NEWCASTLE DISEASE VIROTHERAPY:

A NOVEL IMMUNOTHERAPEUTIC APPROACH IN THE TREATMENT OF HIGH-GRADE GLIOMA

Carolien KOKS, PhD
BANO/BBTS first prize winner 2012
Summary of results obtained following BBTS prize – *in vitro* (1)

1. NDV can kill a range of human and murine HGG cell lines, and virus-induced tumor cell death can be of apoptotic or necrotic nature.
2. Induced tumor cell death is of immunogenic nature

**Surface Exposure**

**Calreticulin**

**Release of Danger Signals**

- **Cell Lysate**
  - 24 h, 72 h, 96 h
  - CTR, NDV
- **Conditioned Medium**
  - 24 h, 72 h, 96 h
  - CTR, NDV

**Secretion of ATP**

**Up-regulation of Tumor-Associated Antigens**

- **Controls**
  - 24 h, 72 h, 96 h
  - PMEL17
- **NDV**
  - 24 h, 72 h, 96 h
  - TRP-2, Actin

Summary of results obtained following BBTS prize – *in vitro* (2)
3. NDV treatment significantly prolongs overall survival and crucially depends on the induction of an adaptive antitumoral immune response that is tumor-specific and long-lasting.

**OVERALL SURVIVAL FOLLOWING NDV THERAPY**

![Graph showing overall survival following NDV therapy](image1)

**LOSS OF THERAPEUTIC EFFICACY IN IMMUNODEFICIENT ANIMALS**

![Graph showing loss of therapeutic efficacy in immunodeficient animals](image2)

**T CELL POPULATION SPECIFICALLY RECOGNIZING THE IMPLANTED TUMOR FOLLOWING OVT**

![Graph showing T cell population](image3)

**LONG-TERM SURVIVORS RESIST SECONDARY GLIOMA INDUCTION**

![Table showing tumor incidence](image4)

<table>
<thead>
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<th>Challenge of age-matched controls</th>
<th>Rechallenge of long-term survivors</th>
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Milestones supported by BANO/BBTS prize

1. **June 2013**: Best poster prize
   7th International Conference on Oncolytic Virus Therapeutics (Quebec)

2. **April 2014**: Best abstract for oral presentation prize
   8th International Conference on Oncolytic Virus Therapeutics (Oxford)

3. **August 2014**:

4. **December 2014**: completion of PhD project, title of Doctor in Biomedical Sciences

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Newcastle disease virotherapy induces long-term survival and tumor-specific immune memory in orthotopic glioma through the induction of immunogenic cell death


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Thank you !!
In my project I’m trying to implement nanoparticles in immune therapy for the treatment of GBM. The hypothesis is that these particles can replace ex vivo grown dendritic cells in immunotherapy.

After in vitro tests have shown uptake by dendritic cells and presentation of pieces of lysate in MHC context, preclinical testing in mice was performed. In a prophylactic setting, subcutaneous injection of lysate coupled to nanoparticles showed an increased median survival of treated mice as compared to untreated mice.

1) The BBTS price money made it possible to attend an international conference, the BioNanoMed 2015, where I was able to present my results to and discuss them with authorities in the nanotechnology field.

Topics including Nanomaterials for Biomedical Applications & Regenerative Medicine; Nanotechnology for Detection, Diagnostics, Therapeutics & monitorings; NanoPharmaceuticals & Drug Delivery Nanotechnology; and Advances in Nano-Oncology. It was during the last session that I presented my data.

2) This autumn I’m planning to go to another conference which will be more in the scope of cancer immunotherapy.
Improving the immunogenicity of whole tumor antigen preparations to enhance the efficacy of tumor antigen-pulsed DC vaccines for the treatment of high-grade glioma

My project focuses on ameliorating the immunogenicity of the death tumor cells:
1) By irradiating the death tumor cells
2) By inducing a special type of cell death, i.e., immunogenic cell death, by treating the cancer cells with hypericin-based photodynamic therapy

Publications:
For part 1: In submission for Onco-Immunology; *Irradiation of necrotic cancer cells, employed for pulsing dendritic cells (DCs), potentiates DC vaccine-induced antitumor immunity against high-grade glioma*
For part 2: In preparation for Science Translational Medicine; *Immunotherapy with dendritic cell vaccines based on immunogenic cell death provides unprecedented survival benefit against high grade glioma*

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Thanks to the BANO/BBTS prize...

- I had/have the opportunity to present my data at the:
  - Annual SITC (Society for Immunotherapy of Cancer) meeting in Washington (Poster presentation)
  - Annual CIMT (Cancer Immunotherapy) meeting in Mainz (Poster presentation)