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POSTER PRESENTATIONS - PROFFERED ABSTRACTS | AUGUST 15 2020

Abstract 333: Development of a biomimetic 3D scaffold to study breast cancer bone metastasis FREE

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Cancer Res (2020) 80 (16_Supplement): 333.

https://doi.org/10.1158/1538-7445.AM2020-333

Abstract

Cancer metastasis is the leading cause of morbidity and cancer-related death. Bone is one of the most favored sites of metastatic spread, particularly from breast cancer. However, our understanding on how the host tissue can impact tumor growth is weak. This is hampered by the lack of a reliable *in vitro* model ables to replicate the complex microenvironment. Indeed, bone microenvironment provides physical support to cells but it can also affect cell behaviour and phenotype.

We developed a hybrid 3D collagen-based scaffold functionalized with hydroxyapatite material (HA) in order to mimic natural bone features. Scaffolds were synthesized in our laboratory through collagen solution mixed and cross-linked with hydroxyapatite. Then, we cultured MDA-MB-231, a triple negative breast cancer cell line and MCF-7, an ER+ breast cancer cell line in collagen or hybrid scaffold, in order to evaluate how extracellular matrix affects cell behavior. Cell growth was evaluated by MTT cell-proliferation assay in a time course analysis. Moreover, we evaluated cell morphology and cell disposition within the scaffold by confocal microscopy. Finally, gene profiling was evaluated by qRT-PCR.

MCF-7 cells acquire an organized and linear structure, whereas MDA-MB-231 an epithelial-like morphology, when cultured in hybrid scaffold. MDA-MB-231 cells proliferate faster than MCF-7 in both models. However, this is not affected by hydroxyapatite since the proliferation rate is similar when cells are cultured in collagen or hybrid scaffold.

MDA-MB-231 grown in hybrid scaffold show a significant increase in *RANKL*/*OPG* ratio, pathway strictly involved in bone homeostasis. Moreover, they show a significant increased expression in *JAG1*, *MMP2* and *SNAIL1*. For MCF-7, we observe a decrease in *CDH1*/*VIM* expression ratio

and a significant decrease in *OPG*, osteoclastogenesis inhibitory factor. Overall, these results suggest a shift induced by hydroxyapatite scaffold towards an osteolytic phenotype.

Whereas collagen-scaffold could better simulate *in vivo* primary tumor (Liverani C. et al, *Sci Rep* 9, 12263, 2019), we highlight that hybrid hydroxyapatite/collagen scaffold is more suitable to study breast cancer cells behaviour in bone metastasis. Then, we will implement it with a direct co-culture of osteoclast and osteoblast cells, in order to better investigate the contribution of the host microenvironment in bone metastasis. This model could provide a reliable *3D in vitro* model for the study of bone metastasis mechanisms and for drug screening assays.

Citation Format: Chiara Spadazzi, Laura Mercatali, Alessandro De Vita, Chiara Liverani, Claudia Cocchi, Giacomo Miserocchi, Alberto Bongiovanni, Federica Recine, Sebastiano Calpona, Nada Riva, Giandomenico Di Menna, Lorena Gurrieri, Valentina Fausti, Silvia Angela De Bonis, Giovanni Martinelli, Nicola Baldini, Toni Ibrahim. Development of a biomimetic 3D scaffold to study breast cancer bone metastasis [abstract]. In: Proceedings of the Annual Meeting of the American Association for Cancer Research 2020; 2020 Apr 27-28 and Jun 22-24. Philadelphia (PA): AACR; Cancer Res 2020;80(16 Suppl):Abstract nr 333.

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