

BIOGRAPHICAL SKETCH

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NAME: Simoes-Costa, Marcos

eRA COMMONS USER NAME (credential, e.g., agency login): scmarcos

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
University of Santa Catarina, Florianopolis, Brazil	BA	02/2004	Biology
University of Sao Paulo, Sao Paulo, Brazil	PHD	04/2009	Cell Biology
California Institute of Technology, Pasadena, CA	Postdoctoral Fellow	10/2016	Developmental Biology

A. Personal Statement

My laboratory investigates how gene regulatory networks control cell identity and behavior in development and disease. We are particularly interested in the molecular mechanisms that orchestrate the development of the progenitors of the central and peripheral nervous systems. We combine spatial transcriptomics, genomic and single-cell analysis to understand how regulatory programs are deployed in the distinct domains of the developing embryo. Here we propose to investigate how the genetic circuits that operate in the formation of the central nervous systems are abnormally reactivated in embryonal tumors. In the last years, we have compiled transcriptomic and epigenomic datasets from the embryonic cells that will give rise to the nervous system. These datasets can now be used as a powerful platform to identify novel regulatory circuits involved in neural development, which may be co-opted in tumorigenesis and metastasis. Several important factors place me in a unique position to pursue the proposed research plan. First, my extensive experience working on gene regulatory networks will be an important asset to tackle this ambitious, high-risk high-reward research program. Second, my new lab, which is already staffed with talented graduate students and a postdoc, has become a dynamic and productive environment. Finally, the supportive and highly collaborative environment of the Department of Molecular Biology and Genetics has been an invaluable asset for my research program. Support from the Sontag Foundation will allow us to pursue this exciting research program at the interface of cancer and developmental biology.

1. Azambuja AP, Simoes-Costa M. (2020). Connectome of neural crest enhancers reveals pervasive regulation by Wnt signaling (submitted).
2. Bhattacharya D, Azambuja AP, Simoes-Costa M. Metabolic reprogramming promotes neural crest migration via Yap/Tead signaling. *Developmental Cell* 2020 (*in press*).
3. Rothstein M, Simoes-Costa M. A Tfap2-mediated molecular switch reshapes the cis-regulatory landscape in neural crest stem cells. *Genome Research* 2020 Jan;30(1):35-48.
4. Bhattacharya D, Rothstein M, Azambuja A, Simoes-Costa M. Control of neural crest multipotency by Wnt signaling and the *Lin28/let-7* axis. *eLife* 2018 Dec 6;7:e40556.

B. Positions and Honors**Positions and Employment**

2016 - Assistant Professor, Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY

Other Experience and Professional Memberships

- 2013 - Member, International Society of Differentiation
2016 - Member, Society for Developmental Biology

Honors

- 2003 Scientific Initiation Program Award, Federal University of Santa Catarina
2004 Top Performance on National Exam of Courses, Brazilian Ministry of Education
2004 Class Valedictorian, Federal University of Santa Catarina
2005 José Carneiro Award (Honorable Mention), University of São Paulo
2005 Aristides Pacheco Leão Award, Brazilian National Academy of Sciences
2006 MBL Fellowship Award (Embryology Course), Marine Biological Laboratory
2008 Pew Latin American Fellow in Biomedical Sciences, Pew Charitable Trusts
2012 Caltech Cell Center Postdoctoral Fellowship, Moore Foundation
2013 MBL Fellowship Award (GRN Course), Marine Biological Laboratory
2014 NIH Pathway to Independence (PI) Award (K99/R00), National Institutes of Health
2016 Nancy and Peter Meinig Family Investigator in the Life Sciences, Cornell University
2018 Basil O'Connor Starter Schollar Award, March of Dimes
2018 Young Scientist 2018, World Economic Forum
2019 NIH New Pioneer Award

