BIOGRAPHICAL SKETCH

NAME: Dong, Xianjun

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

POSITION TITLE: Assistant Professor of Neurology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date	FIELD OF STUDY
Southeast University	BS	07/2002	Biomedical Engineering
Southeast University	MS	07/2005	Biomedical Engineering
Bergen University	PhD	07/2010	Bioinformatics and Genomics
University of Massachusetts Medical School	Postdoctoral Fellow	09/2013	Bioinformatics and Integrative Biology

A. Personal Statement

I am an Assistant Professor in Neurology at Harvard Medical School and head of the Genomics and Bioinformatics Hub at Brigham and Women's Hospital. I have been appointed as the Director of Computational Neuroscience of Precision Neurology Program at Brigham and Women's Hospital since 2016. I was previously granted the American Parkinson's Disease Association (APDA) Research Award twice, once in 2017 for cracking the code of chromosome 17q31 region in Parkinson's disease (Dong et al. ***Nature Neuroscience*** 2018), and once in 2019 for identifying the circRNAs that can explain the genetic risk variants for Parkinson's disease. I am recently funded by ASAP($9M) to deconstruct proximal disease mechanisms across cells, space and progression for Parkinson's disease.

My research interests lie in developing and applying computational methods to integrate and analyze omics and clinical data, in order to understand the functions of the human genome and their roles in neurodegenerative diseases and development. My doctoral studies focused on long-range gene regulation in vertebrates using comparative genomics and epigenomics. I discovered the first set of protein-coding exons that simultaneously serve as enhancers in animal development (Dong et al. ***Nucleic Acids Research*** 2009; Fredman et al. ***Genome Biology*** 2011). I also developed several online tools to study the transcriptional regulation in vertebrate genomes (Dong et al. ***Genome Biology*** 2009; Dong et al. ***BMC Bioinformatics*** 2010). When being trained as a postdoc in Dr. Weng's lab, I've served as an active member of the ENCODE Project (ENCyclopedia Of DNA Elements) consortium. My co-author work (An integrated encyclopedia of DNA elements in the human genome, ENCODE consortium, ***Nature***, 2012; 757 citations in 2013 alone) was recognized as the Top 10 Breakthroughs of the Year 2012 in Science. I designed sophisticated models to quantify the association between gene expression and chromatin features in various cellular contexts and different cell components (Dong et al. ***Genome Biology*** 2012; Dong et al. ***Epigenomics*** 2013). I'm also a co-author of four related publications (in journals such as *PLoS Biology*, *Genome Biology, Genome Research*, and *Nucleic Acids Research*) on various aspects from this milestone "roadmap" of human genome functions. Now, as a young investigator at Harvard Medical School & Brigham and Women's Hospital, I'm fully dedicated to neurological disease research. I wish that with my expertise in Bioinformatics and gene regulation I could make my best contribution to the battle of conquering neurological diseases.

1. Dong X, Liao Z, Gritsch D, Hadzhiev Y, Bai Y, Locascio J, Guennewig B, Liu G, Blauwendraat C, Wang T, Adler CH, Frosch MP, Nelson PT, Rizzu P, Cooper AA, Heutink P, Beach TG, Mattick JS, Mueller F, Scherzer CR. Enhancers active in dopamine neurons are a primary link between genetic variation and neuropsychiatric disease. Nature Neuroscience. 2018 Oct;21(10):1482-1492. PMID: 30224808.
2. An integrated encyclopedia of DNA elements in the human genome. Nature. 2012 Sep 6;489(7414):57-74. PubMed PMID: 22955616; PubMed Central PMCID: PMC3439153.
3. Dong X, Greven MC, Kundaje A, Djebali S, Brown JB, Cheng C, Gingeras TR, Gerstein M, Guigó R, Birney E, Weng Z. Modeling gene expression using chromatin features in various cellular contexts. Genome Biol. 2012 Jun 13;13(9):R53. PubMed PMID: 22950368; PMCID: PMC3491397.

4. Dong X, Navratilova P, Fredman D, Drivenes Ø, Becker TS, Lenhard B. Exonic remnants of whole-genome duplication reveal cis-regulatory function of coding exons. Nucleic Acids Res. 2010 Mar;38(4):1071-85. PubMed PMID: 19969543; PubMed Central PMCID: PMC2831330.

