Søknadsinformasjon

Utlysning	Nordic Cancer Union Research Grant, 2015
Søknad	Optimisation of HPV-based cancer control strategies
Søknadsid	176670
Innsendt av	Joakim Dillner

Oppgave: Progress report

Tilordnet	Joakim Dillner
Status	Arkivert
Opprettet	10.02.2017

RAPPORT

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

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.

Summarize the major findings of the project

During 2016 several major advances on prevention of HPV-associated diseases, from both groups, have been accomplished. A selection of findings that have been reported during 2016:
1) The large phase III trial of bivalent HPV vaccine found no evidence of type replacement (Tota et al). A meta-analysis of global data, included from both the Swedish and Finnish groups, found only inconsistent results on type replacement (Mesher et al).
2) HPV vaccination before treatment of cervical lesions was found to prevent recurrence/development of new lesions (Garland et al).
3) Large-scale safety data on HPV vaccination found no increased risks (Lehtinen et al).
4) Very high risks for cervical precancer in case of HPV persistence for 6 years necessitates close follow-up (Elfgren et al).
5) Cancer risks after low-grade cytological abnormalities are age-dependent. For women below 28 years, a repeat smear is sufficient (Sundström et al).
6) Improved methods for registry-based follow-up of screening (Elfström et al), for measuring HPV antibodies (Faust et al) and for monitoring HPV type-specific disease burden (Lagheden et al).
7) HPV vaccination, with either vaccine, is effective in inducing antibodies among HIV-positive subjects (Faust et al).

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

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. The results have enabled quality control measures that need to be implemented in order to realise these health gains and have further optimised the use of gynecology resources for cancer preventive effect in the era of HPV-based screening.

Outline how Nordic cooperation has added value to this project

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. Jointly, the groups contain 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.
During 2016 three joint studies have been submitted (On mathematical modelling to estimate prevention of infection; on herd immunity when vaccinating boys; on long-term protection also against non-vaccine HPV types) and one manuscript (on effectiveness of HPV vaccination of boys). Two joint projects are well underway (on HPV serological measures of HPV vaccination effectiveness and on cervical screening among HPV vaccinated cohorts). In summary, the joint project has been very productive and has unquestionably produced new data of relevance for optimal cancer control.

