NCU – Summative report for 2014

Report submission date: 20150401

Principal investigator: Joakim Dillner

Project title: Optimisation of HPV-based cancer control strategies

NCU grant received (€): 30 000

Project commencement and completion dates: 2014-01-01 to 2014-12-31 + ongoing extension.

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

   The Human Papillomavirus (HPV) is a major cause of cancer in man. HPV can be prevented by vaccination and the major HPV-caused cancer (cervical cancer) can be prevented by HPV-based screening programs. Finland and Sweden have made substantial contributions to development and validation of HPV vaccination and HPV-based screening and are now leading innovative work for optimising cancer control strategies targeting HPV (vaccination and screening), including randomised clinical trials and long-term follow-up studies using registries and biobanks. Joint Nordic work in this area will provide a stronger evidence base for optimal cancer control.

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

   During 2014, a major milestone has been the appointment on 2014-09-01 of Matti Lehtinen to a strategic visiting professorship at the Karolinska Institutet. This significantly facilitates the continued building of the collaboration that the NCU grant has enabled. The Finnish and Swedish teams have met for a thorough workshop on ongoing activities in HPV-based cancer control and the joint research described in the application has been started. Both groups have at the same time continued to be very active in this area. Major advances are: 1. The description of the nationwide cluster-randomized HPV vaccination trial in Finland (Lehtinen et al). 2. The first preliminary detection of a correlate of immunity for HPV vaccination (minimum antibody level required for protection) (Castellsague et al) 3. Thorough EU-wide description of the quality control used in the HPV vaccination programs and the cervical cancer screening programs in EU

(Elfström et al, a;b). 4. Continued standardisation and quality improvement of HPV testing services from the International HPV Reference Center (Bzhalava et al; Eklund et al). 5. Validation of an HPV monitoring strategy based on residual samples from Chlamydia trachomatis screening programs and the demonstration that HPV vaccination in Sweden is already leading to a decreased circulation of HPV in Sweden (Söderlund-Strand et al, a;b) 6. Long-term follow-up assessment of the importance of different HPV types for causing precursors to cervical cancer (Smelov et al; Elfström et al). 7. Development of a high-quality process for biobanking cervical screening samples (Perskvist et al, a;b) 8. Quantification of the additional benefit for protection of condylomas for each dose of HPV vaccines (Herweijer et al) 9. Establishing a baseline for HPV surveillance (Nygård et al) 10. Development and use of a mathematical model for optimising HPV vaccination strategies (Baussano et al). Finally, we have also been active in public debate, e.g. regarding new evidence suggesting that additional carcinogeniuc HPV types may exist (Arbyn et al) and regarding the importance of Translational Cancer Research for efficient cancer control (Wild et al). Thus, both groups have been very active in the project described in the application and the joint Nordic work is now well underway.

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

Targeting a cancer-causing infection (HPV) is an innovative way to prevent cancer. Our translational studies have shown that, while large health benefits are possible, they will not occur unless there is an ambitious program of translational cancer research that measures the effect of the interventions and optimises improvements of the preventive policies.
Specifically, the findings have implications for organisation of HPV vaccination programs, including age groups to target, gender-neutral vaccination and importance of second generation vaccines containing additional HPV types. On cervical screening, HPV-based strategies have been shown to be more effective, but new quality control measures need to be implemented in order to realise these health gains.

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

The Finnish group is one of the largest in the world in terms of HPV vaccination studies and clinical trials. The Swedish group is running the International HPV Reference Center and is contributing significantly to the field of HPV-based cervical screening. Jointly, the groups contain both all the necessary expertise and joint critical mass to make a decisive impact in the cancer control area. Research using registries and biobanks is also a strategic research area for the Nordic Countries.

5. Publications resulting from the NCU research grant

Characteristics of a cluster-randomized phase IV human papillomavirus vaccination effectiveness trial. **Lehtinen M**, Apter D, Baussano I, Eriksson T, Natunen K, Paavonen J, Vänskä S, Bi D, David MP, Datta S, Struyf F, Jenkins D, Pukkala E, Garnett G, Dubin G.
Vaccine. 2015 Mar 3;33(10):1284-90. doi: 10.1016/j.vaccine.2014.12.019.

Impact of smoking on the quantity and quality of antibodies induced by human papillomavirus type 16 and 18 AS04-adjuvanted **virus**-like-particle vaccine - a pilot study. Namujju PB, Pajunen E, Simen-Kapeu A, Hedman L, Merikukka M, Surcel HM, Kirnbauer R, Apter D, Paavonen J, Hedman K, **Lehtinen M**.
BMC Res Notes. 2014 Jul 11;7:445. doi: 10.1186/1756-0500-7-445.

