developed through experimentation on animal models. This dynamic interplay between clinical practice and experimental oncology faces new challenges, especially when clinicians and biologists interact at the bench. Here, we present our experience in unifying analytical criteria to classify and interpret histopathological studies beyond current standards. In biopsies of human breast carcinomas and mouse tumor xenografts, we evaluated histological and nuclear indexes to establish tumor grade. We evaluated the extent of necrosis in growing and shrinking tumors after therapy and the characteristics of tumor edges, whether they are expansive or infiltrating. After immunohistological studies, we designed a score for particular proteins in the PI3K/AKT/mTOR and cyclin D1/Rb pathways considering the percentage of positive tumor cells and the intensity of the staining. In conclusion, we established new approaches considering the research interest and the standard convention criteria with a dynamic interaction between scientists and pathologists.

Poster Session 4

Chairs
Karen Blyth, University of Glasgow, Glasgow, UK
Gareth Owen, Pontificia Universidad Católica, Santiago, Chile
Carolina Schere Levy, IFIBYNE-UBA-CONICET, Buenos Aires, Argentina

PS4-53 / Exposure to endocrine disruptors induces proangiogenic factors in MDA-MB-231 human breast cancer cells
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Angiogenesis plays a role in local tumor growth and metastasis. Elevated levels of Hypoxia Inducible Factor-1α (HIF-1α) correlate with angiogenesis. HIF-1α induces gene expression like Cyclooxygenase-2 (COX-2), Nitric Oxide Synthase-2 (NOS-2) and Vascular Endothelial Growth Factor (VEGF). COX-2 and NOS-2 promote tumor angiogenesis. VEGF increases endothelial cells proliferation, survival and migration. Endocrine disruptors Hexachlorobenzene (HCB) and Chlorpyrifos (CPF) induce cell proliferation and tumor growth in breast cancer animal models. Our aim was to examine their action on breast cancer angiogenesis. We studied HCB (0.005, 0.05, 0.5 and 5 μM) or CPF (0.05, 0.5, 5 and 50 μM) effect in MDA-MB 231 triple negative breast cancer cells on: HIF-1α, COX-2 and NOS-2 protein levels, VEGF expression and secretion (Western Blot). Our results showed that exposure to 6 h of HCB enhances HIF-1α levels at 0.05, 0.5 and 5 μM, and NOS-2 expression and VEGF secretion at all assayed doses. In addition, at 24 h HCB (0.05 and 5 μM) increases COX-2 levels ($p < 0.05$). Moreover, CPF for 6 h enhances HIF-1α and NOS-2 expression at all assayed doses, as well as VEGF secretion at 0.05, 0.5 and 5 μM. Besides, CPF (0.05, 0.5 and 5 μM) stimulates COX-2 levels at 24 h ($p < 0.05$). We demonstrated that HCB and CPF induce the proangiogenic factors expression. In conclusion, these data highlight that the exposure to endocrine disruptors could contribute to mammary carcinogenesis, inducing angiogenesis proteins.

PS4-54 / Chlorpyrifos subthreshold exposure induces epithelial-mesenchymal transition in breast cancer cells
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Chlorpyrifos (CPF) is one of the most frequently used pesticide in extensive agriculture around the world. The effects of this pesticide on carcinogenesis are not clear and there is no consensus concerning the risks of this compound. In this study we investigate whether CPF promotes epithelial-mesenchymal transition (EMT) in breast cancer cells. Migration and invasion were evaluated by wound healing assay, Boyden Chamber assay and multicellular spheroids (3D). Also, we analyzed the effects of CPF on the number and the area of first (MS1) and second (MS2) generation of MCF-7-mammospheres. We demonstrate that 50 μM CFP induces invasion in MCF-7 and MDA-MB-231 cells (*** $p < 0.001$) when they were grown as a monolayer. In MCF-7-3D culture, we observed that 0.05 μM CPF increased the area of invasion after 7 days (** $p < 0.01$) and CPF at 50 μM increased the area of invasion after 5 (* $p < 0.05$) and 7 days (*** $p < 0.001$) when collagen type 1 was used as matrix model. When Matrigel® was used as substrate, we observed that only 0.05 μM CPF produced an increment of the invasion area after 2 (* $p < 0.05$), 5 (** $p < 0.01$) and 7 days (*** $p < 0.001$). In addition, 0.05 and 50 μM CPF increases migration in both cell lines grown as a monolayer and 3D culture. CPF at 0.05 μM induced an increment of the number and the area of MS1 and MS2 (* $p < 0.05$ and *** $p < 0.001$). Our results show that CPF promotes migration and invasion in breast cancer cells, generating a more aggressive phenotype.

PS4-55 / Environmental exposure and mammary tumors: the pesticides action on LM3 murine breast cancer cells
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Epidemiological studies have shown that pesticide exposure is associated with an increased risk of breast