BIOGRAPHICAL SKETCH

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NAME: DE LA SERNA, IVANA L

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

POSITION TITLE: Associate Professor with tenure

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
Cornell University	BACHELOR OF SCIENCE (BS)	05/1984	Nutritional Biochemistry
University of California, Davis	DOCTOR OF PHILOSOPHY (PHD)	12/1998	Plant Pathology
University of Massachusetts Medical School, Worcester, MA	Postdoctoral Fellow	08/2005	Chromatin Remodeling /Cell Biology

A. Personal Statement

With specialized training and expertise in the study of epigenetics in development and disease, I am well-equipped to undertake the proposed studies. My lab's expertise in gene regulation and chromatin remodeling will enable us to elucidate the mechanisms by which BetaM regulates muscle development and impacts upon metabolism. During my postdoctoral tenure at the University of Massachusetts Medical School, I was trained by a leader in chromatin remodeling, Dr. Anthony Imbalzano. During this time, I achieved a groundbreaking discovery by revealing that SWI/SNF, a multi-subunit ATP-dependent chromatin remodeling complex, activates previously silent muscle specific genes during specification of the muscle lineage. I went on to elucidate a mechanism by which a pioneer transcription factor facilitates MYOD binding and SWI/SNF recruitment to muscle specific promoters.

Building upon this foundation, my laboratory later elucidated transcriptional mechanisms by which SWI/SNF contributes to cardiac hypertrophy. Although much of my lab has focused on melanocytes and cancer, we are actively engaged in investigating the mechanisms by which chromatin remodeling and histone modifications activate gene expression in diverse biological contexts.

We are collaborating with Dr. Modyanov. to elucidate the mechanisms by which BetaM regulates muscle development. Recently, we published findings demonstrating that BetaM upregulates the expression of MyoD, a master regulator of myogenesis, in cultured muscle cells. This regulation occurs through BetaM's binding to the MyoD upstream region, which promotes changes in chromatin structure and enhances the recruitment of SWI/SNF chromatin remodeling enzymes to the DRR region of the MyoD promoter. Our goal is to elucidate how BetaM, through its role in muscle development, influences whole body metabolism in vivo. The following contributions highlight my expertise in these areas, underscoring my significant advancements in understanding the regulation of gene expression during muscle differentiation.

1. Ahmad N, de la Serna IL, Marathe HG, Fan X, Dube P, Zhang S, Haller ST, Kennedy DJ, Pestov NB, Modyanov NN. Eutherian-Specific Functions of BetaM Acquired through Atp1b4 Gene Co-Option in the Regulation of MyoD Expression. Life (Basel). 2023 Feb 2;13(2) PubMed Central PMCID: PMC9962273.
2. Marathe HG, Mehta G, Zhang X, Datar I, Mehrotra A, Yeung KC, de la Serna IL. SWI/SNF enzymes promote SOX10- mediated activation of myelin gene expression. PLoS One. 2013;8(7):e69037. PubMed Central PMCID: PMC3712992.
3. de la Serna IL, Ohkawa Y, Higashi C, Dutta C, Osias J, Kommajosyula N, Tachibana T, Imbalzano AN. The microphthalmia-associated transcription factor requires SWI/SNF enzymes to activate melanocyte-specific genes. J Biol Chem. 2006 Jul 21;281(29):20233-41. PubMed PMID: 16648630.

4. de La Serna IL, Carlson KA, Hill DA, Guidi CJ, Stephenson RO, Sif S, Kingston RE, Imbalzano AN. Mammalian SWI-SNF complexes contribute to activation of the hsp70 gene. Mol Cell Biol. 2000 Apr;20(8):2839-51. PubMed Central PMCID: PMC85505.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2013 -	Associate Professor with tenure, University of Toledo College of Medicine and Life Sciences, Toledo, OH
2006 - 2013	Assistant Professor, University of Toledo College of Medicine and Life Sciences, Toledo, OH
2005 - 2006	Assistant Professor, Medical College of Ohio, Toledo, OH

Honors

2002 - 2004	Medical Foundation Postdoctoral Research Fellowship, June Rockwell Levy Foundation and the Charles A. King Trust
2000 - 2003	NIH Public Health Service Individual National Research Service Award (Postdoc grant), National Institute of Health
2022	Shout out for Innovative Faculty, University of Toledo
2016	Outstanding Mentor Award, University of Toledo
2013	Melanoma Research Award, Melanoma Know More Association
2012	Discover Award, Ohio Cancer Research Associates
2010	Outstanding New Investigator Award, University of Toledo

