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PhD Student (5th year)

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Vichithra Liyanage received her B.Sc in Molecular Biology and Biotechnology from University of Peradeniya Sri Lanka in 2009, with First Class Honors. She was awarded with the Award of Academic Excellence from University of Peradeniya for her achievements. She then completed research training in Gene Technology at the Genetech Research Institute, Sri Lanka. After completing her undergraduate studies, Vichithra joined the Department of Molecular Biology and Biotechnology, Faculty of Science, University of Peradeniya, Sri Lanka as an assistant lecturer. She also worked as a visiting assistant lecturer/instructor at the Department of Pharmacy and Postgraduate Institute of Science, University of Peradeniya until 2010. She started her M.Sc. graduate studies at the University of Manitoba, Canada in 2011 by joining Dr. Mojgan Rastegar's Epigenetics and Neurogenesis lab. She successfully transferred to PhD program in 2012.

Her graduate studies at the University of Manitoba were continuously funded by Manitoba Health Research Council (MHRC)/ University of Manitoba Graduate Fellowship (UMGF)/ Research Manitoba studentships (2011-2013; 2013-2015; 2015-2017). Moreover, she was awarded with several Faculty of Graduate Studies scholarships for international students including International Graduate Student Entrance Scholarship (2011) and International Graduate Student Scholarship (2013, 2014). Her academic achievements in Human Genetics were appreciated by the President's Graduate scholarship in Human Genetics in 2013/14 (single award presented each year). Her hard work and contribution to Medical Genetics were paid off by the receipt of the Department of Biochemistry and Medical Genetics outstanding graduate student awards in three consecutive years, 2013, 2014 and 2015 [Mindel Rady Olenick Fellowship in Human Genetics (2014/15; 2013/14) and Phyllis J. McAlpine Graduate Fellowship (2012/13). To present her research work, Vichithra had attended many national and international neuroscience conferences where she had presented more than 20 posters. She was awarded with 6 travel awards including NeuroDevNet Brain Development Conference Travel Scholarship (2013, 2014), Manitoba Medical College Foundation travel award (awarded as a recognition for excellence in Manitoba poster competition 2014), Faculty of Graduate Studies Graduate student travel award (2013, 2012) and Canadian Association of Neuroscience Travel award (2012). She has also won 3 poster awards; Manitoba Medical Service Foundation award for excellence in Manitoba Health Research Poster competition 2014, Silver award: Canadian Institute of Health Research (CIHR) national research Poster competition 2014 and 7th Annual Child Health Research Day Symposium 2011. Vichithra also received Outstanding Master's student Departmental Seminar Presentation of the year 2011-2012.

As scholarly activities, she volunteers as a reviewer in scientific journals such as Obstetrics and Gynaecology Cases – Reviews, the Journal of Sports and Health Sciences- Elsevier, the Journal of Emerging Investigators: An open-access journal biological and physical sciences for middle and high school students and OMICS International Group: Journal of Stem Cell Research & Therapy. She has volunteered as a judge for Winnipeg School Science Fair for three years (2014-2016) under the categories of Biology and Sustainable Development. Vichithra is also involved in knowledge translation activities through Discovery Days, (one-day workshops for high school children and teachers) organized by Canadian Medical Hall of Fame since 2012.

RESEARCH OVERVIEW

Epigenetic Regulation of MeCP2 in Brain

Methyl CpG Binding Protein 2 (MeCP2) is a major transcriptional regulator in brain. Mutations, deficiency or overexpression of which lead to severe neurological disorders including, Rett Syndrome (RTT), MECP2 duplication syndrome (MDS) and alcohol-induced neurological disorders such as Fetal Alcohol Spectrum Disorders (FASD). Alternative splicing of MECP2/Mecp2 gene generates two isoforms MeCP2E1 and MeCP2E2, which differ in terms of their expression, functions and neuronal phenotypes caused by overexpression/deficiency. Therefore, tight regulation of both Mecp2/MeCP2 isoforms in brain cell types is essential. However, regulatory mechanisms of Mecp2/MeCP2 expression largely remain elusive. Therefore, the main objective of my current studies is to investigate the role of epigenetic mechanisms in regulating Mecp2 isoforms in neurons, the major cell type of the brain. My studies so far have shown that DNA methylation at Mecp2 regulatory elements found within the Mecp2 promoter and intron 1 plays a role in regulating Mecp2/MeCP2 expression in differentiating neural stem cells (Liyanage et al., 2013, Molecular Autism, Liyanage et al., 2015, Experimental Neurology) and in adult mouse brain (Olson et al., 2014, Plos One). My research work will contribute significantly to the understanding of regulatory mechanisms of Mecp2/MeCP2 isoforms in the major cell type of the brain and provide checkpoints that could be targeted in drug therapy to modulate their expression in MeCP2-related neurological disorders.

