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Irradiation of mouse mammary gland stimulates the migration of triple negative breast cancer cells and development of lung metastases

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Emergence of migratory phenotype is believed to be the consequence of acquired mutations in cancer cells. Alone, this mutation-based hypothesis cannot explain the progression of all tumors. Since inflammation can be associated with the promotion of metastases, it is important to determine whether radiation-induced inflammation in healthy breast could stimulate the migration of cancer cells and ultimately favor the formation of metastases. Our study was done with the D2A1 breast cancer cells which are triple negative (TNBC), a subgroup of breast cancer at higher risk of early recurrence. A single mammary gland of Balb/c mice was irradiated with 4 fractions of 6 Gy given at 24h interval. After the last irradiation, D2A1 breast cancer cells were implanted close to the nipple. This protocol eliminated confounding effects that could occur by irradiating the tumor and the mammary gland at the same time, such as selection of a subpopulation of cancer cells that could be more likely to migrate. Pre-irradiation of mammary gland before implantation increased the migration of cancer cells, the quantity of circulating cancer cells and the number of lung metastases. These adverse effects were associated with induction of pro-inflammatory molecules such as COX-2 and IL-6. In conclusion, we propose an alternative mechanism to explain the higher risk of early recurrence for TNBC based on pro-migratory molecules induced by radiation.

Biography

Benoit Paquette is a radiobiologist who studies the biological consequences of radiation therapy. His research is oriented towards improving radiotherapy for brain and breast cancer, as well as preventing cancer cell invasion induced by radiation. His team has pioneered the use of the Gamma Knife for irradiating localized patches of cortex in rodents. Two clinical trials based on results obtained in his laboratory are currently underway in brain tumor patients. He is the Director of the Department of Nuclear Medicine and Radiobiology, University of Sherbrooke, and he is the Vice-president of the International Society of Radiobiology in French Language.

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