C. Contribution to Science

1. During my tenure as a postdoctoral fellow, little was known about the cellular functions of SWI/SNF chromatin remodeling complexes. I discovered that SWI/SNF activates gene expression in response to heat shock and other external stimuli. I also made the seminal discovery that SWI/SNF interact with lineage specific factors to play critical roles in diverse cellular contexts. These include differentiation of muscle, melanocyte, and Schwann cell lineages. These papers demonstrate our contributions to our understanding of SWI/SNF chromatin remodeling enzymes in the regulation of cellular differentiation and response to external stimuli in mammalian cells. Among these papers, we have recently elucidated a novel mechanism by which Atp1b4 has been co-opted in placental mammals to interact with SWI/SNF and regulate MyoD expression in muscle cells.

    a. Marathe HG, Watkins-Chow DE, Weider M, Hoffmann A, Mehta G, Trivedi A, Aras S, Basuroy T, Mehrotra A, Bennett DC, Wegner M, Pavan WJ, de la Serna IL. BRG1 interacts with SOX10 to establish the melanocyte lineage and to promote differentiation. Nucleic Acids Res. 2017 Jun 20;45(11):6442-6458. PubMed Central PMCID: PMC5499657.
    b. Marathe HG, Mehta G, Zhang X, Datar I, Mehrotra A, Yeung KC, de la Serna IL. SWI/SNF enzymes promote SOX10- mediated activation of myelin gene expression. PLoS One. 2013;8(7):e69037. PubMed Central PMCID: PMC3712992.
    c. de la Serna IL, Ohkawa Y, Higashi C, Dutta C, Osias J, Kommajosyula N, Tachibana T, Imbalzano AN. The microphthalmia-associated transcription factor requires SWI/SNF enzymes to activate melanocyte-specific genes. J Biol Chem. 2006 Jul 21;281(29):20233-41. PubMed PMID: 16648630.
    d. de La Serna IL, Carlson KA, Hill DA, Guidi CJ, Stephenson RO, Sif S, Kingston RE, Imbalzano AN. Mammalian SWI-SNF complexes contribute to activation of the hsp70 gene. Mol Cell Biol. 2000 Apr;20(8):2839-51. PubMed Central PMCID: PMC85505.

2. Our laboratory has made significant strides in understanding the intricate mechanisms through which SWI/SNF regulates genes involved implicated in cancer etiology. Additionally, our research has delved into the complexities of chromatin remodeling in melanoma and potential as a therapeutic target in cancer, as evidenced by our insightful review articles. These endeavors underscore our noteworthy contributions to the realms of melanocyte and melanoma research.

a. Dreier MR, Walia J, de la Serna IL. Targeting SWI/SNF Complexes in Cancer: Pharmacological Approaches and Implications. Epigenomes. 2024 Feb 4;8(1) PubMed Central PMCID: PMC10885108.
b. Saladi SV, Wong PG, Trivedi AR, Marathe HG, Keenen B, Aras S, Liew ZQ, Setaluri V, de la Serna IL. BRG1 promotes survival of UV-irradiated melanoma cells by cooperating with MITF to activate the melanoma inhibitor of apoptosis gene. Pigment Cell Melanoma Res. 2013 May;26(3):377-91. PubMed Central PMCID: PMC3633630.
c. Saladi SV, Keenen B, Marathe HG, Qi H, Chin KV, de la Serna IL. Modulation of extracellular matrix/adhesion molecule expression by BRG1 is associated with increased melanoma invasiveness. Mol Cancer. 2010 Oct 22;9:280. PubMed Central PMCID: PMC3098014.
d. Keenen B, Qi H, Saladi SV, Yeung M, de la Serna IL. Heterogeneous SWI/SNF chromatin remodeling complexes promote expression of microphthalmia-associated transcription factor target genes in melanoma. Oncogene. 2010 Jan 7;29(1):81-92. PubMed Central PMCID: PMC2803337.

3. My research has investigated the role of epigenetic regulators in diverse biological contexts as targets for epigenetic therapies. We found that the BET-bromodomain containing proteins and Class IV bromodomain-containing proteins promote melanocyte differentiation and expression of genes that promote pigmentation. This work has therapeutic implications for disorders such as vitiligo and melasma. Obesity and heart disease represent significant challenges to human health and well-being, exerting a widespread impact on mortality. In the pursuit of innovative therapeutic avenues, chromatin remodelers emerge as promising targets for drug development in addressing these conditions. Our studies identified FTO and SETD7, in obesity and cardiac function. As a collaborative researcher, we delved into unraveling novel epigenetic mechanisms associated with gene expression regulation during adipogenesis, with a focus on understanding the functional role of FTO.

