

Søknadsinformasjon

Utlysning	Nordic Cancer Union Research Grant, 2014
Søknad	Optimisation of HPV-based cancer control strategies
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Innsendt av	Joakim Dillner

Oppgave: Progress report

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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 2015 several major advances on prevention of HPV-associated diseases, from both groups, have been accomplished. The following findings have been reported:

- 1) The final results of the large phase III trial of bivalent HPV vaccine concluded that vaccination has a substantial impact on the overall incidence of high-grade cervical abnormalities associated with high risk HPV-16 and/or -18 (Apter et al).
- 2) A novel combined protocol based on mathematical modelling has been worked out, proposing that by expanding the indications for HPV vaccination and much greater use of HPV testing in screening programmes the potential to accelerate the decline in cervical cancer incidence is increased (Bosch et al).
- 3) Women with atypical glandular cells found at cervical screening have a substantial and long-term increased risk of cervical cancer. Better follow-up strategies will be needed. The study suggests that monitoring should include an additional tissue sampling within a year and a more active follow-up. A regionally centralized specialist care for the management of these women is another possibility (Wang et al).
- 4) As primary cervical screening with HPV is being introduced in many countries, strategies to ensure quality of routine HPV testing need to be well developed. The same audit strategy as that used for cytology is now suggested to be used routinely also for HPV testing. A higher sensitivity for HPV than for cytology is proposed as audit target.
- 5) Participation in HPV vaccination was found to also increase the interest for participating also in cervical screening (Herweijer et al).
- 6) HPV vaccination strategies based on catch-up vaccination of females and vaccination of males are effective for accelerating HPV prevalence reduction. Inclusion of routine male vaccination improves the resilience of vaccination programs (Elfström et al).
- 7) Stability of HPV antibodies after vaccination also on the long term was demonstrated (Nygård et al).
- 8) Among women with minor cytological abnormalities, HPV status is the most significant determinant of developing high-grade cervical disease during follow-up (Persson 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, but new quality control measures need to be implemented in order to realise these health gains.

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 and is contributing significantly to the field of HPV-based cervical screening. 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 2015 two highly innovative review articles on new endpoints for vaccination trials and on a new strategy to combine vaccination and screening were published with both PIs as co-authors. Both groups continued to be highly productive in their respective areas. Several joint studies are now in manuscript format. Also, Matti Lehtinen has hired a full time postdoctoral researcher in biostatistics, stationed at the Karolinska Institute in Sweden, further implying that the amount of joint work increases.

List the publications resulting from the NCU research grant

Author(s), title, journal and edition	PMID (8 digits, only if possible)
Lehtinen M, Apter D. Gender-neutrality, herd effect and resilient immune response for sustainable impact of HPV vaccination. <i>Curr Opin Obstet Gynecol.</i> 2015 Oct;27(5):326-32. doi: 10.1097/GCO.	26308204
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. <i>Nat Rev Clin Oncol.</i> 2016 Feb;13(2):119-32. doi: 10.1038/nrclinonc.2015.146.	26323382
Lowy DR, Herrero R, Hildesheim A; Participants in the IARC/NCI workshop on Primary Endpoints for Prophylactic HPV Vaccine Trials. Primary endpoints for future prophylactic human papillomavirus vaccine trials: towards infection and immunobridging. <i>Lancet Oncol.</i> 2015 May;16(5):e226-33. doi: 10.1016/S1470-2045(15)70075-6.	25943067
Apter D, Lehtinen M, Dubin G; HPV PATRICIA Study Group. Efficacy of human papillomavirus 16 and 18 (HPV-16/18) AS04-adjuvanted vaccine against cervical infection and precancer in young women: final event-driven analysis of the randomized, double-blind PATRICIA trial. <i>Clin Vaccine Immunol.</i> 2015 Apr;22(4):361-73. doi: 10.1128/CVI.00591-14.	25651922
Struyf F, Colau B, Wheeler CM, Naud P, Garland S, Quint W, Chow SN, Salmerón J, Lehtinen M, et al; HPV PATRICIA Study Group. Post hoc analysis of the PATRICIA randomized trial of the efficacy of human papillomavirus type 16 (HPV-16)/HPV-18 AS04-adjuvanted vaccine against incident and persistent infection with nonvaccine oncogenic HPV types using an alternative multiplex type-specific PCR assay for HPV DNA. <i>Clin Vaccine Immunol.</i> 2015 Feb;22(2):235-44	25540273
Lehtinen M, Nieminen P, Apter D, Paavonen J. Prevention of HPV disease burden. <i>Womens Health (Lond Engl).</i> 2014 Jul;10(4):341-3. doi: 10.2217/whe.14.35.	25259894
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. <i>BMJ.</i> 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. <i>J Clin Virol.</i> 2016 Feb;75:33-6. doi: 10.1016/j.jcv.2015.12.007. Epub 2015 Dec 24.	26748032
Herweijer E, Feldman AL, Ploner A, Arnheim-Dahlström L, Uhnöo I, Netterlid E, Dillner J, Sparén P, Sundström K. The Participation of HPV-Vaccinated Women in a National Cervical Screening Program: Population-Based Cohort Study. <i>PLoS One.</i> 2015 Jul 28;10(7):e0134185. doi: 10.1371/journal.pone.0134185.	26218492
Dillner J. Near full control of human papillomavirus vaccine types. <i>Lancet Infect Dis.</i> 2015 Nov;15(11):1251-2. doi: 10.1016/S1473-3099(15)00085-7.	26201301
Elfström KM, Lazzarato F, Franceschi S, Dillner J, Baussano I. Human Papillomavirus Vaccination of Boys and Extended Catch-up Vaccination: Effects on the Resilience of Programs. <i>J Infect Dis.</i> 2016 Jan 15;213(2):199-205. doi: 10.1093/infdis/jiv368. Epub 2015 Jul 3.	26142436
Nygård M, Saah A, Munk C, Tryggvadottir L, Enerly E, Hortlund M, Sigurdardottir LG, Vuocolo S, Kjaer SK, Dillner J. Evaluation of the Long-Term Anti-Human Papillomavirus 6 (HPV6), 11, 16, and 18 Immune Responses Generated by the Quadrivalent HPV Vaccine. <i>Clin Vaccine Immunol.</i> 2015 Aug;22(8):943-8. doi: 10.1128/CVI.00133-15.	26084514
Dillner J. Prevention of human papillomavirus-associated cancers. <i>Semin Oncol.</i> 2015 Apr;42(2):272-83. doi: 10.1053/j.seminoncol.2014.12.028.	25843731
Persson M, Elfström KM, Olsson SE, Dillner J, Andersson S. Minor Cytological Abnormalities and up to 7-Year Risk for Subsequent High-Grade Lesions by HPV Type. <i>PLoS One.</i> 2015 Jun 17;10(6):e0127444. doi: 10.1371/journal.pone.0127444.	26083247

Brief overview of expenditures for last year 1 vedlegg (NCU financial report 2015_160218.doc)