

## Crosstalk between Mesenchymal Stem Cells and tumor cells: the role of inflammation

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Mesenchymal Stem Cells (MSCs) are self-renewal multipotent cells that can be isolated from different adult tissues. There is a growing interest in the role exerted by MSCs in cancer progression. MSCs exhibit a marked tropism for tumors and participate to the creation of the stroma and related inflammation, which has a critical role in carcinogenesis, progression and metastasis. Nevertheless, while many studies showed that MSCs promote tumor progression and metastasis, others reported that MSCs suppress tumor growth. These contradictory results may be due to the origin of the MSCs, their degree of differentiation, the tumor model and other factors that are not yet elucidated. Aim of this work was to establish the role of the paracrine effect exerted by MSCs isolated from inflamed (I-MSCs) and control (C-MSCs) tissues towards human MCF7 and KI-JK cell lines, respectively derived from a breast cancer and an anaplastic large T cell lymphoma (ALCL). After stemness characterization, MSCs were indirectly co-cultured with MCF7 or KI-JK for 7 days; subsequently the proliferation rate and the expression of specific genes were tested. Genes were selected according to their role in inflammation and cancer previously reported in literature and explicate their action by different mechanisms: chemokines with pro-(CXCL2, CXCL9) or anti-angiogenic effect (CXCL10); chemokines (CCL2, CXCL12, CXCL5) for the recruitment of myeloid-derived suppressor cells (MDSCs); interleukins distinctive for chronic (IL2, IL4) and acute (IL8, IL16) inflammation; cytokines belonging to the Th2 subset (CCL22, IL13, IL22, CCL17, CCL18); cytokines (IL6, IL10 and TGF $\beta$ 1) involved in the manipulation of the antigen-presenting cells function. Our data confirm a role of MSCs in cancer; an increase of pro-angiogenic chemokines as well as of interleukin related to acute phase of inflammation, a general switch of the T cell response from the Th1 cell subset to the Th2 subset and the induction of MDSCs were observed. Surprisingly, these effects have been mainly found in both cancer cell lines after co-culture with C-MSCs; it may mean that I-MSCs, suffering of chronic inflammation, are less responsive than C-MSCs to new stress/stimuli. Further experiments will be necessary to better address the role of MSCs and inflammation on cancer progression; nevertheless, this study highlight as MSCs are not simply guardian but active actors in cancer fate.

### References

- [1] Orciani et al. (2013) The response of breast cancer cells to mesenchymal stem cells: a possible role of inflammation by breast implants. *Plast Reconstr Surg.* 132:899; doi: 10.1097/01.prs.0000434401.98939.60.
- [2] Elinav et al. (2013) Inflammation-induced cancer: crosstalk between tumours, immune cells and microorganism. *Nat Rev Cancer* 13: 759; doi: 10.1038/nrc3611.

### Keywords

MSCs; inflammation; paracrine effect; tumours.