GESINAS - ImmunoTools Award 2014

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INFLUENCE OF THE LOCAL AND DISTANT MICROENVIRONMENT ON THE PROGRESSION OF MAMMARY CANCER

Between the epithelial cells and the fibroblastic/adipose stroma there is a constant exchange of information, essential for normal functionality and morphogenesis, as well as for the development of cancer. This project will focus on mammary cancer because of its high incidence among women. We will study normal human mammary adipose tissue (NHMAT) obtained from patients without mammary tumours (from repair/aesthetic surgery) and human cancer mammary adipose tissue (THMAT) from radical or partial mastectomies. In the cases of mastectomies, we will analyse cells derived from adipose tissue surrounding the tumour as well as 2 cm afar. From these tissues we will isolate stem adipose cells (SAC) because of the potential role as both possible therapeutic agents as well as their importance in regulating tumour development and metastasis. We will investigate the role of soluble factors, released from the adipose tissue (AT) as well as insoluble factors (for example components of the extracellular matrix) on proliferation, migration, cell adhesion and metalloproteinase expression, and using different human cancer cell lines (MDA-MB-231, IBH7, MCF-7 y T47D) or non-cancer (MCF10-A). This project should allow us to widen the concept of cancer, once centred on oncogenes and tumour suppressor genes to one that proposes a dynamic and reciprocal interaction between the mutated epithelia and the microenvironment, both coevolving. According to this theory, one could possibly alter or reverse the tumour behaviour/phenotype through regulation or modification of its microenvironment and/or the interactions the tumour establishes with it. We have published some papers on the subject: - Human adipose tissue from normal and tumoral breast regulates the behavior of mammary epithelial cells. Pistone Creydt V, Fletcher SJ, Giudice J, Bruzzone A, Chasseing NA, Gonzalez EG, Sacca PA, Calvo JC. Clin Transl Oncol. 15(2): 124-31, 2013; - Human periprostatic adipose tissue: its influence on prostate cancer cells. Sacca, Paula Alejandra; Pistone Creydt, Virginia; Choi, Hosoon; Mazza, Osvaldo Néstor; Fletcher, Sabrina Johanna; Fernández Vallone, Valeria Beatriz; Scorticati, Carlos; Chasseing, Norma Alejandra; Calvo, Juan Carlos. Cellular Physiology and Biochemistry 30: 113-122, 2012; - Adipocyte differentiation influences the proliferation and migration of normal and tumoral breast epithelial cells. Pistone Creydt V, Sacca PA, Tesone AJ, Vidal L, Calvo JC. Molecular Medicine Reports 3: 433-439, 2010. Our working hypothesis is that in tumour development and maintenance of a cancer phenotype, being this invasive or not, a bidirectional communication between epithelial cells and stromal environment is necessary. This communication could elicit a cancerous

behaviour or be instrumental in its maintenance, as well as play a crucial role in an involution or regression to a non-cancerous phenotype. In order to be able to conduct this research, we need access to flow cytometry reagents, cytokines, ELISA kits for cytokine determination, as well as growth factors that are essential for cell cultures. For example, the identification of the stem cell derived from adipose tissue requires the use of flow cytometry, and the use of fluorescent labelled antibodies against CD44, CD34, CD90, CD73, CD105, CD14, CD45. In the process of obtaining those cells, it is imperative to quantify possible contaminants from the immune system, as well as from other cell types and this justifies the use of a variety of CD combination. It is well known that adipocytes are essentially and endocrine gland producing adipokines, cytokines or cytokine-like molecules (IL-6, leptin, adiponectine, TNF-alpha), growth factors (TGF-beta, IGF-1), and so we could expect a release of most of this factors into the culture medium. The use of antibodies against some of these factors, and ELISA kits for their determination will provide us with excellent tools that will help in the analysis of the conditioned media.

GESINAS-Award: I am personally actively involved in bringing Science to people through different activities. I have published a book for the general public, titled “Qué porquería las hormonas” (Hormones suck) intended to explain the general population how hormones work. Every year I participate as invited speaker for high school students, as well as for soon to be high school teachers in Science (mainly Biology and Chemistry). At the IBYME I participate in a week long activity called “Puertas Abiertas” (Open doors) where students from different high schools come to our Institute and we or our fellows offer lectures on the different research activities that take place in the laboratories. This is intended to incite a taste for scientific careers in those students. For the general population I participate in the “Feria del Libro” (Book Fair) where, again, representing CONICET I bring scientific topics, such as hormones, cloning, reproduction to anyone interested in attending those talks.

GESINAS ImmunoTools AWARD for

Juan Carlos Calvo includes 50 reagents

FITC - conjugated anti-human CD19, CD24, CD29, CD45, Control-IgG1, Annexin V,

PE - conjugated anti-human CD3, CD34, CD105, Control-IgG2a,

APC - conjugated anti-human CD9, CD44, Control-IgG2b,

CD3 FITC / CD8 PE / CD45 PE-Dy647,

human ELISA-set for 96 wells, IFN-gamma, IL-6, IL-10, human IL-12p40 total (detect IL-23 as well), human TNF-a (each 3 reagents),

recombinant human cytokines: rh BMP-2, rh G-CSF, rh HGF, rh RANTES / CCL5, rh RANKL, rh SDF-1α / CXCL12a, rh TGF-beta3, rh TRAIL / CD253, rh TSLP, rh EGF, rh FGF-b, rh Galectin-1, rh Galectin-3, rh IFNgamma, rh IL-6, rh IL-10, rh IL-12, rh Leptin, rh VEGF-A/VEGF-165 DETAILS more AWARDS