Barts Cancer Institute
Queen Mary University of London

Cancer Gene Therapy

Why we focus on cancer gene therapy

Despite advances in our understanding of the processes involved in the development and progression of cancer, treatment options for many patients are limited and prognosis still remains poor. Surgery followed by chemotherapy or radiation therapy have been the main treatment options available for cancer patients, however many cancers are resistant to these standard therapies. At the BCI, we are developing experimental treatments that can target these resistant cancers. We are particularly focusing on development of gene therapy strategies to target pancreatic, prostate and ovarian cancers, which have mortality rates that have not significantly improved in the past two decades.

What we do

- The gene therapy program focuses on the development of engineered viruses that selectively replicate in and kill cancer cells (oncolysis).
- We use Adenovirus and Vaccinia virus, which we are modifying to enhance oncolytic efficacy against tumour cells, while maintaining safety. These viruses are used to deliver genes designed to influence the tumour environment and improve the efficacy of treatment.
- We are investigating the host immune response to both the virus and the tumour in order to maximise the potential of our viruses to boost anti-tumour immunity.
- Studies at the BCI also involve the determination of how genetic alterations in the tumour modulate viral potency and how the viruses interact with current therapies.
- We are identifying predictive biomarkers for virus activity in tumour cells and exploring how the inflammatory response to viral infection can be modified to augment virus-induced cell death.

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Key Publications

- Spurrell *et al*. STAT1 interaction with E3-14.7K in monocytes affects the efficacy of oncolytic adenovirus. *J Virol*. 2014 88(4): 2291-300
- Young AM *et al*. Failure of Translation of Human Adenovirus mRNA in Murine Cancer Cells Can be Partially Overcome by L4-100K Expression In Vitro and In Vivo. *Molecular Therapy* 2012; 20: 1676-88.
- Tysome *et al*. A novel therapeutic regimen to eradicate established solid tumors with an effective induction of tumor-specific immunity. *Clin Cancer Res*. 2012; 18(24):6679-89
- Adam *et al*. Synergistic and Selective Cancer Cell Killing Mediated by the Oncolytic Adenoviral Mutant AdΔΔ and Dietary Phytochemicals in Prostate Cancer Models. *Hum Gene Ther*. 2012; 23(9):1003-15.
- Miranda *et al*. Adenovirus-mediated sensitization to the cytotoxic drugs docetaxel and mitoxantrone is dependent on regulatory domains in the E1ACR1 gene-region. *PLOS ONE*. 2012; 7(10):e46617.
- Connell *et al*. Genomic DNA damage and ATR-Chk1 signaling determine oncolytic adenoviral efficacy in human ovarian cancer cells. *J Clin Invest*. 2011; 121: 1283-97.
- Salako, M.A., Kulbe, H., Ingemarsdotter, C.K., Pirlo, K.J., Williams, S.L., Lockley, M., Balkwill, F.R., McNeish, I.A. Inhibition of the inflammatory cytokine TNF-a increases adenovirus activity in ovarian cancer via modulation of cIAP1/2 expression. *Mol. Ther* (2011) 19 (3): 490-9

Who does the research

Prof. Nick Lemoine	Use of Adenovirus and Vaccinia virus to target pancreatic cancer
Dr .Gunnel Halldén	Exploiting synergistic efficacy of novel oncolytic adenoviruses and anticancer drugs in prostate and pancreatic cancers
Dr. Michelle Lockley	Inflammatory cytokines and oncolytic Adenoviruses in ovarian cancer
Dr. Yaohe Wang	Use of Adenovirus and Vaccinia virus to target pancreatic and head and neck cancer

Major Funders

- Cancer Research UK
- Medical Research Council
- Pancreatic Cancer Research Fund
- Pancreatic Cancer UK