Prof. Dr. Dirk de Ruysscher

Immune therapy with stereotactic ablative radiotherapy (SABR) – partners in crime?

Shortly after the discovery of the mammalian anticancer immune system in the last century, science started to unveil the effects of ionising radiation to the immune system, as well. Early experiments showed the decrease or even the eradication of T cells in tumours after the treatment with ionizing radiation. These early insights into the interplay of radiation therapy and subsequent cancer-related immune response were followed by manifold further investigations: Application of ionising radiation results in a strong activation of beneficial anti-tumour immune responses, for example the reprogramming of tumour-associated macrophages, activation of dendritic cells, upregulation of tumour-associated antigens and the induction of immunogenic cell death. Additionally, ionising radiation has been shown to cause T cell priming, trafficking and infiltration into malignant tissues, an effect which can be imagined as an *in situ* vaccination. One approach of combining radio and immunotherapy is the application of immunocytokines in order to specifically target tumour tissue with IL-2. IL-2 is an interleukin which has been shown to downregulate tumourigenic processes. It is attached to L19-antibody, a carrier being directed to fibronectin and subsequently enriched at sites of angiogenesis, thus tumourigenic areas. In combination with ionising radiation, IL-2 therapy caused the curation of carcinogenic animals (Rekers et al., Nature Communications 2015). Although these effects have been monitored in a preclinical study, a proof-of-concept study has already been conducted in patients (Golden et al., Lancet Oncology, 2015).

However, although ionising radiation as a sole therapy approach triggers anti-cancer immune responses initially, negative feedback occurs. For example, pro-tumourigenic regulatory T cell responses are dampened upon radiotherapy, but may increase again within a few days. Hence, the combination of radio- and immunotherapy appears favourable. The mechanisms underlying the negative re-occurrence of pro-tumourigenic processes requires further investigation.

Anna Broich