NCU – Summative report for 2013

Report submission date: 2014-03-15

Principal investigator: Fredrik Wiklund

Project title: Genetic epidemiology of prostate cancer prognosis

NCU grant received (€): 65.000

Project commencement and completion dates: 2013-01-01—2013-12-31

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1. Briefly describe the project in a language understandable to non-scientists (max. 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 (max. 400 words)

Sample collection
We have completed record linkage between the national CONOR biobank and the Norwegian Cancer Registry. This resulted in identification of 4,923 men with a diagnosis of prostate cancer in the CONOR population. Through complete follow-up regarding vital status up to 2013-06-15 1,133 patients had died due to prostate cancer. A nested cases-case design has been implemented matching a non-lethal case to each patient that has died due to prostate cancer. Retrieval of genomic DNA from these cases is ongoing. Through this effort we will have available genomic DNA from approximately 18,000 prostate cancer patients from Norway, Sweden and Finland of which 2,100 had a lethal outcome.

Exome sequencing
We have performed a whole exome sequencing project of lethal prostate cancer patients. In total 75 Swedish and 50 Finnish patients that have died due to their disease at a very young age (below 65 years) have been selected for sequencing. Exonic sequences was enriched using a Nimblegen capture kit. The enriched DNA was fragmented, tagged and sequenced using Illumina

sequencing allowing for high diploid coverage of the individual exomes. All data has been aligned against a reference genome. Overall the quality of derived data his high with over 80% of the captured regions having a coverage of 20X or higher. Presently we are contrasting the prostate cancer exome data against a reference population set of 1,200 populations control ascertained in a Swedish Schizophrenia study.

Replication analysis
We are still performing a GWAS study of prostate cancer survival utilizing the PRACTICAL/iCOGS consortium. We expect to complete this assessment during spring 2014 and will then take forward indicated genomic regions associated with prostate cancer survival for replication analysis in our Nordic populations (see above).

3. Describe how the project has increased our knowledge of the prevention, cause and/or cure for cancer (max. 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 research performed to date to identify these variants has been limited by small study populations (low statistical power). Therefore our efforts with ascertaining large prostate cancer study populations from the Nordic countries are of great importance to increase our possibility to succeed with our overall aim.

4. Outline how Nordic cooperation has added value to this project (max. 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 the NCU research grant

No publications so far.