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Biography

Chann Lagadec has spent five years as a Post-doctoral fellowship in Dr. Pajonk'lab, a pioneer in CSC research field. Within the time at UCLA in the Radiation Oncology Department, he got trained in CSC and was the first to demonstrate the phenotype plasticity of CSC induced by radiation treatment. Since 2012, he set up his own team in the INSERM U908 lab in Lille, France, where he studies the molecular mechanisms involved in the reprogramming process. He develops molecular tools and an animal model to track and characterize CSC and iCSC. His domain of interest enlarges recently to understand the potential role of reprogramming in tumor dormancy and metastasis development.

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Note:

INFLAMMATORY CYTOKINES, INDUCED BY IONIZING RADIATION, REPROGRAM NON-TUMORIGENIC CANCER CELLS INTO CANCER STEM CELLS IN BREAST CANCER

Identification of cancer stem cells (CSC) in solid tumours – with self-renewal, multipotency, tumorigenesis, and therapy resistance capacities – has opened path to new targeting therapeutic approaches. However, CSC targeting alone might not be sufficient to eradicate a tumour. Indeed, recent studies showed that cancer cells are plastic, and conventional therapies, such as radiotherapy, can lead to cancer cells (non-CSC) reprogramming into iCSC (induced-CSC). The goal of our work is to identify the molecular mechanisms responsible for treatment-induced CSC emergence. First, we have shown that conditioned media from irradiated non-CSC is sufficient to induce iCSC reprogramming. These results suggest that cell plasticity might be actively regulated by diffusible factors secreted by irradiated cells. By using proteins arrays and ELISA, we demonstrated that the secretion of a specific cocktail of chemokines is induced by ionizing radiation, such as CXCL1 and CCL5. Interestingly, recombinant CXCL1 and CCL5 treatments increase the sphere forming capacity (SFC) of isolated non-CSC treated population. Concomitantly, treatment with neutralizing antibodies targeting CXCL1 and CCL5 leads to a decreased CSC number (ALDH+ cells). Most importantly, treatment with neutralising antibodies through radiation treatment of xenograft in SCID mice double the survival time of the mice. Preclinical study show predictive value of CXCL1 and CCL5 expression. We also studied the expression of the corresponding chemokines receptors, by flow cytometry. First, we saw that reprogrammable ALDH- cells are enriched for CXCL1 and CCL5 receptors expressing cells compare to unsorted population or ALDH+ population (CSC). We analysed the reprogramming potential of isolated ALDH-/receptor-positive cells versus ALDH-/receptor-negative cells. The ALDH-/receptor-positive-derived cell population is more able to form spheres and overcomes the receptor-negative-derived population when the two populations are mixed and tested for their sphere forming capacity. The use of pharmacological inhibitors against the receptors induce a slight decrease of CSC. Taken together, our results indicate the involvement of chemokines, in particular CXCL1 and CCL5, in the reprogramming mechanism.