List the publications resulting from the NCU research grant

Author(s), title, journal and edition	PMID (8 digits, only if possible)
Tota JE, Struyf F, Merikukka M, Gonzalez P, Kreimer AR, Bi D, Castellsagué X, de Carvalho NS, Garland SM, Harper DM, Karkada N, Peters K, Pope WA, Porras C, Quint W, Rodriguez AC, Schiffman M, Schussler J, Skinner SR, Teixeira JC, Hildesheim A, Lehtinen M; Costa Rica Vaccine Trial and the PATRICIA study groups. Evaluation of Type Replacement Following HPV16/18 Vaccination: Pooled Analysis of Two Randomized Trials. J Natl Cancer Inst. 2017 Jan 28;109(7). pii: djw300. doi: 10.1093/jnci/djw300.	28132019
Lehtinen M, Eriksson T, Apter D, Hokkanen M, Natunen K, Paavonen J, Pukkala E, Angelo MG, Zima J, David MP, Datta S, Bi D, Struyf F, Dubin G. Safety of the human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine in adolescents aged 12-15 years: Interim analysis of a large community-randomized controlled trial. Hum Vaccin Immunother. 2016 Dec;12(12):3177-3185. doi: 10.1080/21645515.2016.1183847.	27841725
Mesher D, Soldan K, Lehtinen M, Beddows S, Brisson M, Brotherton JM, Chow EP, Cummings T, Drolet M, Fairley CK, Garland SM, Kahn JA, Kavanagh K, Markowitz L, Pollock KG, Söderlund-Strand A, Sonnenberg P, Tabrizi SN, Tanton C, Unger E, Thomas SL. Population-Level Effects of Human Papillomavirus Vaccination Programs on Infections with Nonvaccine Genotypes. Emerg Infect Dis. 2016 Oct;22(10):1732-40. doi: 10.3201/eid2210.160675.	27648688
Garland SM, Paavonen J, Jaisamrarn U, ..., Lehtinen M, Dubin G; HPV PATRICIA Study Group. Prior human papillomavirus-16/18 AS04-adjuvanted vaccination prevents recurrent high grade cervical intraepithelial neoplasia after definitive surgical therapy: Post-hoc analysis from a randomized controlled trial. Int J Cancer. 2016 Dec 15;139(12):2812-2826.	27541373
Bosch FX, Robles C, Díaz M, Arbyn M, Baussano I, Clavel C, Ronco G, Dillner J, Lehtinen M, Petry KU, Poljak M, Kjaer SK, Meijer CJ, Garland SM, Salmerón J, Castellsagué X, Bruni L, de Sanjosé S, Cuzick J. HPV-FASTER: broadening the scope for prevention of HPV-related cancer. Nat Rev Clin Oncol. 2016 Feb;13(2):119-32. doi: 10.1038/nrclinonc.2015.146.	26323382
Elfgren K, Elfström KM, Naucler P, Arnheim-Dahlström L, Dillner J. Management of women with human papillomavirus persistence: long-term follow-up of a randomized clinical trial. Am J Obstet Gynecol. 2016 Nov 5. pii: S0002-9378(16)30978-4. doi: 10.1016/j.ajog.2016.10.042.	27825977
Sundström K, Lu D, Elfström KM, Wang J, Andrae B, Dillner J, Sparén P. Follow-up of women with cervical cytological abnormalities showing atypical squamous cells of undetermined significance or low-grade squamous intraepithelial lesion: a nationwide cohort study. Am J Obstet Gynecol. 2017 Jan;216(1):48.e1-48.e15. doi: 10.1016/j.ajog.2016.07.042	27457115
Lagheden C, Eklund C, Kleppe SN, Unger ER, Dillner J, Sundström K. Validation of a standardized extraction method for formalin-fixed paraffin-embedded tissue samples. J Clin Virol. 2016 Jul;80:36-9. doi: 10.1016/j.jcv.2016.04.016	27148635
Elfström KM, Sparén P, Olausson P, Almstedt P, Strander B, Dillner J. Registry-based assessment of the status of cervical screening in Sweden. J Med Screen. 2016 Dec;23(4):217-226.	27068429
Faust H, Eklund C, Sukvirach S, Ngamkham J, Dillner J. Sourcing of the WHO human papillomavirus type 18 international standards for HPV antibody levels. J Clin Virol. 2016 May;78:89-92. doi: 10.1016/j.jcv.2016.03.014.	27002710
Faust H, Toft L, Sehr P, Müller M, Bonde J, Forslund O, Østergaard L, Tolstrup M, Dillner J. Human Papillomavirus neutralizing and cross-reactive antibodies induced in HIV-positive subjects after vaccination with quadrivalent and bivalent HPV vaccines.Vaccine. 2016 Mar 18;34(13):1559-65. doi: 10.1016/j.vaccine.2016.02.019.	26896686
Wang J, Andrae B, Sundström K, Ström P, Ploner A, Elfström KM, Arnheim-Dahlström L, Dillner J, Sparén P. Risk of invasive cervical cancer after atypical glandular cells in cervical screening: nationwide cohort study. BMJ. 2016 Feb 11;352:i276. doi: 10.1136/bmj.i276.	26869597
Hortlund M, Sundström K, Lamin H, Hjerpe A, Dillner J. Laboratory audit as part of the quality assessment of a primary HPV-screening program. J Clin Virol. 2016 Feb;75:33-6. doi: 10.1016/j.jcv.2015.12.007.	26748032

Brief overview of expenditures for last year 1 vedlegg (NCU financial report 2016_170221.pdf)

NCU – Financial report for 2016

Report submission date: 2017-03-01

Principal investigator: Joakim Dillner

Project title: Optimisation of HPV-based cancer control strategies

NCU grant received (€): 50 000

Project commencement and completion dates: 2016-01-01 – 2016-12-31

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1. Brief overview of expenditures for 2016

	€
Salary (C. Lagheden, BMSc)	36498
Travel (C. Lagheden, BMSc)	1011
Materials	35
HPV-analyses	3107
Overhead costs	9349
Total:	**50000**