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European Journal of Histochemistry

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The *European Journal of Histochemistry* was founded in 1954 by Maffo Vialli and published until 1979 under the title of *Rivista di Istochimica Normale e Patologica*, from 1980 to 1990 as *Basic and Applied Histochemistry* and in 1991 as *European Journal of Basic and Applied Histochemistry*. It is published under the auspices of the University of Pavia, Italy.

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The Journal publishes Original Papers, Technical Reports, Reviews, Brief Reports, Letters to the Editor, Book Reviews, Views and Comments, concerning investigations performed with the aid of biophysical, biochemical, molecular-biological, enzymatic, immunohistochemical, cytometric, and image analysis techniques.

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MULTIOMICS ANALYSIS OF S100 PROTEINS IN BREAST CANCER

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The S100 gene family is the largest subfamily of calcium binding proteins of EF-hand type, expressed in tissue and cell-specific manner. S100 proteins act as intracellular regulators and as extracellular signaling. Within cells, S100 have been involved in the regulation of proliferation, differentiation, apoptosis, energy metabolism, inflammation, migration and invasion via interactions with a variety of target proteins. Extracellular S100 proteins act in an autocrine and paracrine manner through the activation of surface receptors that regulate cell proliferation, differentiation, survival and migration. More recently, there is growing interest in the S100 proteins and their relationship with different cancers because of their involvement in a variety of biological events closely related to tumorigenesis and cancer progression¹. However, the occurrence, the role and the possible coordination of this group of proteins in breast cancer is still poorly known. We previously describe a large-scale proteomic investigation performed on breast cancer patients for the screening of multiple forms of S100 proteins^{2,3}. Our results have shown that the majority of S100 proteins are preferentially expressed in the tumor mass compared with the normal adjacent tissue and that some S100 protein members were ubiquitously expressed in almost all patients, while others appeared more sporadic among the same group of patients. More interestingly, patients which developed distant metastases showed a general tendency of higher S100 protein expression, compared to the disease-free group. Present study was aimed to assess the gene expression levels of the S100 protein family members utilizing a breast cancer dataset generated on Affymetrix microarrays technologies⁴. GOBO (Gene expression-based Outcome for Breast cancer Online) is a user-friendly online tool that allows, also, the identification of co-expressed genes and association with outcome in an 1881 breast cancer samples. Other important association with breast cancer outcome was carried out by Kaplan Meir-plotter database⁵. Integrating results obtained by proteomic and transcriptomic analysis of S100 proteins highlight their important involvement in breast cancer progression, and support the idea that S100 proteins are important prognostic factors, related to survival period of tumor patients. However, the specific mechanisms by which S100 proteins affect progression of breast require further study.

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CURCUMIN REDUCES INFLAMMATORY EFFECTS EXERTED BY 6-MER HYALURONAN IN HUMAN CHONDROCYTES

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Hyaluronan (HA) fragments produced during many pathological conditions may contribute to amplify pro-inflammatory response during tissue injury¹. HA oligosaccharides may enhance an inflammatory response by interacting with the toll-like receptor 4 (TLR-4), toll-like receptor 2 (TLR-2) and CD44. The TLRs activation triggers a pathway that leads to the nuclear translocation of the transcriptional nuclear factor kappaB (NF-κB), that in turn induces the expression of different inflammatory mediators².

Curcumin (diferuloylmethane) is a phytochemical with anti-inflammatory and anti-oxidant properties. It has been shown to have suppressive effect on NF-κB signaling pathway in various cell types, including chondrocytes³.

The aim of this study was to investigate the effect of curcumin treatment in a human chondrocyte cell line stimulated with 6-mer hyaluronan oligosaccharides.

6-mer HA treatment induced up-regulation of CD44, TLR4 and TLR-2 mRNA expression and related protein levels, and NF-κB activation, that in turn increased iNOS, IL-1beta, IL-6, MMP-9 e MMP-13 expression. Treatment with curcumin decreased NF-κB activation and pro-inflammatory mediators, while had no effect on CD44 and TLRs activation.

These data showed that curcumin is able to reduce pro-inflammatory effect induced by HA oligosaccharides in chondrocytes. Since it has been suggested that HA fragments contribute to develop joint inflammation and cartilage damage in rheumatoid arthritis, curcumin may could be beneficial in the management of this chronic disease as a suitable adjunct to conventional pharmaceutical therapy.

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EFFECTS OF CANCER AND STROMAL CELLS CROSSTALK ON HYALURONAN AMOUNT IN AN *IN VITRO* TUMOUR ENVIRONMENT

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Extracellular matrix (ECM) is a complex network of macromolecules and secreted factors that ensures the tissue integrity and physiologic properties by modulating the hydration and osmotic balance in the tumor microenvironment. It is well known that dysregulation of the composition of the ECM is associated with several pathologies, such as breast cancer¹. Among various ECM glycosaminoglycans, hyaluronan (HA) has a remarkable structural importance² but also a role in regulating cellular processes through a binding with membrane receptors and activation of signalling pathways. The role of HA in tumour cells' functions depends on its molar mass. Moreover, matrix with high amount of HA around tumours favour the cancer cells migration and infiltration of newly formed blood vessels³. At all stages of tumorigenesis, stromal cells become "activated" and release growth factors and cytokines that further increase HA synthesis in both stromal and tumour cells. In our laboratory we performed studies on the cross-talk between tumour and surrounding stroma using co-culture sys-