Søknadsinformasjon

Utlysning	Nordic Cancer Union Research Grant, 2014
Søknad	Molecular epidemiology of familial ocular and cutaneous malignant melanoma; a Swedish-Danish collaboration
Søknadsid	155357
Innsendt av	Göran Jönsson

Oppgave: Progress report

Tilordnet	Göran Jönsson
Status	Arkivert
Opprettet	04.02.2016

RAPPORT

Briefly describe the project in a language understandable to non-scientists

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, 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 believe that tumor molecular information in tumors from familial melanoma may help to understand the development of the disease.

Summarize the major findings of the project

Thus far, we have firmly established that BAP1 is an 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. In addition, we are involved in the search for cutaneous melanoma susceptibility genes and a study on this was recently published in Journal of the National Cancer Institute. We are currently performing targeted DNA sequencing of 100 ocular melanomas which will be compared to 100 cutaneous melanomas. The targeted gene panel includes all genes previously reported as mutated in melanoma. The technical validation of this technique is ongoing and is a challenging as we are working with paraffin embedded tissue samples. In a second project we have investigated 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 was found between the

Describe how the project has increased our knowledge of the prevention, cause and/or cure for cancer

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

Outline how Nordic cooperation has added value to this project

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 technical and genomic expertise combined with extensive tumor cohorts has been very rewarding in this collaboration.
The three collaborating research groups have different areas of expertise, which all three groups and the research have benefitted from.

List the publications resulting from the NCU research grant

Author(s), title, journal and edition	PMID (8 digits, only if possible)
Wadt KA, Aoude LG, Johansson P, Solinas A, Pritchard A, Crainic O, Andersen MT, Kiilgaard JF, Heegaard S, Sunde L, Federspiel B, Madore J, Thompson JF, McCarthy SW, Goodwin A, Tsao H, Jönsson G, Busam K, Gupta R, Trent JM, Gerdes AM, Brown KM, Scolyer RA, Hayward NK. A recurrent germline BAP1 mutation and extension of the BAP1 tumor predisposition spectrum to include basal cell carcinoma. Clin Genet. 2014 Sep 15	25225168
Wadt KA, Aoude LG, Krogh L, Sunde L, Bojesen A, Grønskov K, Wartacz N, Ek J, Tolstrup-Andersen M, Klarskov-Andersen M, Borg Å, Heegaard S, Kiilgaard JF, Hansen TV, Klein K, Jönsson G, Drzewiecki KT, Dunø M, Hayward NK, Gerdes AM. Molecular characterization of melanoma cases in denmark suspected of genetic predisposition. PLoS One. 2015 Mar 24;10(3):e0122662	25803691
Aoude LG, Pritchard AL, ...,Gruis NA, Trent JM, Jönsson G, Bishop DT, Mann GJ, Newton-Bishop JA, Brown KM, Adams DJ, Hayward NK. Nonsense mutations in the shelterin complex genes ACD and TERF2IP in familial melanoma. J Natl Cancer Inst. 2014 Dec 13;107(2)	25505254
Staaf J, Harbst K, Lauss M, Ringnér M, Måsbäck A, Howlin J, Jirström K, Harland M, Zebary A, Palmer JM, Ingvar C, Olsson H, Newton-Bishop J, Hansson J, Hayward N, Gruis N, Jönsson G; Melanoma Genetics Consortium. Primary melanoma tumors from CDKN2A mutation carriers do not belong to a distinct molecular subclass. J Invest Dermatol. 2014 Dec;134(12):3000-3	24999598

Brief overview of expenditures for last year 1 vedlegg (Göran Jönsson NCU 2015.pdf)

Informasjon om vedlegg "Göran Jönsson NCU 2015.pdf"

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