BIOGRAPHICAL SKETCH

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NAME: Mojgan Rastegar, PhD	POSITION TITLE Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login)	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Tehran University, Iran	BSc	07/1988	Microbiology
Tehran University of Medical Sciences, Iran	MSc	07/1992	Medical Bacteriology
Université Catholique de Louvain (UCL), Belgium	DEA*	09/1998	Biochemistry and Human Cellular Biology
Université Catholique de Louvain (UCL), Belgium	PhD	02/2000	Biomedical Sciences
Indiana Purdue University (IUPUI), Indiana, IN, USA	Post-doc	06/2001	Pharmacology & Toxicology
McGill Cancer Centre, Montréal, QC, Canada	Post-doc	11/2004	Epigenetics

Diplôme d'Etudes Approfondies

A. Personal Statement

Chemical modifications on DNA molecules known as DNA methylation refer to a major type of epigenetic modifications. My research program focuses on the role of DNA methylation, and a DNA methylation-binding protein (MeCP2) in brain development and neurodevelopmental disorders. I am particularly interested on the differential function and regulation of the two MeCP2 protein variants (isoforms), MeCP2E1 and MeCP2E2. Abnormal DNA methylation; altered MeCP2 expression or compromised MeCP2 protein function leads to impaired brain function, Rett Syndrome, autism, and is linked to fetal alcohol spectrum disorders (FASD). Accordingly, MeCP2 is a major epigenetic factor in brain that is critical for normal brain development and function. In my lab, we have established reproducible neural stem cell differentiation systems to study early events during brain development. I believe that our studies will help towards improved therapeutic strategies for neurological diseases that currently have no cure, such as Rett Syndrome, FASD and autism.

The following research areas in my lab link epigenetics, neuroscience, mental health, and regenerative medicine:

1. Role of MeCP2 in neurons and neurological disorders.
2. Regulation of MeCP2 isoforms during brain development.
3. Epigenetic control of gene regulatory networks in brain-derived neural stem cells.

B. Positions and Honors

Positions and Employment

12/2004-08/2005 **Research Associate**, Oncology Dept., McGill Cancer Centre, Montréal, QC, Canada
09/2005-08/2008 **Research Associate**, Dev. & Stem Cell Biol., Sickkids Hospital, U. Toronto, ON, Canada
09/2008-12/2008 **Visiting Professor**, Biochem & Medical Genetics, U. Manitoba, Winnipeg, MB, Canada
01/2009-03/2015 **Assistant Professor**, Biochem & Medical Genetics, U. Manitoba, Winnipeg, MB, Canada
03/2015-present **Associate Professor**, Biochem & Medical Genetics, U. Manitoba, Winnipeg, MB, Canada

Honors and Awards

1996-7 Doctoral Fellowship, Fonds de Développement Scientifique, UCL, Brussels, Belgium
1998-9 Doctoral Fellowship, Patrimoine Facultaire, UCL, Brussels, Belgium
2000 Subside Scientifique Complémentaire, Patrimoine Facultaire, UCL, Brussels, Belgium
2001 Canderel Fellowship Award, McGill University, Montréal, QC, Canada
2002 Dr. David T. W. Lin Fellowship Award, Faculty of Medicine, McGill University, Montréal, QC, Canada
2002 CIHR Cancer Consortium Training Grant Fellowship Award, McGill University, Montréal, QC, Canada
2003 Conrad F. Harrington Fellowship Award, McGill University, Montréal, QC, Canada
2004 CIHR Cancer Consortium Training Grant Fellowship Award, McGill University, Montréal, QC, Canada
2005 Miriam & SAUL Goldberg Innovative Research Award, McGill University, Montréal, Canada (declined)
2008 Stem Cell Network Canadian Alumni Award, Stem Cell Network, Canada
2012 NSERC-Early Career Researcher Supplement Award

Expertise

Epigenetics, DNA methylation, Cellular and Molecular Biology, Histone Modifications, Neural Stem Cells, Stem Cell Differentiation, MeCP2 Isoforms, Transcriptional Regulation, Chromatin Remodeling, Rett Syndrome, Neurodevelopmental Disorders