B. Positions and Honors

Positions and Employment

2005 - 2010	Research Assistant, Computational Biology Unit, University of Bergen
2010 - 2013	Postdoctoral Fellow, Program in Bioinformatics and Integrative Biology, UMass Medical School, Worcester, MA
2013 -	Faculty, Department of Neurology, Brigham and Women's Hospital, Boston, MA
2013 - 2020	Instructor, Department of Neurology, Harvard Medical School, Boston, MA
2016 -	Director of Computational Neuroscience, Precision Neurology Program, Brigham and Women's Hospital, Boston, MA
2020 -	Director, Genomics and Bioinformatics Program, Brigham and Women's Hospital, Boston, MA
2020 -	Assistant Professor, Department of Neurology, Harvard Medical School, Boston, MA

Other Experience and Professional Memberships

2006 -	Member, International Society for Computational Biology (ISCB)
2013 -	Member, American Society for Human Genetics (ASHG)
2015 - 2015	Judge, The 10th National DNA Day Essay Contest, American Society for Human Genetics
2016 -	Member, American Academy of Neurology (AAN)

Honors

2000	*Liu Yonglin* Fellowship, Southeast University, China
2000	Excellent Undergraduate Scholarship, Southeast University, China
2000	Second Prize of National Undergraduate Mathematical Contest in Modeling, CSIAM (China Society for Industrial and Applied Mathematics)
2001	Meritorious Winner, International Mathematical Contest in Modeling (MCM)
2001	First Prize of National Undergraduate Electronic Design Contest, Ministry of Education, China
2001	Excellent Undergraduate Scholarship, Southeast University, China
2002	Excellent Undergraduate Scholarship, Southeast University, China
2009	Travel Fellowship, MCB Research School, University of Bergen, Norway
2009	Full Travel Scholarship, "Chromatin Domains and Insulators" Workshop, Spain
2010	Chinese Government Award for Outstanding Self-financed Students Abroad, Ministry of Education, China
2015	Reviewers' Choice Abstract, American Society of Human Genetics (ASHG) meeting
2018	Finalist of the PacBio Structural Variant SMRT Grant program
2018	Research Excellence Award, Brigham and Women's Hospital
2019	Center for Advanced Parkinson's Research (CAPR) Seed Award

C. Contribution to Science

1. **Transcriptional and epigenetic regulation of neurodegenerative diseases**

   We have performed the laser-capture microdissection total RNAseq for different neuron types in 130 human brains. We found that surprisingly more than 60% of human genome are transcribed in dopamine neurons alone. 71,022 transcribed non-coding elements (TNEs) were identified and many of them are active enhancers (eRNAs) in dopamine neurons. Active enhancers were shown to be a primary link between genetic variation and neuropsychiatric disease. We also performed integrative analysis on the transcriptome and H3K4me3 epigenomes of human prefrontal cortex neurons obtained using fluorescence-activated nuclei sorting. We identified genomic regions (both promoters and enhancers) with differential H3K4me3 signals in

the prefrontal cortex neurons of individuals diagnosed with Huntington's disease. We also found the likely genetic markers associated with the early development and fast decline of Parkinson's disease.

a. Dong X, Liao Z, Gritsch D, Hadzhiev Y, Bai Y, Locascio J, Guennewig B, Liu G, Blauwendraat C, Wang T, Adler CH, Frosch MP, Nelson PT, Rizzu P, Cooper AA, Heutink P, Beach TG, Mattick JS, Mueller F, Scherzer CR. Enhancers active in dopamine neurons are a primary link between genetic variation and neuropsychiatric disease. Nature Neuroscience. 2018 Oct;21(10):1482-1492. PMID: 30224808.
b. Dong X, Tsuji J, Labadorf A, Roussos P, Chen JF, Myers RH, Akbarian S, Weng Z. The Role of H3K4me3 in Transcriptional Regulation Is Altered in Huntington's Disease. PLoS One. 2015;10(12):e0144398. PubMed PMID: 26636336; PubMed Central PMCID: PMC4670094.
c. Liu G, Boot B, Locascio JJ, Jansen IE, Winder-Rhodes S, Eberly S, Elbaz A, Brice A, Ravina B, van Hilten JJ, Cormier-Dequaire F, Corvol JC, Barker RA, Heutink P, Marinus J, Williams-Gray CH, Scherzer CR. Specifically neuropathic Gaucher's mutations accelerate cognitive decline in Parkinson's. Ann Neurol. 2016 Nov;80(5):674-685. PubMed PMID: 27717005; PMCID: PMC5244667.
d. Mittal S, Bjørnevik K, Im DS, Flierl A, Dong X, Locascio JJ, Abo KM, Long E, Jin M, Xu B, Xiang YK, Rochet JC, Engeland A, Rizzu P, Heutink P, Bartels T, Selkoe DJ, Caldarone BJ, Glicksman MA, Khurana V, Schüle B, Park DS, Riise T, Scherzer CR. β2-Adrenoreceptor is a regulator of the α-synuclein gene driving risk of Parkinson's disease. Science. 2017 Sep 1;357(6354):891-898. PubMed PMID: 28860381.

