BIOGRAPHICAL SKETCH

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NAME: Levine, Michael S.

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

POSITION TITLE: Director, Lewis-Sigler Institute for Integrative Genomics

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 California, Berkeley, CA	BA	06/1976	Genetics
Yale University, New Haven, CT	PHD	09/1981	Biophysics, Biochemistry
Universität Basel, Switzerland (W.Gehring)	Postdoctoral Fellow	09/1983	Molecular Genetics
University of California, Berkeley, CA (G. Rubin)	Postdoctoral Fellow	06/1984	Molecular Genetics

A. Personal Statement

I have studied gene regulation in development for nearly 40 years. These studies led to the discovery of the homeobox (with Bill McGinnis at the Univ Basel—McGinnis, Levine et al. Nature 1984), the first identification of Hox protein recognition sequences (Hoey and Levine, Nature 1988), the characterization of the eve stripe 2 developmental enhancer (Stanojevic et al. Science 1991), and the affinity threshold model for the differential regulation of dorsal-ventral patterning genes by the Dorsal (fly NF-kB) regulatory gradient (Jiang and Levine, Cell 1993). In more recent years my lab has elucidated mechanisms of transcriptional precision: the reliable deployment of key patterning genes during the critical one-hour period (2-3 hrs following fertilization) when the blueprint of the adult fly is established. Particular efforts focus on paused RNA polymerase II (Pol II) and shadow enhancers, which mediate synchronous and reliable activation of gene expression even under stressful conditions such as increases in temperature. Newly developed live-imaging methods suggest that enhancers control the frequency of transcriptional bursts during development, and that single enhancers can coordinately activate distantly mapping regulatory genes. During the past 25 years my lab has also examined gene regulatory networks underlying the specification of the chordate body plan in a simple proto-vertebrate, the sea squirt Ciona intestinalis. Using single cell RNA sequencing methods my lab has created comprehensive transcriptome lineages for most of the ~60 cell types in the Ciona tadpole, including each of the 15 different neural cell types comprising the sensory vesicle (simple brain) of swimming tadpoles. Over 40 of my former grad students and postdocs are now Asst, Assoc, or Full Professors at major universities in Asia, the US and Europe.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2015 -	Director, Lewis-Sigler Institute for Integrative Genomics, Princeton University
2015 -	Professor, Department of Molecular Biology, Princeton University
2012 - 2015	Chair, Chancellor’s Advisory Committee for Biology, UC Berkeley
2007 - 2011	Head, Division of Genetics, Genomics, & Development, UC Berkeley
2003 - 2015	Co-Director, Center for Integrative Genomics, UC Berkeley
2001 - 2002	Associate Director, Functional Genomics, Joint Genome Institute
2000 -	Deputy Editor, Science Advances, American Association for the Advancement of Science
1999 - 2000	Visiting Professor, University of Zurich, Switzerland
1996 -	Member of the Scientific Advisory Committee, Stowers Institute for Medical Research
1996 - 2015	Professor, Department of Molecular and Cell Biology, UC Berkeley
1991 - 1996	Professor, Department of Biology, University of California, San Diego
1988 - 1990	Professor, Department Biological Sciences, Columbia University

1986 - 1988	Associate Professor, Department of Biological Sciences, Columbia University
1984 - 1986	Assistant Professor, Department of Biological Sciences, Columbia University

Honors

2016	Elected to EMBO, European Molecular Biology Organization
2015	Conklin Medal, Society for Developmental Biology
2015	Anthony B. Evnin Professor of Genomics, Princeton University
2012	President, Society for Developmental Biology
2010	Einstein Professor, Chinese Academy of Sciences
2009	Wilbur Cross Medal, Yale University
2009	Faculty Research Lecturer, UC Berkeley
2007	Commencement Speaker, UC Berkeley, Dept. MCB
2006	Gavin Borden Fellow, Cold Spring Harbor Laboratory
2004	ISI Highly Cited Investigator, Molecular Biology & Genetics
2003	Singer Medal, Society for Developmental Biology; MERIT Award NIH
2002	Frances Williams Chair in Genetics, UC Berkeley
1999	Harvey Lecture, The Harvey Society, New York
1998	Elected to the National Academy of Sciences, National Academy of Sciences
1996	National Academy of Sciences Award in Molecular Biology, National Academy of Sciences
1996	Fellow, American Academy of Arts & Sciences
1995	Chancellor’s Associates Chair in Biology, UCSD
1985	Searle Scholars Fellow, Alfred P. Sloan Fellow
1982	Jane Coffin Childs Postdoctoral Fellow, Jane Coffin Childs Memorial Fund for Medical Research

