

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Erasmus MC
Project Title:	Oncolytic virotherapy as a treatment for pancreatic adenocarcinoma.
Abstract:	<p>Pancreatic adenocarcinoma is a devastating disease, with less than 5% of patients surviving after five years. Currently, only a small minority of patients (15%) can be cured by radical surgery at initial diagnosis, and thus new therapies are needed. The application of oncolytic viruses in cancer patients is a promising treatment strategy with encouraging results for a variety of tumors. Newcastle disease virus(NDV) is a naturally occurring oncolytic virus with proven clinical efficacy against several human tumor types. In our effort to develop oncolytic virotherapy using NDV for pancreatic cancer patients, we have constructed recombinant NDVs (rNDV) with immune modulatory genes as well as rNDV with increased virulence. These viruses were tested for immunomodulating and oncolytic efficacy in human pancreatic adenocarcinoma cells, mice models as well as in non-human primates for safety issues. However, the efficacy of this virus still needs improvement. Our aim is to construct a highly-virulent recombinant NDV harboring immune modulatory genes to target pancreatic tumors. You will be part of a team working on constructing new recombinant viruses and testing their (and other already available recombinant viruses) behavior in various <i>in vitro</i> and <i>in vivo</i> model systems as well as looking into their effect on signaling pathways.</p>
Requirements of candidate:	<p>Master: Yes.</p> <p>Background: You have a background in molecular and cellular biology and preferably basic knowledge of virology. You are experienced with molecular, biological and immunological laboratory techniques and are highly motivated to perform basic translational research. Experience with animal handling is desired but not necessary.</p> <p>IELTS Grade of 7.0 (minimal 6.0 per component) or TOEFL: 100 (minimal 20 per component).</p>

<p>Supervisor information:</p>	<p>Prof. dr. C.H.J. van Eijck (c.vaneijck@erasmusmc.nl) and Dr. B. van den Hoogen (b.vandenhoogen@erasmusmc.nl)</p> <p><u>Selected Publications Prof. dr. C.H.J. van Eijck</u></p> <ol style="list-style-type: none"> 1. Vitale G, van Eijck CH, van Koetsveld Ing PM, Erdmann JI, Speel EJ, van der Wansem Ing K, Mooij DM, Colao A, Lombardi G, Croze E, Lamberts SW, Hofland LJ. Type I interferons in the treatment of pancreatic cancer: mechanisms of action and role of related receptors. Ann Surg. 2007 Aug;246(2):259-68. 2. Erdmann J, Vitale G, van Koetsveld PM, Croze E, Sprij-Mooij DM, Hofland LJ, van Eijck CH. Effects of interferons alpha/beta on the proliferation of human micro- and macrovascular endothelial cells. J Interferon Cytokine Res. 2011 May;31(5):451-8. 3. Morak MJ, van Koetsveld PM, Kanaar R, Hofland LJ, van Eijck CH. Type I interferons as radiosensitisers for pancreatic cancer. Eur J Cancer. 2011 Sep;47(13):1938-45. 4. Booy S, Hofland LJ, Waaijers AM, Croze E, van Koetsveld PM, de Vogel L, Biermann K, van Eijck CH. Type I Interferon Receptor Expression in Human Pancreatic and Periampullary Cancer Tissue. Pancreas. 2014 Jul 28. 5. Booy S, van Eijck CH, Dogan F, van Koetsveld PM, Hofland LJ. Influence of type-I Interferon receptor expression level on the response to type-I Interferons in human pancreatic cancer cells. J Cell Mol Med. 2014 Mar;18(3):492-502. 6. Buijs PR, van Eijck CH, Hofland LJ, Fouchier RA, van den Hoogen BG. Different responses of human pancreatic adenocarcinoma cell lines to oncolytic Newcastle disease virus infection. Cancer Gene Ther. 2014 Jan;21(1):24-30. 7. Sideras K, Braat H, Kwekkeboom J, van Eijck CH, Peppelenbosch MP, Sleijfer S, Bruno M. Role of the immune system in pancreatic cancer progression and immune modulating treatment strategies. Cancer Treat Rev. 2014 May;40(4):513-22. <p><u>Selected Publications Dr. B. van den Hoogen</u></p> <ol style="list-style-type: none"> 1. Buijs PA, van Amerongen G, van Nieuwkoop S, Bestebroer T, van Run P, Kuiken T, Fouchier R, van Eijck R, and van den
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	<p>Hoogen BG. Intravenously injected Newcastle disease virus in non-human primates is safe to use for oncolytic virotherapy. Accepted Cancer Gene Ther. 2014</p> <p>2. de Wilde AH, Jochmans D, Posthuma CC, Zevenhoven-Dobbe JC, van Nieuwkoop S, Bestebroer TM, van den Hoogen BG, Neyts J, Snijder EJ. Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture. Antimicrob Agents Chemother. 2014 May 19. pii: AAC.03011-14.</p> <p>3. van den Hoogen BG, van Boheemen S, de Rijck J, van Nieuwkoop S, Smith DJ, Laksono B, Gultyaev A, Osterhaus AD, Fouchier RA. Excessive Production and extreme editing of Human Metapneumovirus Defective Interfering RNA is Associated with Type I Interferon Induction. J Gen Virol. 2014 Apr 23. doi: 10.1099/vir.0.066100-0.</p> <p>4. Buijs PR, van Eijck CH, Hofland LJ, Fouchier RA, van den Hoogen BG. Different responses of human pancreatic adenocarcinoma cell lines to oncolytic Newcastle disease virus infection. Cancer Gene Ther. 2014 Jan;21(1):24-30.</p> <p>5. Nguyen DT, de Vries RD, Ludlow M, van den Hoogen BG, Lemon K, van Amerongen G, Osterhaus AD, de Swart RL, Duprex WP. Paramyxovirus infections in ex vivo lung slice cultures of different host species. J Virol Methods. 2013 Oct;193(1):159-65.</p> <p>6. de Wilde AH, Ray VS, Oudshoorn D, Bestebroer TM, van Nieuwkoop S, Limpens RW, Posthuma CC, van der Meer Y, Bárcena M, Haagmans BL, Snijder EJ, van den Hoogen BG. MERS coronavirus replication induces severe in vitro cytopathology and is strongly inhibited by cyclosporin A or interferon-alpha treatment. J Gen Virol. 2013 Aug;94(Pt 8):1749-60.</p> <p>7. Schildgen V, van den Hoogen B, Fouchier R, Tripp RA, Alvarez R, Manoha C, Williams J, Schildgen O. Human Metapneumovirus: lessons learned over the first decade. Clin Microbiol Rev. 2011 Oct;24(4):734-54.</p> <p>8. Verkaik NJ, Nguyen DT, de Vogel CP, Moll HA, Verbrugh HA, Jaddoe VW, Hofman A, van Wamel WJ, van den Hoogen BG, Buijs-Offerman RM, Ludlow M, de Witte L, Osterhaus AD, van Belkum A, de Swart RL. Streptococcus pneumoniae exposure is associated with human metapneumovirus seroconversion and</p>
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	increased susceptibility to in vitro HMPV infection. Clin Microbiol Infect. 2011 Dec;17(12):1840-4.
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