2. **Direct contributions to the international ENCODE project, which was selected as one of the *Top 10 Breakthroughs of the Year 2012 in Science***

As the next milestone after the Human Genome Project, the ENCODE Project aimed to identify all functional elements in the human genome. When working as a postdoctoral in Dr. Zhiping Weng's lab, I have served as an active member of the ENCODE consortium. In September 2012, the ENCODE project released a series of important scientific discoveries in 30 papers published simultaneously in several top journals, including the landmark article in Nature ("An integrated encyclopedia of DNA elements in the human genome", ENCODE consortium, Nature, 2012; 757 citations in one year). Many of the discoveries are revolutionary. For example, we found that the vast majority (80.4%) of the human genome, not just 5-10% as we thought before the start of the project, participates in at least one biochemical RNA or chromatin-associated event in at least one cell type (ENCODE Consortium, Nature, 2012). Out of the 30 papers, 7 publications were from me, including one co-author in Nature, one first-author in Genome Biology, one first-author in Epigenomics, one co-author in PLoS Biology, one co-author in Nucleic Acids Research, and two in Genome Research.

a. Dong X, Greven MC, Kundaje A, Djebali S, Brown JB, Cheng C, Gingeras TR, Gerstein M, Guigó R, Birney E, Weng Z. Modeling gene expression using chromatin features in various cellular contexts. Genome Biol. 2012 Jun 13;13(9):R53. PubMed PMID: 22950368; PMCID: PMC3491397.
b. Wang J, Zhuang J, Iyer S, Lin X, Whitfield TW, Greven MC, Pierce BG, Dong X, Kundaje A, Cheng Y, Rando OJ, Birney E, Myers RM, Noble WS, Snyder M, Weng Z. Sequence features and chromatin structure around the genomic regions bound by 119 human transcription factors. Genome Res. 2012 Sep;22(9):1798-812. PubMed PMID: 22955990; PubMed Central PMCID: PMC3431495.
c. Cheng C, Alexander R, Min R, Leng J, Yip KY, Rozowsky J, Yan KK, Dong X, Djebali S, Ruan Y, Davis CA, Carninci P, Lassman T, Gingeras TR, Guigó R, Birney E, Weng Z, Snyder M, Gerstein M. Understanding transcriptional regulation by integrative analysis of transcription factor binding data. Genome Res. 2012 Sep;22(9):1658-67. PubMed PMID: 22955978; PMCID: PMC3431483.
d. An integrated encyclopedia of DNA elements in the human genome. Nature. 2012 Sep 6;489(7414):57-74. PubMed PMID: 22955616; PubMed Central PMCID: PMC3439153.

3. **Discovery of the first genome-wide set of cis-regulatory elements in exons in the human genome**

My early publications were focusing on discovering long-range regulatory elements, such as enhancers, using comparative genomics. An enhancer is a short stretch of DNAs that is located distal, upstream or downstream, to the transcription start site (TSS) of a target gene. Nearly all enhancer studies so far are

limited to look for enhancers in the space of non-coding regions. For the very first time, I have successfully demonstrated via a genome-wide study that enhancers can be also found in the exon of the protein-coding genes. By systematically tracking the fate of genomics regulatory blocks (GRBs) along the evolution of vertebrates, I have discovered a list of 38 exonic enhancers with high confidence and had largely expanded the space of searching for regulatory elements.

a. Akalin A, Fredman D, Arner E, Dong X, Bryne JC, Suzuki H, Daub CO, Hayashizaki Y, Lenhard B. Transcriptional features of genomic regulatory blocks. Genome Biol. 2009;10(4):R38. PubMed PMID: 19374772; PubMed Central PMCID: PMC2688929.
b. Dong X, Navratilova P, Fredman D, Drivenes Ø, Becker TS, Lenhard B. Exonic remnants of whole-genome duplication reveal cis-regulatory function of coding exons. Nucleic Acids Res. 2010 Mar;38(4):1071-85. PubMed PMID: 19969543; PubMed Central PMCID: PMC2831330.
c. Fredman D, Dong X, Lenhard B. Making enhancers from spare parts of the genome. Genome Biol. 2011 Dec 29;12(12):138. PubMed PMID: 22206586; PubMed Central PMCID: PMC3334608.

4. **Revealing the predictive association between gene expression and epigenetic marks with a novel two-step model**

Gene expression can be controlled not only by the genetic elements inherited in DNA, but also regulated by the factors that are not inherited in DNA, so-called epigenetic factor, such as histone modifications. Unlike the genetic elements, epigenetic elements are more relevant to the environmental factor, which contribute significantly to the change of disease or physiological traits. Taking advantage of the big data from the ENCODE project, I could investigate the relationship of gene transcription and epigenetic modification in a genome-wide large-scale manner, for both cancer cell lines and normal cells. The novel two-step model I developed can predict both the 'on/off' status and quantification level of gene expression. It not only assures the previous finding but also provides new insights for the mechanism of transcriptional regulation.

a. Dong X, Greven MC, Kundaje A, Djebali S, Brown JB, Cheng C, Gingeras TR, Gerstein M, Guigó R, Birney E, Weng Z. Modeling gene expression using chromatin features in various cellular contexts. Genome Biol. 2012 Jun 13;13(9):R53. PubMed PMID: 22950368; PMCID: PMC3491397.
b. An integrated encyclopedia of DNA elements in the human genome. Nature. 2012 Sep 6;489(7414):57-74. PubMed PMID: 22955616; PubMed Central PMCID: PMC3439153.
c. Dong X, Weng Z. The correlation between histone modifications and gene expression. Epigenomics. 2013 Apr;5(2):113-6. PubMed PMID: 23566087; PubMed Central PMCID: PMC4230708.

