

## Immune system activation through Carbon ion irradiation (Ab-scopal effect)\*

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Metastasis and tumor recurrence are the main cancer poor prognosis cause. Carbon Ion radiation is one of the most innovative, powerful and for sure the less invasive methods for cancer treatment. Besides the well-known advantages derived from the better capacity to kill the tumor cells and to spare the healthy tissues around, tumor irradiation has been shown to produce in a statistical low number of cases not only the neoplastic malignant shrinking but also the shrink of metastasis located out of the irradiation field, a rare phenomenon known as ab-scopal effect. Despite the effect is extremely rare, its consequence on the cancer can be stunning, leading to the disappearance of malignant growths throughout the entire body also about the distal metastasis out of the irradiation field [1]. Study about how this happen is still on going, but is absolutely clear now that the immune system, and more specifically dendritic cells and T cells, is involved. Radiation would produce a complete rearrangement of the membrane cell antigens. This new "antigens set" would then be recognized by the dendritic cells as "not self" anymore and targeted by T cells [1]. The purpose of our project is to study the carbon irradiation effects on the immune-system.

C3H female mice were used for our experiments. Seven days before irradiation, 106 squamous carcinoma cells (SCCVII) were injected in both mice posterior limbs. Mice left tumor were irradiated at day zero with a 15 Gy SOBP of 6 cm at HIMAC-NIRS facility. PCR array (Qiagen immune and adaptive response pathway), blood PGE2 and HMGB1 ELISA and immuno-hystochemistry analysis at days 9, 16 and 25 of both tumor has been done (irradiated tumor and the abscopal tumor out of the irradiation field).

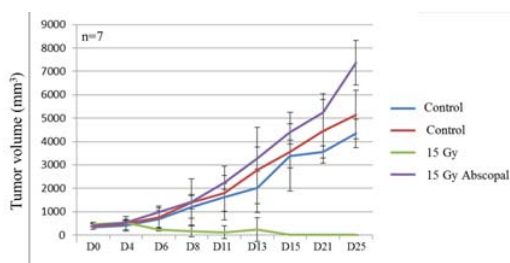


Figure 1: Twenty-five days tumor growth curve.

Twenty-five days after irradiation the ab-scopal tumor

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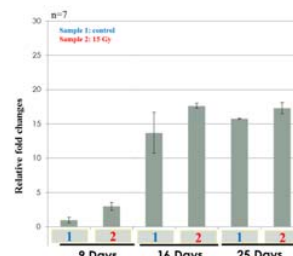


Figure 2: PGE2 ELISA relative fold changes for in vivo C3H female mice experiments after 9, 16 and 25 days. All the results have been normalized for the 9 days control.

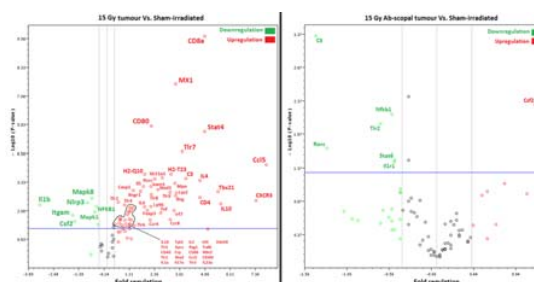


Figure 3: PCR array results of 15 Gy irradiated tumor (left) compared with the 15 Gy abscopal (right).

(out of the irradiation field) was bigger than the tumor control (Fig 3). This could be because of the increased PGE2 release after irradiation that could produce the Phoenix rising effect [2]. Furthermore PGE2 could be responsible for the T regulatory cells increase a well-known immune suppressor kind of cells [3]. ELISA blood analysis has been done (Fig 4). Nine days after irradiation the PGE2 was 3-4 times higher than the control. Sixteen and 25 days after irradiation the PGE2 level is not significant different from the control. Anyway PGE2 release level has not been normalized for the tumor mass. PCR array have been used for a gene expression array pathway. Clear immune-system activation has been found in the 15 Gy irradiated tumor while no activation has been found for the abscopal tumor.

## References

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