

Radiation dose-effect relationship: an old story? (1)

Monday, September 9, 2024 9:45 AM (1 hour)

The DNA centered view of radiobiology was comforted in the last century by the finding that the level of unrepaired DNA lesions can be correlated with the cell sensitivity to radiation. This drove efforts to improve tumor cell killing, by focusing on enhancing tumors radiation dose and producing deleterious DNA damage. However, events occurring in the cytoplasm or at the cell membrane also have consequences on nuclear DNA. The contribution of these extranuclear effects to cell death needs to be accurately assessed.

In addition, a paradigm shift that recognizes the essential role of the immune system in cancer development and progression has become broadly accepted. Several clinical cases support revisiting the radiobiology DNA-centered view, by demonstrating for instance that targeted alpha therapy is efficient in quite large tumors, which sizes are beyond the radiation range, with biological effects observed also away from irradiated cells. These distant effects are called bystander effects when occurring at short distance ($< 1\text{mm}$), and systemic effects when occurring at much longer distance, implicating the immune system. Altogether, these findings showed that cells can die without receiving any radiation dose, and that a more complex and integrated view of radiobiology is required. Finally, these immune stimulatory effects of radiation have become clinically relevant in the current era of cancer immunotherapy, rendering systemic responses in patients an attainable aim.

The first hour of these lectures will focus on the in vitro aspects and its limitations entitled “From cancer cell to tumor microenvironment”, and the second hour will focus on the in vivo aspects entitled “From rodent to clinical radiobiology”.

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