

## The inflamed microenvironment: role on MSCs immunobiology and cancer

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Inflammation and cancer are an inseparable binomial. The majority of cancers are triggered by somatic mutations and environmental factors with a common element: inflammation. Inflammation creates a microenvironment in which neoplastic cells can profit from the trophic factors secreted by inflammatory cells, useful to interfere with the anti-tumor response. Among the others, mesenchymal stem cells (MSCs) participate to microenvironment creation by a strong paracrine effect. The linkage between MSCs and inflammation is bidirectional: the inflamed microenvironment affects the complex MSCs immunobiology, but also MSCs can sustain inflammation. Here, we tried to clarify the influence of inflammation on the immunobiology of MSCs and deepen the paracrine effect of MSCs on tumor growth. MSCs were isolated from periprosthetic capsule caused by breast implant, affected by inflammation (I-MSCs). The contralateral part of the same patient, not inflamed, was used as control (C-MSCs). A panel of selected cytokines were analyzed by Real-Time PCR and ELISA. The cytokines expression was different in I-MSCs compared to C-MSCs, revealing that inflammation affects MSCs immunobiology. Then, C- and I-MSCs were indirectly co-cultured with MCF7 cells from breast adenocarcinoma. New analyses on proliferation rate and cytokines expression were performed. C- and I-MSCs gave almost the same results. The over-secretion of all the cytokines referred to the Th1 pathway and the decrease of those belonging to the Th2 pathway revealed the absence of a switch from Th1 to Th2 important to induce a chronic inflammation. The levels of TGF- $\beta$  and G-CSF linked to the skill to damage the antigen-presenting cell function were decreased. In conclusion, even if MCF-7 proliferation increased after co-culture with I-MSCs, MSCs-derived paracrine effect does not sustain breast adenocarcinoma. These results absolve the breast implants from the insult to enhance adenocarcinoma onset.

### References

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### Keywords

Inflammation; mesenchymal stem cells; cancer; immunobiology.