C. Contribution to Science

1. During my postdoctoral training with Dr. Marianne Bronner, I explored the regulatory mechanisms controlling the cranial neural crest, due to its key role in craniofacial development. I have shown that specification of cranial and trunk neural crest cells requires distinct genetic programs, a finding which might account for differences in cell behavior and developmental potential observed between these populations. I characterized axis-specific enhancers that are active in different subpopulations of neural crest and are valuable tools for scrutinizing the molecular underpinnings of neural crest formation. These enhancers were used to isolate pure populations of cranial neural crest cells for transcriptome analysis, which revealed an early bias to a cartilage or bone fate and uncovered novel regulators and biological pathways that are important for craniofacial development.
 - a. Simões-Costa M, Bronner ME. Reprogramming of avian neural crest axial identity and cell fate. *Science*. 2016 Jun 24;352(6293):1570-3. PubMed PMID: [27339986](#); PubMed Central PMCID: [PMC5100669](#).
Simões-Costa M, Stone M, Bronner ME. Axud1 Integrates Wnt Signaling and Transcriptional Inputs to Drive Neural Crest Formation. *Dev Cell*. 2015 Sep 14;34(5):544-54. PubMed PMID: [26256212](#); PubMed Central PMCID: [PMC4573882](#).
 - b. Simões-Costa M, Tan-Cabugao J, Antoshechkin I, Sauka-Spengler T, Bronner ME. Transcriptome analysis reveals novel players in the cranial neural crest gene regulatory network. *Genome Res*. 2014 Feb;24(2):281-90. PubMed PMID: [24389048](#); PubMed Central PMCID: [PMC3912418](#).
 - c. Simões-Costa MS*, McKeown SJ*, Tan-Cabugao J, Sauka-Spengler T, Bronner ME. Dynamic and differential regulation of stem cell factor FoxD3 in the neural crest is encrypted in the genome. *PLoS Genet*. 2012;8(12):e1003142. PubMed PMID: [23284303](#); PubMed Central PMCID: [PMC3527204](#).
2. One of my main research interests is how the emergence and evolution of neural crest cells impacted the vertebrate body plan. To gain further insight in the origin and diversification of this clade, we have employed comparative gene regulatory studies in basal vertebrate species such as the amphioxus (which lacks neural crest) and the lamprey (which lacks major neural crest derivatives). The results from these studies suggest that progressive elaboration of the neural crest gene regulatory network allowed for the

emergence of quintessential features of the vertebrate body plan, such as a complex craniofacial skeleton and peripheral nervous system.