Risk of newly detected infections and cervical abnormalities in women seropositive for naturally acquired human papillomavirus type 16/18 antibodies: analysis of the control arm of PATRICIA. Castellsagué X, Naud P, Chow SN, Wheeler CM, Germar MJ, **Lehtinen M**, Paavonen J, Jaisamrarn U, Garland SM, Salmerón J, Apter D, Kitchener H, Teixeira JC, Skinner SR, Limson G, Szarewski A, Romanowski B, Aoki FY, Schwarz TF, Poppe WA, Bosch FX, de Carvalho NS, Peters K, Tjalma WA, Safaeian M, Raillard A, Descamps D, Struyf F, Dubin G, Rosillon D, Baril L.
J Infect Dis. 2014 Aug 15;210(4):517-34. doi: 10.1093/infdis/jiu139.

Cervical cancer screening in Europe: Quality assurance and organisation of programmes.
Elfström KM, Arnheim-Dahlström L, von Karsa L, **Dillner J**.
Eur J Cancer. 2015 Mar 25. pii: S0959-8049(15)00224-5. doi: 10.1016/j.ejca.2015.03.008.

Organization and quality of HPV vaccination programs in Europe.
Elfström KM, **Dillner J**, Arnheim-Dahlström L.
Vaccine. 2015 Mar 30;33(14):1673-81. doi: 10.1016/j.vaccine.2015.02.028.

International standardization and classification of human papillomavirus types.
Bzhalava D, Eklund C, **Dillner J**.
Virology. 2015 Feb;476:341-4. doi: 10.1016/j.virol.2014.12.028.

Global improvement in genotyping of human papillomavirus DNA: the 2011 HPV LabNet International Proficiency Study.
Eklund C, Forslund O, Wallin KL, **Dillner J**.
J Clin Microbiol. 2014 Feb;52(2):449-59. doi: 10.1128/JCM.02453-13.

Change in population prevalences of human papillomavirus after initiation of vaccination: the high-throughput HPV monitoring study.
Söderlund-Strand A, Uhnoo I, **Dillner J**.
Cancer Epidemiol Biomarkers Prev. 2014 Dec;23(12):2757-64. doi: 10.1158/1055-9965.EPI-14-0687.

Evaluation of human papillomavirus DNA detection in samples obtained for routine Chlamydia trachomatis screening. Söderlund-Strand A, Wikström A, **Dillner J**.
J Clin Virol. 2015 Mar;64:88-91. doi: 10.1016/j.jcv.2015.01.008.

Long-term HPV type-specific risks of high-grade cervical intraepithelial lesions: a 14-year follow-up of a randomized primary HPV screening trial. Smelov V, Elfström KM, Johansson AL, Eklund C, Naucler P, Arnheim-Dahlström L, **Dillner J**.
Int J Cancer. 2015 Mar 1;136(5):1171-80. doi: 10.1002/ijc.29085.

Long-term HPV type-specific risks for ASCUS and LSIL: a 14-year follow-up of a randomized primary HPV screening trial. Elfström KM, Smelov V, Johansson AL, Eklund C, Naucler P, Arnheim-Dahlström L, **Dillner J**.
Int J Cancer. 2015 Jan 15;136(2):350-9. doi: 10.1002/ijc.28984.

The Process of Moving from a Regionally Based Cervical Cytology Biobank to a National Infrastructure. Perskvist N, Norlin L, **Dillner J**.
Biopreserv Biobank. 2015 Jan 19.

A complex intervention for workflow enhancement at the Swedish cervical cytology biobank. Perskvist N, Björklund C, **Dillner J**.
Biopreserv Biobank. 2014 Feb;12(1):69-73. doi: 10.1089/bio.2013.0068.

Association of varying number of doses of quadrivalent human papillomavirus vaccine with incidence of condyloma. Herweijer E, Leval A, Ploner A, Eloranta S, Simard JF, **Dillner J**, Netterlid E, Sparén P, Arnheim-Dahlström L.
JAMA. 2014 Feb 12;311(6):597-603. doi: 10.1001/jama.2014.95.

Targeting human papillomavirus to reduce the burden of cervical, vulvar and vaginal cancer and pre-invasive neoplasia: establishing the baseline for surveillance.
Nygård M, Hansen BT, **Dillner J**, Munk C, Oddsson K, Tryggvadottir L, Hortlund M, Liaw KL, Dasbach EJ, Kjær SK.
PLoS One. 2014 Feb 5;9(2):e88323. doi: 10.1371/journal.pone.0088323.

Upscaling human papillomavirus vaccination in high-income countries: impact assessment based on transmission model.
Baussano I, **Dillner J**, Lazzarato F, Ronco G, Franceschi S.
Infect Agent Cancer. 2014 Jan 20;9(1):4. doi: 10.1186/1750-9378-9-4.

Are 20 human papillomavirus types causing cervical cancer? Arbyn M, Tommasino M, Depuydt C, **Dillner J**.
J Pathol. 2014 Dec;234(4):431-5. doi: 10.1002/path.4424

Translational cancer research: balancing prevention and treatment to combat cancer globally. Wild CP, Bucher JR, de Jong BW, **Dillner J**, von Gertten C, Groopman JD, Herceg Z, Holmes E, Holmila R, Olsen JH, Ringborg U, Scalbert A, Shibata T, Smith MT, Ulrich C, Vineis P, McLaughlin J.
J Natl Cancer Inst. 2014 Dec 16;107(1):353. doi: 10.1093/jnci/dju353.