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Impact of Ionising Radiation on Inflammation and Carcinogenesis

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Recent research revealed that DNA-damage responses and inflammatory reactions can be interconnected. Radiation of distinct doses, qualities and dose rates thereby impact on tissue microenvironments and induce tissue damage. The latter is alerted by release of immune modulating danger signals, the so called damage associated molecular patterns (DAMPs). Of note is that a pre-existing inflammatory status affects the radiation-induced immune response and the shape of dose response: low and intermediate dose of radiation exert anti-inflammatory effects and higher doses of radiation foster acute inflammation and anti-tumour reactions.

The talk will focus on how low and intermediate doses of irradiation impact on the inflammatory phenotype of macrophages, being key players in initiation and resolution of inflammation, and consecutively on T cell responses and the phenotype of dendritic cells (bystander effects). In vivo experiments revealed that the inflammatory and erosive area in human-TNF-alpha transgenic mice, that develop a chronic polyarthritis, is reduced by intermediate doses of ionising radiation. Then, the role of DAMPs such as HMGB1, ATP and Hsp70 in the induction of non-targeted effects of ionising radiation alone and especially with further immune stimulation will be outlined. Systemic anti-tumour cell immune responses are inducible by modification of the phenotype of tumour cells and their microenvironment by radiation.

The shape of dose response regarding modulation of inflammation and immune responses is manifold, since many immunological pathways are affected by radiation. Since radiation modulates inflammation that impacts on non-cancer diseases, carcinogenesis and anti-tumour responses, future work has to be performed examining mechanisms that couple radiation-induced DNA-damage responses and consecutive immune modulations.