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New concepts and challenges in radio-immunotherapies

Udo S. Gaipl*

Translational Radiobiology, Department of Radiation Oncology, Uniklinikum Erlangen, Erlangen, Germany

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***Correspondence:** Udo S. Gaipl Translational Radiobiology, Department of Radiation Oncology, Uniklinikum Erlangen, Erlangen, Germany
E-mail: udo.gaipl@uk-erlangen.de
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Abstract

During the last decades it has become obvious that radiation has manifold biological consequences ranging from DNA damage to local and systemic immune alterations. Thereby, it has taken a long time to understand how local radiation exposure leads to immune changes that are not just immune suppressive ones. Cells that are exposed to radiation react with a stress response and, when the trigger is strong enough, undergo cell death. In these processes the cells interact with the immune system with consequences on molecular, cellular and organism level. In the talk connection between radiation-induced DNA damage, DNA damage responses and immunological consequence will be elucidated. The dependence of immunological consequences of radiation exposure on dose, dose rate (FLASH-radiotherapy), fractionation, and the tumor micro-environment including lymph nodes will be outlined. Immune signatures being prognostic for radio-immunotherapies will be introduced and challenges to make use of such signatures for understanding radiation-specific immune alterations that persist will be discussed, taking also into consideration the dynamics of immune reactions. Ultimately, it should become clear that radiation and the immune system belong together and that radiation-induced immune changes can and should be used therapeutically for solid tumors in combination with distinct immune therapies such as immune checkpoint inhibition, vaccination and CAR T cell therapy.