C. Selected Peer-reviewed Publications (Trainees are underlined)

1. **Rastegar M**, Szpirer C, Rousseau GG, and Lemaigre FP. Hepatocyte nuclear factor 6: organization and chromosomal assignment of the rat gene and characterization of its promoter. *Biochemical Journal* 1998; 334: 565-569
2. **Rastegar M**, Lemaigre FP, and Rousseau GG. HNF-6: Pièce maîtresse d'un réseau de facteurs de transcription hépatiques contrôlé par l'hormone de croissance. *Médicine /Sciences 2000*; 16: 1106-1108
3. **Rastegar M**, Lemaigre FP, and Rousseau GG. Control of gene expression by growth hormone in liver: Key role of a network of transcription factors. *Molecular and Cellular Endocrinology* 2000; 164: 1-4
4. Lahuna O*, **Rastegar M***, Maiter D, Thissen J-P, Lemaigre F.P. and Rousseau G.G. Involvement of STAT5 and HNF-4 in the transcriptional control of the *hnf6* gene by growth Hormone. *Molecular Endocrinology* 2000; 14: 285-94
   Equal contribution.
5. **Rastegar M**, Rousseau GG, and Lemaigre FP. CCAAT/Enhancer Binding Protein alpha (C/EBPα) is a mediator of growth hormone action in the liver and controls the expression of Hepatocyte Nuclear Factor-6 (HNF-6). *Endocrinology* 2000; 141: 1686-92
6. Wu CH, **Rastegar M**, Gordon J, and Safa AR. β2-microglobulin induces apoptosis in HL-60 human leukemia cells and its multidrug resistant variants overexpressing MRP1 but lacking Bax or overexpressing P- glycoprotein. *Oncogene* 2001; 25: 7006-7020
7. Wu CH, Gordon J, **Rastegar M**, Ogretmen B, and Safa AR. Proteinase-3, a serine protease which mediates doxorubicin-induced apoptosis in the HL-60 leukemia cell line is down-regulated in its doxorubicin-resistant variant. *Oncogene* 2002; 21: 5160-5174
8. Gordon J, Wu CH, **Rastegar M**, and Safa AR. ß2-microglobulin induces caspase-dependent apoptosis in CCRF-HBS-2 human leukemia cell line independently of caspase-3, -8, and -9 pathways but through increased reactive oxygen species. *International Journal of Cancer* 2003; 103: 316-327
9. **Rastegar M**, Kobrossy L, Nagy Kovàcs E, Rambaldi I, and Featherstone M. Sequential histone modifications at *Hoxd4* regulatory regions distinguish anterior from posterior embryonic compartments. *Molecular and Cellular Biology* 2004; 24: 8090-8103

10. Huang H, **Rastegar M**, Bodner C, Goh SL, Rambaldi I, and Featherstone M. Meis C-termini harbor transcriptional activation domains that respond to cell signaling. *The Journal of Biological Chemistry* 2005; 280:10119-27

11. Kobrossy L, **Rastegar M**, Featherstone M. Interplay between chromatin and *trans*-acting factors regulating the *Hoxd4* promoter during neural differentiation. *Journal of Biological Chemistry* 2006; 281:25926-39

12. Nolte C*, **Rastegar M***, Amores A, Bouchard M, Grote D, Maas R, Nagy Kovacs E, Postlethwait J, Rambaldi I, Rowan Sh, Zhang F, and Featherstone M. Stereospecificity and PAX6 function direct *Hoxd4* neural enhancer activity along the antero-posterior axis. *Developmental Biology* 2006; 15-299(2): 582-93
Equal contribution.

13. Ellis J, Hotta A, and **Rastegar M.** Retrovirus silencing by an epigenetic TRIM. *Cell* 2007**;** 131(1), 13-14

14. Delcuve GP, **Rastegar M,** and Davie JR. Epigenetic Control. *Journal of Cellular Physiology* 2009**;** 219(2): 243-50. *Artwork selected for the cover*

15. **Rastegar M**, Hotta A, Pasceri P, Makarem M, Cheung A, Elliot S, Adachi M, Jones FS, Park KJ, Clarke I, Dirks P, and Ellis J. MECP2 Isoform-Specific Vectors with Regulated Expression for Rett Syndrome Gene Therapy. *PLOS ONE* 2009**;** 4(8): 1-15. e6810. doi: 10.1371

16. Barber B & **Rastegar M.** Epigenetic Control of *Hox* Genes during Neurogenesis, Development and Disease. *Annals of Anatomy* 2010; 192(5): 261-74. *Artwork selected for cover.*

17. Sandhu S, Wu X, Nabi Z, **Rastegar M,** Kung S, Mai S, and Ding H. Loss of HLTF Promotes Intestinal Carcingogenesis. *Molecular Cancer* 2012; 27; 11(1): 18: 1-16.

18. Zachariah RM, and **Rastegar M.** Linking Epigenetics to Human Disease and Rett Syndrome; The Emerging Novel and Challenging Concepts in MeCP2 Research. *Neural Plasticity* 2012. 2012:415825. 1-11. doi: 10.1155/2012/415825

19. Olynik B, and **Rastegar M**. The Genetic and Epigenetic Journey of Embryonic Stem Cells into Mature Neuronal Cell Types. *Frontiers in Genetics* 2012; 3(81):1-16. doi: 10.3389/fgene.2012.00081.

20. Zachariah RM*, Olson C*, Ezeonwuka CD, and **Rastegar M.** Novel MeCP2 Isoform-Specific Antibody Reveals the Endogenous MeCP2E1 Expression in Murine Brain, Primary Neurons and Astrocytes. *PLOS ONE* 2012; 7(11):1-10. e49763. doi: 10.1371/ journal.pone.0049763
Equal contribution.

