Paola Betancur

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Professional Focus

Dr Betancur?s long-term research goal is to understand the mechanisms encoded in the DNA by which cancerous cells avoid being detected and destroyed by the host?s immune system. Toward this goal, her lab examines the interactions between epigenetic modifiers, transcription factors and the genomic enhancers of target genes that abnormally activate the immune evasion program in cancer cells.

Prior to Joining UCSF as Faculty, Dr. Betancur studied the transcriptional regulation of CD47 (an immune evasion cell-surface signal present in all cells) that provides a ?don?t eat me? signal to macrophages, and other immune cells, thus protecting cells from being targeted and

cleared by the immune system. Damaged cells when ready to be cleared by macrophages downregulate CD47 transcript and protein expression. However, most cancer cells fail to do so. Through computational genomic analyses, experimental isolation and biochemical characterization of enhancers and transcription factors complexes, Dr. Betancur exposed for the first time the complexity of CD47 gene regulation, which is remarked across different cancer types by the activation of distinct enhancers or super-enhancers (SEs) that are inactive in healthy counterparts. Moreover, she found that CD47 expression is increased by pro-inflammatory signals and blocking these signals in combination with a CD47 blocking antibody treatment, potentiates immune clearance of breast cancer cells.

Using this information as a platform Dr Betancur?s lab is currently assembling a gene regulatory network (GRN) to clarify all upstream CD47 activators and novel genes that together with CD47 activate the immune evasion program. This virtual map will address how these interactions, within the immune evasion GRN, are altered, particularly, through increased inflammation during radiation therapy. Such information will be crucial to develop tools to deactivate this program in cancer and prevent cancer cells or other diseased cells from escaping immunosurveillance. In addition, A GRN of immune evasion will point at effective immunotherapies that can be combined with radiation therapy to engage the immune system and improve the treatment of cancer.

Education

2003	Stony Brook University, New York	BS	Biology
2010	California Institute of Technology	PhD	Developmental Cell Biology and Genetics

Professional Experience

2019-present	University of California, San Francisco	Assistant Professor	Department of Radiation Oncology
2011-2019	Stanford University	Postdoctoral Fellow/Instructor	Institute for Stem Cell Biology and Regenerative Medicine
2010-2011	California Institute of Technology	Postdoctoral Fellow	Department of Developmental and Cell Biology

Recent Significant Publications:

Betancur P, Abraham B.J, Yiu Y.Y, Willingham S, Khameneh F, Zarnegar M, Kuo A.H, McKenna K, Kojima Y, Leeper N.J, Ho P, Gip P, Swigut T, Sherwood R, Clarke M.F, Somlo G, Young R.A, Weissman I.L. **A CD47-associated Super-enhancer Links Pro-inflammatory Signaling to CD47 Upregulation in Breast Cancer.** Nat Comm 8:14802, 2017

Kojima Y, Volkmer J.P, McKenna K, Civelek M, Lusis A.J, Miller C, Direnzo D, Nanda V, Brady S, Connolly A, Schadt E, Quertermous T, Betancur P, Hansson G, Maegdefessel

L,Perisic L, Hedin U, Weissman I.L, Leeper N. **CD47 Blocking Antibodies Restore Phagocytosis and Prevent Atherosclerosis.** Nature 536(7614):86-90, 2016.

Betancur P, Simoes-Costa M, Sauka-Spengler T, Bronner M. **Expression and Function of Transcription Factor cMyb During Cranial Neural Crest Development.** Mech Dev 132:38-43, 2014.

Betancur P, Sauka-Spengler T, Bronner M. **A Sox10 Enhancer Common to the Otic Placode and Neural Crest is Activated by Tissue Specific Paralogs.** Development 138(17):3689-98, 2011.

Betancur P, Bronner-Fraser M, Sauka-Spengler T. **Assembling Neural Crest Regulatory Circuits into a Gene Regulatory Network.** Annu Rev Cell Dev Biol 26:581-603, 2010.

Betancur P, Bronner-Fraser M, Sauka-Spengler T. **Genomic Code for Sox10 Activation Reveals a Key Regulatory Enhancer for Cranial Neural Crest.** Proc Natl Acad Sci USA (107)8:3570-75, 2010.

Sutton M.A, Ito H.T, Cressy P, Kempf C, Woo J.C, **Schuman M.E. Miniature Neurotransmission Stabilizes Synaptic Function Via Tonic Suppression of Local Protein Synthesis.** Cell (125)4:785-799, 2006.

Lwigale P.Y, Cressy P.A, Bronner-Fraser M. **Corneal Keratocytes Retain Neural Crest Progenitor Cell Properties.** Dev Biol 288(1):284-293, 2005.

Patents:

Isolation of neural crest enhancers that can be used to generate ?reporters? that indicate when a cell adopts neural crest traits. Sauka-Spengler T, McKeown S, Betancur P and Bronner-Fraser M. Serial number: 61/203,334; CIT file number: 5293-P. Patent filed (2008).

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