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Metarrestin, a new approach to metastasis

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While the advances in cancer biology and treatment have significantly reduced cancer mortality over all, pancreatic cancer remains a deadly disease. The American Cancer Society estimates about 45,220 new cases and 38,460 deaths from pancreatic cancer alone in the United States for the year 2013. Survival rates, which rank among the lowest for any solid organ cancer, have not changed over the last three decades. 72 to 90 percent of patients succumb to the disease within the first year after receiving a diagnosis of pancreatic cancer. Reports of long term survival or cure are anecdotal in nature, even for patients where an early disease state was treated with complete surgical resection as the disease inevitably recurs. The failure of decades of effort is partly due to the lack of strategies that are effectively against metastasis, the cause for nearly all pancreatic cancer deaths. We have identified and developed a first in class compound, Metarrestin, that selectively blocks metastasis in an orthotopic pancreatic metastatic cancer model without any detectable adverse impact on tested animals. Metarrestin was identified from a high-throughput high-content screen (HTS) that was followed by an extensive medicinal chemistry optimization campaign, against a cellular subnuclear structure, the perinucleolar compartment (PNC), whose formation reflects the metastatic capability of cancer cells. Metarrestin has excellent oral bioavailability and tolerability displaying also shows promising results in metastatic xenograft models of prostate and breast cancer. Rational for this new therapeutic approach, together with medicinal chemistry, pharmacokinetics and biological results will be presented.

Biography

Juan Jose Marugan has been involved for more than twenty years in the translational field working in several aspects of drug discovery in academia, pharmaceutical industry and NIH. He is the author of more than 50 peer review publications and 31 patents, he also has extensive experience as team leader of programs in preclinical lead optimization (Antivirals, Antibiotics, Cardiovascular, CNS, Oncology, Rare and Neglected Diseases, etc.), with many of them advancing toward preclinical development or clinical trials. Since 2008 he holds a group leader position at NCATS.

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