   a. Basuroy T, Dreier M, Baum C, Blomquist T, Trumbly R, Filipp FV, de la Serna IL. Epigenetic and pharmacological control of pigmentation via Bromodomain Protein 9 (BRD9). Pigment Cell Melanoma Res. 2023 Jan;36(1):19-32. PubMed Central PMCID: PMC10091956.
   b. Trivedi A, Mehrotra A, Baum CE, Lewis B, Basuroy T, Blomquist T, Trumbly R, Filipp FV, Setaluri V, de la Serna IL. Bromodomain and extra-terminal domain (BET) proteins regulate melanocyte differentiation. Epigenetics Chromatin. 2020 Mar 10;13(1):14. PubMed Central PMCID: PMC7063807.
   c. Basuroy T, de la Serna IL. SETD7 in cardiomyocyte differentiation and cardiac function. Stem Cell Investig. 2019;6:29. PubMed Central PMCID: PMC6789293.
   d. Wu Q, Saunders RA, Szkudlarek-Mikho M, Serna Ide L, Chin KV. The obesity-associated Fto gene is a transcriptional coactivator. Biochem Biophys Res Commun. 2010 Oct 22;401(3):390-5. PubMed Central PMCID: PMC2963669.

4. The control of gene expression, encompassing both transcriptional and post-transcriptional levels, plays a pivotal role in the development of both benign and malignant neoplasms. My research has significantly advanced our understanding of multiple levels of gene regulation by uncovering novel molecular pathways that regulate gene expression within neoplastic cells. Collaborating with fellow investigators, our projects leveraged my expertise in gene expression, chromatin assays, and other cutting-edge techniques. This collaborative effort yielded successful completion of research projects focused on melanoma, breast cancer, and prostate cancer.

   a. Subramaniyan B, Sridharan S, M Howard C, M C Tilley A, Basuroy T, de la Serna I, Butt E, Raman D. Role of the CXCR4-LASP1 Axis in the Stabilization of Snail1 in Triple-Negative Breast Cancer. Cancers (Basel). 2020 Aug 21;12(9) PubMed Central PMCID: PMC7563118.
   b. Datar I, Kalpana G, Choi J, Basuroy T, Trumbly R, Chaitanya Arudra SK, McPhee MD, de la Serna I, Yeung KC. Critical role of miR-10b in B-RafV600E dependent anchorage independent growth and invasion of melanoma cells. PLoS One. 2019;14(4):e0204387. PubMed Central PMCID: PMC6469749.
   c. Ren G, Baritaki S, Marathe H, Feng J, Park S, Beach S, Bazeley PS, Beshir AB, Fenteany G, Mehra R, Daignault S, Al-Mulla F, Keller E, Bonavida B, de la Serna I, Yeung KC. Polycomb protein EZH2 regulates tumor invasion via the transcriptional repression of the metastasis suppressor RKIP in breast and prostate cancer. Cancer Res. 2012 Jun 15;72(12):3091-104. PubMed PMID: 22505648; NIHMSID: NIHMS371335.

d. Ren G, Feng J, Datar I, Yeung AH, Saladi SV, Feng Y, de la Serna I, Yeung KC. A Micro-RNA Connection in BRaf(V600E)-Mediated Premature Senescence of Human Melanocytes. Int J Cell Biol. 2012;2012:913242. PubMed Central PMCID: PMC3348633.

5. Across my professional journey, I have played a pivotal role in advancing our comprehension of chromatin remodeling, particularly in fundamental biological processes. My contributions extend across diverse realms, encompassing critical facets such as cell cycle regulation, DNA replication, nuclear architecture, and DNA repair mechanisms. In essence, my career is marked by a commitment to unraveling the mysteries of chromatin remodeling, providing key insights into its role in governing fundamental biological processes that underpin cellular function and genomic stability.

   a. Hill DA, de la Serna IL, Veal TM, Imbalzano AN. BRCA1 interacts with dominant negative SWI/SNF enzymes without affecting homologous recombination or radiation-induced gene activation of p21 or Mdm2. J Cell Biochem. 2004 Apr 1;91(5):987-98. PubMed PMID: 15034933.
   b. Moen PT Jr, Johnson CV, Byron M, Shopland LS, de la Serna IL, Imbalzano AN, Lawrence JB. Repositioning of muscle-specific genes relative to the periphery of SC-35 domains during skeletal myogenesis. Mol Biol Cell. 2004 Jan;15(1):197-206. PubMed Central PMCID: PMC307540.
   c. de la Serna IL, Imbalzano AN. Unfolding heterochromatin for replication. Nat Genet. 2002 Dec;32(4):560-2. PubMed PMID: 12457187.
   d. de la Serna IL, Roy K, Carlson KA, Imbalzano AN. MyoD can induce cell cycle arrest but not muscle differentiation in the presence of dominant negative SWI/SNF chromatin remodeling enzymes. J Biol Chem. 2001 Nov 2;276(44):41486-91. PubMed PMID: 11522799.

My Bibliography: https://www.ncbi.nlm.nih.gov/myncbi/1JIpfenUVaKAQ/bibliography/40797168/public/