NCU – Summative report for 2013

Report submission date: 04.03.14

Principal investigator: Göran Jönsson

Project title: Molecular epidemiology of familial ocular and cutaneous malignant melanoma; a Swedish-Danish collaboration

NCU grant received (€): 60,000

Project commencement and completion dates:

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1. **Briefly describe the project in a language understandable to non-scientists (max. 100 words)**

In current project we aim to investigate familial ocular and cutaneous melanoma which will lead to a better understanding of these diseases that are tightly linked but still different on a biological level. In familial cutaneous melanoma germline mutations in CDKN2A is a well established susceptibility gene. We are investigating tumor molecular properties from CDKN2A germline mutated patients with the aim of defining distinct features in such tumors. Familial ocular melanoma is rare and recently we and others have described inherited mutations in the BAP1 gene in ocular melanoma families. We are now aiming at investigating tumors from these individuals. In summary, we belive that tumor molecular information in tumors from familial melanoma may help to understand the development of the disease.

2. **Summarize the major findings of the project (max. 400 words)**

Thus far, we have firmly established that BAP1 is a ocular melanoma susceptibility gene. In addition, we show that individuals with a BAP1 mutation also confer an increased risk to other cancers such as mesothelioma. We are currently collecting tumors from individuals with familial ocular melanomas that will be compared to non-familial ocular melanomas. In a second project we have investiagetd the gene expression landscape of 43 cutaneous melanomas from CDKN2A mutation carriers. As a comparison we have gene expression data from 223 sporadic melanomas. Overall, no distinct difference were found between the familial and sporadic cases suggesting that the tumor aberrations found in sporadic melanomas are similar to those found in familial melanoma.

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

The project has increased our knowledge on how melanoma arises and in particular that BAP1 germline mutations confer risk of ocular melanoma. Furthermore, the project has increased our understanding with regards to tumor biology of familial cutaneous melanoma.

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

It has been very valuable with the Nordic Cooperation. In this way, it has been possible to examine a larger cohort of patients. We examine common and rare genetic forms of predisposition to cancer, and in this setting it is very valuable to be able to recruit material from large cohorts.
The three collaborating research groups have different areas of expertise, which all three groups and the research has benefitted from.

5. **Publications resulting from the NCU research grant**

Aoude LG, Wadt K, Bojesen A, Crüger D, Borg Å, Trent JM, Brown KM, Gerdes AM, Jönsson G, Hayward NK. A BAP1 mutation in a Danish family predisposes to uveal melanoma and other cancers. *PLoS One* 2013 Aug 19;8(8)