C. Contribution to Science

1. I began my independent lab at Columbia University in 1984 with the goal of understanding how Hox proteins control the patterning of the Drosophila embryo. My lab examined both the regulation of HOX gene expression during development, and how their encoded proteins function as sequence-specific transcription factors. We also performed an in-depth analysis of the regulation of the homeobox gene *even-skipped* (eve), including the characterization of the stripe 2 enhancer:

    a. Hoey T, Levine M. Divergent homeo box proteins recognize similar DNA sequences in Drosophila. Nature. 1988 Apr 28;332(6167):858-61. PubMed PMID: 2895896.

    b. Stanojevic D, Small S, Levine M. Regulation of a segmentation stripe by overlapping activators and repressors in the Drosophila embryo. Science. 1991 Nov 29;254(5036):1385-7. PubMed PMID: 1683715.

    c. Stanojević D, Hoey T, Levine M. Sequence-specific DNA-binding activities of the gap proteins encoded by hunchback and Krüppel in Drosophila. Nature. 1989 Sep 28;341(6240):331-5. PubMed PMID: 2507923.

2. We next employed quantitative imaging methods to study mechanisms of transcriptional precision. These studies led to the identification of paused Pol II and shadow enhancers. Live imaging methods suggest that transcriptional bursting is a core property of gene expression in development:

    a. Boettiger AN, Levine M. Synchronous and stochastic patterns of gene activation in the Drosophila embryo. Science. 2009 Jul 24;325(5939):471-3. PubMed Central PMCID: PMC4280267.

    b. Fukaya T, Lim B, Levine M. Enhancer Control of Transcriptional Bursting. Cell. 2016 Jul 14;166(2):358-368. PubMed Central PMCID: PMC4970759.

    c. Hong JW, Hendrix DA, Levine MS. Shadow enhancers as a source of evolutionary novelty. Science. 2008 Sep 5;321(5894):1314. PubMed Central PMCID: PMC4257485.

3. In recent years we used a combination of genome editing, Hi-C contact maps, and live imaging to explore the role of genome organization in the regulation of enhancer-promoter interactions. These studies led to the identification of a new class of 3D organizational DNAs, tethering elements:

    a. Batut PJ, Bing XY, Sisco Z, Raimundo J, Levo M, Levine MS. Genome organization controls transcriptional dynamics during development. Science. 2022 Feb 4;375(6580):566-570. PubMed PMID: 35113722. PMC Journal In Process
    b. Levo M, Raimundo J, Bing XY, Sisco Z, Batut PJ, Ryabichko S, Gregor T, Levine MS. Transcriptional coupling of distant regulatory genes in living embryos. Nature. 2022 May;605(7911):754-760. PubMed PMID: 35508662. PMC Journal In Process

4. For the past 25 years my lab has helped establish the sea squirt, *Ciona intestinalis*, as a simple model system for studying the development of chordate development. The adults are primitive filter feeders that live in shallow ocean waters, but their embryos and larvae have many of the properties of vertebrate tadpoles. We have helped develop a variety of whole-genome methods for the analysis of gene regulatory networks, including high throughput transgenesis via electroporation:

    a. Abitua PB, Wagner E, Navarrete IA, Levine M. Identification of a rudimentary neural crest in a non-vertebrate chordate. Nature. 2012 Dec 6;492(7427):104-7. PubMed Central PMCID: PMC4257486.
    b. Abitua PB, Gainous TB, Kaczmarczyk AN, Winchell CJ, Hudson C, Kamata K, Nakagawa M, Tsuda M, Kusakabe TG, Levine M. The pre-vertebrate origins of neurogenic placodes. Nature. 2015 Aug 27;524(7566):462-5. PubMed Central PMCID: PMC5008972.
    c. Farley EK, Olson KM, Zhang W, Brandt AJ, Rokhsar DS, Levine MS. Suboptimization of developmental enhancers. Science. 2015 Oct 16;350(6258):325-8. PubMed Central PMCID: PMC4970741.
    d. Horie R, Hazbun A, Chen K, Cao C, Levine M, Horie T. Shared evolutionary origin of vertebrate neural crest and cranial placodes. Nature. 2018 Aug;560(7717):228-232. PubMed Central PMCID: PMC6390964.

5. Finally, we generated high resolution single cell datasets to create comprehensive lineage maps and gene regulatory networks for the different neural cell types comprising the CNS of swimming tadpoles:

    a. Cao C, Lemaire LA, Wang W, Yoon PH, Choi YA, Parsons LR, Matese JC, Wang W, Levine M, Chen K. Comprehensive single-cell transcriptome lineages of a proto-vertebrate. Nature. 2019 Jul;571(7765):349-354. PubMed Central PMCID: PMC6978789.
    b. Lemaire LA, Cao C, Yoon PH, Long J, Levine M. The hypothalamus predates the origin of vertebrates. Sci Adv. 2021 Apr;7(18) PubMed Central PMCID: PMC8081355.