5. **Developing novel web-based bioinformatics tools and services, which have significantly facilitated the researchers in the community of bioinformatics**

Since 2005, I have developed four novel web-based tools (Synorth, Translog, Factorbook.org, humanbraincode.org) to facilitate the research of evolutionary biology and gene regulation. They are all published in renowned journals, such as *Genome Biology*, *BMC Bioinformatics*, and *Nucleic Acids Research*. I also developed the bioinformatics site ("One Tip Per Day", http://onetipperday.blogspot.com) to share technical notes and tips of bioinformatics with the other users in the community. Now as the founding director of the Genomics and Bioinformatics Hub at BWH, we offer bioinformatics training and support to the research community in Brigham and Women's Hospital.

a. Dong X, Fredman D, Lenhard B. Synorth: exploring the evolution of synteny and long-range regulatory interactions in vertebrate genomes. Genome Biol. 2009;10(8):R86. PubMed PMID: 19698106; PubMed Central PMCID: PMC2745767.
b. Dong X, Akalin A, Sharma Y, Lenhard B. Translog, a web browser for studying the expression divergence of homologous genes. BMC Bioinformatics. 2010 Jan 18;11 Suppl 1:S59. PubMed PMID: 20122234; PubMed Central PMCID: PMC3009532.
c. Wang J, Zhuang J, Iyer S, Lin XY, Greven MC, Kim BH, Moore J, Pierce BG, Dong X, Virgil D, Birney E, Hung JH, Weng Z. Factorbook.org: a Wiki-based database for transcription factor-binding data generated by the ENCODE consortium. Nucleic Acids Res. 2013 Jan;41(Database issue):D171-6. PubMed PMID: 23203885; PubMed Central PMCID: PMC3531197.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/labs/bibliography/1TWL5qfAudt/bibliography/public/

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

Ongoing Research Support

Research Grant, American Parkinson Disease Association
Dong, Xianjun (PI) 09/01/19-08/30/20 (NCE 05/31/21)
Circular RNAs: A novel link between genetic susceptibility and Parkinson's disease?
Role: PI

Michael J. Fox Foundation Research Grant / Aligning Science Across Parkinson's (ASAP)
Scherzer, Levin, Dong, Feany, Zhang (PI) 10/01/20 - 08/31/23
Parkinson5D: Deconstructing Proximal Disease Mechanisms across Cells, Space and Progression
Role: Co-PI

NIH 1U01NS120637-01, National Institute of Health (NIH)
Dong, Scherzer (PI) 11/01/20 - 10/31/21
AI2AMP-PD: Accelerating Parkinsons Diagnosis Using Multi-Omics and Artificial Intelligence
Role: Co-PI

NIH 1R01AG057331-01, National Institute of Health (NIH)
Feany, Fraenkel, Scherzer (PI) 09/15/17-06/30/22
Integrative Multi-Omic Discovery of Proximal Mechanisms Driving Age-Dependent Neurodegeneration
Role: Co-Investigator

Brigham Research Institute (BRI) NextGen Awards, Brigham and Women's Hospital
Dong, Xianjun (PI) 12/31/18-06/30/19 (NCE 06/30/20)
Bioinformatics Club: A Weekly Meetup to Learn and Share Bioinformatics at BWH
Role: PI

Michael J. Fox Foundation Research Grant
Scherzer, Riise (PI) 05/01/19 - 04/30/21
400 Virtual Clinical Trials for Parkinson's Disease
Role: Bioinformatics Engineer

Completed Research Support

U01 NS095736-01A1, National Institute of Health (NIH)
Scherzer (PI) 09/30/16-08/31/19
Parkinson Disease: Predicting the Future
Role: Co-Investigator

Research Grant, American Parkinson Disease Association
Dong, Xianjun (PI) 01/01/17-01/01/18
Cracking the Code on Chromosome 17q21 for Parkinson: From GWAS to Novel Drug Targets
Role: PI

Center for Advanced Parkinson's Research (CAPR) Seed Award
Dong, Fanning, Scherzer (PI) 09/28/18-09/28/19
Translating GWAS peaks into novel drug targets
Role: Co-PI