- a. Martik ML, Gandhi S, Uy BR, Green SA, Gillis JA, Simoes-Costa M, Bronner ME. Evolution of the vertebrate New Head by progressive acquisition of neural crest regulatory subcircuits. *Nature*. 2020 Oct;574(7780):675-678.
 - b. Green SA, Simoes-Costa M, Bronner ME. Evolution of vertebrates as viewed from the crest. *Nature*. 2015 Apr 23;520(7548):474-482. PubMed PMID: [25903629](#); PubMed Central PMCID: [PMC5100666](#).
 - c. Uy BR, Simoes-Costa M, Koo DE, Sauka-Spengler T, Bronner ME. Evolutionarily conserved role for SoxC genes in neural crest specification and neuronal differentiation. *Dev Biol*. 2015 Jan 15;397(2):282-92. PubMed PMID: [25286121](#); PubMed Central PMCID: [PMC4545591](#).
 - d. Simões-Costa M, Bronner ME. Insights into neural crest development and evolution from genomic analysis. *Genome Res*. 2013 Jul;23(7):1069-80. PubMed PMID: [23817048](#); PubMed Central PMCID: [PMC3698500](#).
3. As a graduate student with Dr. José Xavier-Neto in the University of São Paulo, I pursued my profound interest in the complexity of developmental mechanisms by exploring the role of signaling systems in development and evolution. I investigated the evolution of the retinoic acid signaling pathway, the evolutionary origins of the vertebrate heart, and how these two processes were interlinked. My experience in the lab made me well versed in important concepts such as molecular evolution and the role of signaling systems and transcriptional regulators in control of developmental programs.
- a. Sobreira TJ*, Marlétaz F*, Simões-Costa M*, Schechtman D, Pereira AC, Brunet F, Sweeney S, Pani A, Aronowicz J, Lowe CJ, Davidson B, Laudet V, Bronner M, de Oliveira PS, Schubert M, Xavier-Neto J. Structural shifts of aldehyde dehydrogenase enzymes were instrumental for the early evolution of retinoid-dependent axial patterning in metazoans. *Proc Natl Acad Sci U S A*. 2011 Jan 4;108(1):226-31. PubMed PMID: [21169504](#); PubMed Central PMCID: [PMC3017150](#).
 - b. Simões-Costa MS, Azambuja AP, Xavier-Neto J. The search for non-chordate retinoic acid signaling: lessons from chordates. *J Exp Zool B Mol Dev Evol*. 2008 Jan 15;310(1):54-72. PubMed PMID: [17109394](#).
 - c. Xavier-Neto J, Castro RA, Sampaio AC, Azambuja AP, Castillo HA, Cravo RM, Simões-Costa MS. Parallel avenues in the evolution of hearts and pumping organs. *Cell Mol Life Sci*. 2007 Mar;64(6):719-34. PubMed PMID: [17380312](#).
 - d. Simões-Costa MS, Vasconcelos M, Sampaio AC, Cravo RM, Linhares VL, Hochgreb T, Yan CY, Davidson B, Xavier-Neto J. The evolutionary origin of cardiac chambers. *Dev Biol*. 2005 Jan 1;277(1):1-15. PubMed PMID: [15572135](#).
4. As an undergraduate student, I worked in the Development and Reproduction Lab at the Federal University of Santa Catarina, where I characterized the morphological features of embryonic development of native freshwater prawn species and investigated aspects of crustacean reproduction. My research training as an undergraduate resulted in four publications and consolidated my desire to become an independent investigator in the field of developmental biology. It also taught me the value of being inventive, diligent, and to make the most of the resources at hand.
- a. Muller YM, Pacheco C, Simoes-Costa MS, Ammar D, Nazari EM. Morphology and chronology of embryonic development in *Macrobrachium acanthurus*. *Invertebrate Reproduction and Development*. 2007; 50(2):67.
 - b. Simoes-Costa MS, Pacheco C, Nazari EM, Muller YM, Ammar D. *Macrobrachium olfersi* (Wiegman) embryonic staging through morphological landmarks. *Revista Brasileira de Zoologia*. 2005; 22(2):501.
 - c. Nazari EM, Simoes-Costa MS, Muller YM, Ammar D, Dias M. Comparisons of fecundity, egg size, and egg mass volume of the freshwater prawns *Macrobrachium potiuna* and *Macrobrachium olfersi* (Decapoda, Palaemonidae). *Journal of crustacean biology*. 2003; 23(4):862.
 - d. Muller YM, Nazari EM, Simoes-Costa MS. Embryonic stages of the freshwater prawn *Macrobrachium olfersi* (Decapoda, Palaemonidae). *Journal of Crustacean Biology*. 2003; 23(4):869.

Complete List of Published Work in My Bibliography:
<http://bit.ly/2b5Okrw>

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

DP2 HD102043, (Simoes-Costa M, PI) — 2019-2024
New Innovator Award, National Institutes of Health
Award Title: Spatial Control of Pattern Formation in Early Vertebrate Development
Awarded funds (direct): USD 300,000/year (5 years)

R01DE028576, (Simoes-Costa M, PI) — 2019-2024
National Institute of Dental and Craniofacial Research, NIH
Award Title: Genomic control of neural crest identity by signaling systems
Awarded funds (direct): USD 237,000/year (5 years)

Basil O'Connor Starter Scholar Award (Simoes-Costa M, PI) — 2018-2020
March of Dimes Foundation
Award Title: Genomic analysis of neural crest skeletogenic differentiation
Awarded funds: USD 150,000 (2 years)

Stem Cell Program Seed Grant (Simoes-Costa M, PI) — 2019-2020
Cornell University
Award Title: A single-cell platform for network analysis of neural crest differentiation
Awarded funds (direct): USD 15,000/year

Completed Research Support

R00 DE024232-03 (Simoes-Costa, PI) 12/1/2016 – 11/30/2019
NIH/NIDCR Pathway to Independence Award
Title: Integrating signaling and transcriptional inputs during neural crest specification
Awarded funds (direct): \$645,320