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CENTRO DE INVESTIGACION

Seminario CIPF

pH homeostasis and cancer

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Abstract: Cancer is a disease of mechanisms controlling cell growth and proliferation. In the past emphasis was on biochemical mechanisms of signal transduction involving growth factors and their receptors, protein kinases, G proteins, transcription factors and chromatin modification systems. Cell growth also requires biophysical mechanisms involved in proton extrusion and, accordingly, tumors have higher intracellular pH (pHi) and lower extracellular pH (pHo) than normal tissues. High pHi was considered a permissive factor without regulatory function. However, genetic manipulation of pHi in mouse fibroblast with a yeast proton pumping ATPase resulted in tumorigenic transformation. And low pHo has recently been shown to be required for metastasis. Two important things prevented consideration of these results by the scientific community: ignorance of mechanisms and lack of therapeutical consequences. These obstacles are in process of been overcome: mechanisms of pHi and pHo effects on cell growth and proliferation are being clarified and novel therapies are emerging. Low pHo activates secreted lysosomal proteases promoting disruption of extracellular matrix and it can be counteracted by bicarbonate. High pHi seems to activate TORC1 and G1 cyclins and could be counteracted by weak organic acids.

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