

## Breast Implant Associated-ALCL: a possible role for inflammation and Mesenchymal Stem Cells

Monia Orciani, Miriam Caffarini, Raffaella Lazzarini, Giulia Sorgentoni, Roberto Di Primio

Department of Clinical and Molecular Sciences- Histology; Università Politecnica delle Marche, 60126 Ancona, Italy

In the last years, the use of breast implants has been cyclically associated with an enhanced risk of Anaplastic Large Cell Lymphoma (ALCL) onset (Breast Implant Associated-ALCL, BIA-ALCL). For the development of other different tumors, the involvement of Inflammation has been suggested. The use of breast implants often breaks out to inflammation, as proved by the formation of the periprosthetic capsule. Tumors take advantage of inflammation to influence and interfere with the host immune response by secreting multiple factors, and their onset and survival is in turn affected by the he paracrine effects from mesenchymal stem cells (MSCs). Our previous work [1] revealed the MSCs derived from inflamed capsules are different from those derived from control tissues. Here we deepen this dysregulation and test, by the criteria evinced from Elinav [2], if MSCs from inflamed tissues may exert a different paracrine effect (immunobiology) that in turn increases the risk of ALCL development.

MSCs derived from both inflamed (I-MSCs) and control (C-MSCs) tissues were isolated and co-cultured with an ALCL cell line. Proliferation rate and the expression of selected cytokines related to inflammation were tested.

Our results show that I-MSCs secrete higher levels of cytokine related to chronic inflammation than C-MSCs. After co-cultures with KI-JK cells, C- and I-MSCs show the same variation in the cytokines expression, with an increase of IL2, IL4, IL5, IL10, IL13, TNF- $\alpha$ , TGF- $\beta$  and G-CSF. Proliferation of ALCL cells was not influenced by co-cultures.

In conclusion our results state: i) inflamed microenvironment affects the immunobiology of MSCs modifying the expression of cytokines related to inflammation; ii) the paracrine effects exerted by MSCs on ALCL cells is not influenced by inflammation. ALCL cells are able to manipulate the MSCs immunoregulatory properties to evade the host immune control but this ability is not associated with inflammation and the question about BIA-ALCL is not proved by our experiments.

### 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* 132:899e-910e
- [2] Elinav et al. (2013) Inflammation-induced cancer: crosstalk between tumours, immune cells and microorganisms *Nat Rev Cancer* 13: 759-771.

### Keywords

Inflammation, mesenchymal stem cells, breast implants, ALCL