling existing prostate cancer resources in Norway, Sweden and Finland strong synergy effect is achieved by creating a large Nordic population-based cohort of prostate cancer patients with complete information regarding clinical characteristics, treatment, and disease-specific follow-up. These are necessary prerequisite to successfully identify genetic determinants for prostate cancer prognosis. Our Nordic cooperation are therefore of outermost importance to achieve our aim.

5. Publications resulting from this grant

No publications so far.