21. Barber B*, Liyanage VRB*, Zachariah RM, Olson CO, Bailey M, and **Rastegar M**. Dynamic Expression of MEIS1 Homeoprotein in E14.5 Forebrain and Differentiated Forebrain-Derived Neural Stem Cells. *Annals of Anatomy* 2013**;** 195(5):431-40. doi: 10.1016/j.aanat.2013.04.005.20.
Equal contribution.

22. Liyanage VRB, Zachariah RM, and **Rastegar M**. Decitabine Alters the Expression of *Mecp2* Isoforms *via* Dynamic DNA Methylation at the *Mecp2* Regulatory Elements in Neural Stem Cells. *Molecular Autism* 2013; 4:46. 1-21. doi:10.1186/2040-2392-4-46

23. Ezeonwuka CD, & **Rastegar M**. MeCP2-Related Diseases and Animal Models. *Diseases.* 2014*;* 2(1):45-70

24. Liyanage VRB, Jarmasz J, Murugeshan N, Del Bigio MR, **Rastegar M**, and Davie JR. DNA Modifications: Function and Applications in Normal and Disease States. *Biology.* 2014; 22;3 (4):670-723. doi: 10.3390/biology3040670.

25. Yasui DH, Aflatooni AO, Gonzales ML, Hu DJ, Gavino BJ, Golub MS, Vincent JB, Schanen NC, Olson CO, **Rastegar M,** and LaSalle JM. Mice with an Isoform-ablating *Mecp2*-exon 1 Mutation Recapitulates the Neurologic Deficits of Rett syndrome. *Human Molecular Genetics* 2014; 23(9):2447-58. doi: 10.1093/hmg/ddt640.

26. Liyanage VRB, and **Rastegar M**. Rett Syndrome and MeCP2. *NeuroMolecular Medicine.* 2014; 16(2):231-64. doi.10.1007/s12017-014-8295-9

27. Olson CO*, Zachariah RM*, Ezeonwuka CD*, Liyanage VRB, and **Rastegar M.** Brain Region-Specific Expression of MeCP2 Isoforms Correlates with DNA Methylation within *Mecp2* Regulatory Elements. *PLOS ONE* 2014**;** 9(3) 1-16: e90645. doi: 10.1371/journal.pone.0090645
Equal contribution.

28. Marzban H, Del Bigio MR, Alizadeh J, Ghavami S, Zachariah RM, and **Rastegar M.** Cellular Commitment in the Developing Cerebellum. *Frontiers in Cellular Neuroscience*, 2015; *8(450): 1-26. Doi: 10.3389/fncel.2014.00450*

29. Liyanage VRB, Zachariah RM, Davie JR, and **Rastegar M**. Ethanol Deregulate Mecp2/MeCP2 in Differentiating Neural Stem Cells via Interplay Between 5-methylcytosine and 5-hydroxymethylcytosine at the Mecp2 Regulatory Elements. *Experimental Neurology* 2015; 265 102-117. Doi: 10.1016/j.expneurol.2015.01.006

D. Research Support (current and past three years)

Ongoing Research Support

- **International Rett Syndrome Foundation (IRSF)** (2016-2018)
  Investigating the Molecular Mechanisms of MeCP2 Isoform-Specific Regulation in Brain Cells. $100,000 USD

- **CIHR Team Grant Canadian Epigenetics, Environment, and Health Research Consortium (CEEHRC)** (2013-2018) (Co-PI and project leader) - [Team Leader: James Davie]
  Discovering the Epigenetic Signatures Associated with Fetal Alcohol Spectrum Disorders. $1,377,000

- **CFI-IOF** (2012-2018) $47,550 (PI)

- **Children's Hospital Research Institute of Manitoba (CHRIM)** (2015-2016)
  DNA Methylation Analysis of Post-mortem Brain from a Rett Syndrome Patient. $5,000

- **University Research Grant Program (URGP)** (2015-2016) Studying Disease-Associated Role of MeCP2 in Rett Syndrome using Clinically Relevant Biological Samples. $7,500

Completed Research Support

- **NSERC Discovery Grant-372405-2009** (2009-2016)
  HOX Regulatory Network during Neural Stem Cell Differentiation. $175,000

- **Health Sciences Centre Foundation** (2013-2016)
  Modeling Childhood ASD and FASD Disorders by Investigating MeCP2 in Neural Stem Cells. $70,000

- **CIHR Catalyst Grant: Environments, Genes and Chronic Disease** (2013-2014) (Co-PI: J. Davie)
  Investigating the Cell Type-Specific Regulatory Role of Ethanol on MeCP2 Expression**.** $100,000

- **Scottish Rite Charitable Foundation of Canada-10110 (SRCFC)** (2010-2014)
  High Resolution Study of MeCP2 Isoforms in Neurons for Therapy in Rett Syndrome. $105,000

- **Manitoba Medical Service Foundation (MMSF)** (2012-2013). $20,000