SCIENTIFIC SEMINAR

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Understanding and combating therapeutic resistance in breast and pancreatic cancers

Resistance to targeted therapies in cancer is a major clinical challenge. Therefore, there is an urgent need to elucidate the molecular mechanisms that drive resistance and use this insight to develop more effective combination therapies that will induce deeper initial responses and delay or ideally prevent relapse. In pancreatic cancer, we have found that Ras pathway inhibition upregulates the anti-apoptotic protein Mcl-1 by triggering its association with its deubiquitinase USP9X, resulting in acute Mcl-1 stabilization and protection from apoptosis. Direct Mcl-1 inhibitors and transcriptional cyclin-dependent kinase (CDK) inhibitors, which suppress Mcl-1 transcription, prevent this protective response and induce tumor regression when combined with MEK inhibitors. In a second study, we have developed a combination therapy based on co-targeting oncogenic and epigenetic drivers for HER2+ breast cancer. EZH2 inhibitors revert de novo resistance to HER2 tyrosine kinase inhibitors and enhance their therapeutic response in sensitive breast cancer models in vitro and in vivo.

CIC bioGUNE
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EXCELENCIA SEVERO OCHOA

Thursday
December 14
Atrio 800
12.00H

BRTA
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