Abstract

Title:
Prerequisites for Immunotherapy in Nasopharyngeal Cancer

Background:
Nasopharyngeal cancer (NPC) is frequently associated with Epstein-Barr virus (EBV). Tumour cells in EBV-driven NPC invariably express EBV antigens, which makes NPC a possible target disease for immunotherapeutic treatment. The presence of Epstein–Barr virus-Encoded small RNAs (EBERs) within the tumours is used for verification of EBV-driven NPC. In active immunotherapy, activation of antigen-presenting Dendritic cells (DCs) is essential. DCs have earlier been shown to be present within NPC but data is limited. In activating DCs an appropriate co-activation is needed. This can be obtained through the use of adjuvants. Poly(γ-glutamic acid)-graft-L-phenylalanine ethylester (γ–PGA-Phe) nanoparticles (NPs) are biodegradable nanoparticles capable of functioning as antigen carriers and adjuvants.

Methods and results:
In the first study (published) γ–PGA-Phe NPs administered on rat middle ear mucosa in vivo was shown to produce a dose and time-dependent inflammatory response characterized by generation of pro-inflammatory cytokines (IL-1α, IL-1β, IL-6, MIP-1α, and TNF-α), similar to a type-1 response and with associated histopathological changes.

In the second study (submitted) untreated fresh NPC biopsies (n=5) were subjected to multicolor flow-cytometry focusing on DC subtype markers. Different subpopulations; CD123+ plasmacytoid DCs (pDCs), CD1c+ myeloid DCs (mDCs), CD141+ mDCs, and CD1c−CD141− mDCs were observed. A high frequency of CD1c+ mDCs expressing CD207 was noted; this C-lectin receptor may be targeted to facilitate cross-presentation of antigen and aid cell-mediated anti-tumor effects.
In the third study (ongoing) untreated NPC biopsies from a well-defined historical NPC cohort (n=49) is re-evaluated (histopathology, classification, EBER-status). A quantification of intra-tumoural EBV-DNA has been performed and the results are planned to be compared to EBER-status, tumour stadium and outcome. Finally, a more thorough map of the intra-tumoural distribution of various immune cells and their pattern recognition receptors (PRRs) will be obtained with the help of immunohistochemistry techniques.

Further studies are currently being planned.

**Significance:**

NPC is a serious disorder with varying survival and expected severe side-effects from given treatment. The present studies will add to the knowledge of the disease providing prerequisites for therapy improvement.

**Publications:**