PUBLICATIONS

Journal Articles (research)

- **Liyanage, V.R.B.,** Zachariah, R.M., Davie, J.R., & Rastegar, M. (2015). *Ethanol Deregulates Mecp2/ MeCP2 in Differentiating Neural Stem Cells via Interplay between 5-Methylcytosine and 5- Hydroxymethylcytosine at the Mecp2 Regulatory Elements.* Experimental Neurology. 265: 102-117

- Olson, C.O., Zachariah, R.M., Ezeonwuka, C.D., **Liyanage, V.R.B.,** & Rastegar, M. (2014). *Brain Region-Specific Expression of MeCP2 Isoforms Correlates with DNA Methylation within Mecp2 Regulatory Elements.* PLoS One. 9(3): e90645.

- **Liyanage, V.R.B.,** Zachariah, R.M., & Rastegar, M. (2013). *Decitabine alters the expression of Mecp2 isoforms via dynamic DNA methylation at the Mecp2 regulatory elements in neural stem cells.* Molecular autism. 4(1).

- Barber, B.A.*, **Liyanage, V.R.B*,** Zachariah, R.M., Olson, C.O., Bailey, M.A., & Rastegar, M (2013). *Dynamic expression of MEIS1 homeoprotein in E14.5 forebrain and differentiated forebrain-derived neural stem cells.* Annals of anatomy, 195(5): 431-440.
  ***Equally contributing first authors**

- **Liyanage V.R.B**., Herath, H.M.Y.G.S.B.K., Sirisena, D.N., Abeysekara, S.W. and Samaraweera, P. (2009). *Evaluation of microsatellite markers for selection of salt tolerant rice varieties in Sri Lanka.* Proceedings of the Peradeniya University Research Sessions. 14: 189-191.

Journal Articles (reviews)

- **Liyanage, V.R.B.,*** Jarmasz, J.S.,* Murugeshan, N., Del Bigio, M.R., Rastegar, M., & Davie, J.R. (2014). *DNA Modifications: Function and Applications in Normal and Disease States.* Biology. 3(4).
  ***Equally contributing first authors**

- **Liyanage, V.R.B,** & Rastegar, M. (2014). *Rett Syndrome and MeCP2.* Neuromolecular medicine. 16(2): 231-264.

Book Chapters

- Delcuve, G.P., Khan, DH, **Liyanage, V.R.B.**, Jahan, S, Rastegar, M, Kirshenbaum, LA and Davie, JR. (2016-Accepted). *Epigenetics: Chromatin Organization And Function. Epigenetics in Cardiac Disease.* Springer's "Cardiovascular Biology Series

- **Liyanage, V.R.B.***, Zachariah, R.M.*, Delcuve, G.P., Davie, J.R., Rastegar, M. (2015). *Chromatin Structure and Epigenetics. Advances in Genetics Research.*
  * Equally contributing first authors (Cross Reference)

- **Liyanage, V.R.B.*,** Zachariah, R.M.*, Delcuve, G.P., Davie, J.R., Rastegar, M. (2012). *New Developments in Chromatin Research: An Epigenetic Perspective.* Neil M. Simpson and Valerie J. Stewart. New Developments in Chromatin Research. 1: 29-58.
  ***Equally contributing first authors**

Conference Publications

- **Liyanage, V.R.B.**, Zachariah R., Rastegar (2015). *Epigenetics regulation of MeCP2 in neural stem cells and adult brain: Implication of therapeutic strategies for MeCP2-related neurodevelopmental disorders.* Int J Dev Neurosci 47:64.

Acknowleged in Manuscripts

- Ezeonwuka, C., and Rastegar, M. (2014). *MeCP2-Related Diseases and Animal Models.* Diseases 2, 45-70.
  (for revisions to the review)

- Zachariah RM, Olson CO, Ezeonwuka C and Rastegar M. (2012). *Novel MeCP2 isoform-specific antibody reveals the endogenous MeCP2E1 expression in murine brain, primary neurons and astrocytes.* PLoS One 7: e49763.
  (for designing figures)