BIO SKETCH FORM & Abstract

First Name: JORGE

Last Name: MOSCAT

Please send us a picture in a Jpeg format

Title: Homer T. Hirst III Professor of Oncology, and Vice-Chair for Cell and Cancer Pathobiology, Department of Pathology

Organization Weill Cornel Medical College of Cornell University

Address of the organization: 1300 York Avenue, New York, NY 10065, USA

Phone: (513) 319-7627

e-mail: jom4010@med.cornell.edu

Curent position: Chief, Division of Cell and Cancer Pathobiology, Vice-Chair for Cell and Cancer Pathobiology

Past positions:

2017-2019	Director, Metabolism Initiatives, Sanford Burnham Prebys Institute, La Jolla, CA
2015-2017	Deputy Director/Associate Director, NCI-designated Cancer Center, Sanford Burnham Prebys Institute, La Jolla, CA
2013 - 2019	Director, Cancer Metabolism and Signaling Networks Program, NCI-designated Cancer Center, Sanford Burnham Prebys Institute, La Jolla, CA
2012 - 2019	Scientific Director, Cancer Metabolism, Sanford Burnham Prebys Institute, La Jolla, CA
2011 - 2019	Professor, Sanford Burnham Prebys Institute, La Jolla, CA
2008 - 2011	Professor and Chair, Department of Cancer and Cell Biology, University of Cincinnati College of Medicine, Cincinnati, OH
2007 - 2008	Interim Chairman, Department of Genome Science/Molecular Oncogenesis, University of Cincinnati College of Medicine, Cincinnati, OH
2006 – 2008	Professor, Department of Genome Science, University of Cincinnati College of Medicine, Cincinnati, OH
2004 - 2006	Scientific Director of Biology and Biomedicine, National Research Council, Madrid (Spain)
1998 - 2002	Director of the Institute of Molecular Biology, CSIC, Madrid (Spain)
1993 - 2006	Professor, Centre for Molecular Biology, Madrid (Spain)

Grants / Awards

Ongoing NIH grants:

R01CA275846-01 PI: **Moscat, J** 12/01/2022 - 11/30/2027
Cholesterol metabolism in mesenchymal colorectal cancer
The goal is to determine the role and function of the cholesterol metabolism in the initiation and progression of mesenchymal intestinal tumors.

R01CA265892 PI: **Moscat, J** 12/01/2021 - 11/30/2026
Interferon regulation by NBR1-driven chaperone-mediated autophagy in stellate cells in liver cancer
The goal of this project is to establish the role and mechanism of actions of stromal NBR1 in the progression of hepatocellular carcinomas.

R01CA250025 PI: **Moscat, J** 03/17/2021 - 02/28/2026
Molecular Mechanisms Driving Mesenchymal Colorectal Cancer
The scope of this proposal is to investigate the molecular mechanisms that drive the poor prognosis mesenchymal type of colorectal cancer.

R01 CA246765 PI: Diaz-Meco, MT 05/01/2020 - 04/30/2025
Novel pathways in the control of lineage plasticity in neuroendocrine prostate cancer
To investigate the role and mechanism of action of PKCl/i to orchestrate serine metabolism and epigenetic regulation in NEPC.

Recently completed NIH grants:

R01DK108743 PI: **Moscat, J** 04/01/2016 - 03/31/2022
Control of stellate cells-driven liver cancer by the p62/NBR1 adapters
To determine the mechanisms whereby the stromal microenvironment impacts liver cancer.

R01CA207177 PI: **Moscat, J** 03/21/2017 - 02/28/2022
Mechanisms of cell death and autophagy in intestinal epithelial cells in inflammation and cancer
To define the mechanisms whereby PKCl/i regulates apoptosis and autophagy.

R01CA211794 MPI: **Moscat, J** and Karin, M 02/15/2017 - 01/31/2022
Role of p62/SQSTM1 in obesity-induced liver cancer
To establish the role of autophagy adaptors in tumor hepatocytes

Abstract

Title of your presentation:

Adult stem cell loss and metaplasia during initiation and malignancy in colorectal cancer

Summary of your presentation:
Mesenchymal colorectal cancer (mCRC) is a microsatellite stable (MSS) subtype marked by high desmoplasia, with CD8+ T cells restricted to the stromal periphery, making it resistant to immunotherapy. Low levels of atypical protein kinase Cs (aPKCs) in the intestinal epithelium are linked to poor survival in mCRC. A key feature of mCRC is the accumulation of hyaluronan (HA), which fosters epithelial diversity and leads to the emergence of tumor fetal metaplastic cells (TFMCs) with invasive traits through interactions with activated fibroblasts. TFMCs, which are influenced by HA, have metaplastic markers that serve as prognostic indicators. Experiments show that degrading HA with hyaluronidase reduces tumor growth and liver metastasis in mCRC, enabling immune checkpoint blockade therapy by increasing the infiltration of CD8+ T and B cells, some with resident memory characteristics, and countering immunosuppression. In the early stages of tumor formation, reduced aPKC levels are associated with the loss of intestinal stem cells (ISCs) and activation of revival and metaplastic programs in precancerous lesions. Experimental PKCλ/ι inactivation in mouse models and organoids activates JNK signaling in normal intestinal epithelial cells (IECs), leading to ISC depletion, including LGR5+ stem cells, followed by the emergence of revival stem cells (RSCs) at the crypt base and fetal-metaplastic cells (FMCs) at the surface. These cell types depend on JNK-induced AP-1 and YAP signaling pathways, and their presence persists throughout cancer progression, promoting aggressive CRC characteristics regardless of their serrated or conventional origin. This understanding of HA and aPKC roles in CRC highlights potential therapeutic strategies, such as HA degradation and combination immunotherapies, to improve outcomes in resistant CRC types.
[https://www.moscatdiazmecolab.org]