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Nanoparticle Modulation of therapeutic Response to Radiation Therapy

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Venue of Talk: Colloquium of the Department of Chemical and Biological Engineering (CBI)
Thursday, 29th June 2023, 16.00-17.30, Kurssaal KSI, Cauerstr. 4, 91054 Erlangen (Südgelände)

Abstract:

Metal nanoparticles are in clinical trials and have market approval in Europe. Scope exists to further their mechanistic understanding and improve their action for enhancing the therapeutic ratio in radiotherapy treatment.

We have been investigating nanoparticle structure-function relationships in a radiotherapy context down to the single cell level. To pre-clinically validate two lead nanoparticle formulations in sensitizing triple negative breast cancer to radiotherapy and assess mechanistic action.

A variety of in-vitro studies have been conducted to understand nanoparticle uptake across cell populations (using cross-correlative confocal microscopy and synchrotron X-ray fluorescence), effects on cell metabolism (fluorescence lifetime microscopy), and the nanoparticle-proteome nexus. Radiobiological response studies have advanced to in-vivo studies with immunocompetent Balb/c mice bearing 4T1 tumours as a model of triple negative breast cancer. In a partnership with the Royal Adelaide Hospital we utilise clinical facilities and mice were irradiated with 4x4Gy fractions from a 6 MV linac after systemic administration of nanoparticle formulations functionalised to target cancer cells. Tumour volume and survival were measured for control arms, and radiotherapy treatment with/out receiving nanoparticles. Mechanistic studies monitored metastatic burden in lung and dissociated tumours were characterized at the single cell level with mass cytometry to identify which cell populations the nanoparticles associate and identify manipulation of the tumour cell-composition.

Nanoparticles were associated with a range of cell types despite being targeted to cancer cells and instigated remodelling of the tumour microenvironment. Median time of animal survival improved by 30% and metastatic burden in lungs was reduced by 70% through use of a nanoparticle radiosensitizer in conjunction with radiotherapy compared to radiotherapy alone.

While the initial premise of high atomic number nanoparticle radiosensitization was based on physics theories, the nano-bio interaction appears to ultimately dominate radiobiological response.

Clinical use of nanoparticle radiosensitizers is likely to increase and understanding their mechanistic modes of action will aid in optimizing formulations to promote the best clinical outcomes.

There will be opportunity for discussions after the talk with Beer and Pretzels !!