BIOGRAPHICAL SKETCH

NAME	**POSITION TITLE**
Kothary, Rashmi	Deputy Scientific Director and Senior Scientist Ottawa Hospital Research Institute

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of British Columbia, BC, Canada	B.Sc.	1976-1979	Cell Biology
University of British Columbia, BC, Canada	Ph.D.	1979-1984	Biochemistry
Brock University, St., ON, Canada	PDF	1984-1985	Molecular Embryology
Mount Sinai Hospital Research Institute, ON, Canada	PDF	1985-1987	Molecular Embryology
AFRC, Cambridge, England	PDF	1988-1990	Molecular Genetics

Dr. Kothary is the Deputy Scientific Director and Senior Scientist at the Ottawa Hospital Research Institute (OHRI). He received a Ph.D. in Biochemistry from the University of British Columbia and pursued postdoctoral research in the laboratories of Dr. Janet Rossant at the Mount Sinai Hospital Research Institute in Toronto and Dr. Azim Surani in Cambridge, U.K. It was during these formative years that Dr. Kothary developed his interests in pre-clinical models to study disease pathology. He has held the University Health Research Chair in Neuromuscular Disorders and is a Professor at the University of Ottawa. His current research focuses on investigating extrinsic and intrinsic factors important for oligodendrocyte mediated myelination and remyelination of the CNS (in the context of Multiple Sclerosis) and understanding Spinal Muscular Atrophy pathogenesis to identify novel therapeutics for this devastating children's disease. He currently sits on the CIHR IMHA advisory board and on the SMA Beyond advisory board, has served on the scientific advisory board for MDA and Cure SMA, and is a reviewer for the CIHR, NIH and Shriners Hospitals for Children.

A. Positions Held

July 1990 – June 1996: Department of Medicine, University of Montreal, Assistant Professor
June 1996 – April 1998: Department of Medicine, University of Montreal, Associate Professor
July 1990 – April 1998: Institut du cancer de Montreal, Montreal, Canada, Scientist
April 1998 – April 2002: Department of Medicine, and Department of Cellular and Molecular Medicine, University of Ottawa, Associate Professor
May 2002 – present: Department of Medicine, and Department of Cellular and Molecular Medicine, University of Ottawa, Professor
April 1998 – present: Ottawa Hospital Research Institute, Regenerative Medicine Program, Senior Scientist
June 1999 – Sept 2003: Center for Neuromuscular Disease, University of Ottawa/OHRI, Founder and Co-Director
April 2001 – Oct 2012: Ottawa Hospital Research Institute, Associate Scientific Director
April 2007 – July 2007: Interim CEO and Scientific Director, OHRI, Interim Vice President Research, Ottawa Hospital
Oct 2012 – present: Ottawa Hospital Research Institute, Deputy Scientific Director

B. Academic Awards

1985 – 1987: National Cancer Institute of Canada, Junior Fellowship
1987 – 1990: Medical Research Council of Canada, Postdoctoral Fellowship
1990 – 1995: Medical Research Council of Canada, Scholar
1995 – 1998: Fonds de la Recherche en Santé du Québec, Scholar
2006 – 2016: University Health Research Chair in Neuromuscular Disorders
2008 Excellence in Mentoring Award, Faculty of Medicine, University of Ottawa
2010 Dr. David Green Founder's Award, National Researcher of the Year, presented by Muscular Dystrophy Canada
2010 Dr. David Green Founder's Award, Ontario Region, presented by Muscular Dystrophy

	Canada
2011	Dr. J. David Grimes Research Career Achievement Award, OHRI
2019	Faculty of Medicine Mentor of the Year Award - Basic Sciences, University Ottawa

C. Professional Affiliations and Activities (last 3 years)

Journal Reviewer

PLOS One; Human Molecular Genetics; Scientific Reports; Expert Opinion on Investigational Drugs; Molecular Therapy; BioMed Research International; Neuromuscular Disorders; Journal of Neurochemistry; Trends in Molecular Medicine; Gene Therapy; Nature Reviews Neurology; Journal of Neurological Disease; Molecular Brain; Journal of Neuroscience; Journal of Clinical Investigation; BBA; European Journal of Medical Genetics; Cellular and Molecular Life Sciences; Experimental Neurology; etc.

Grant Reviewer

Committees

2012-2018	NIH – NSD-B study section
2014-2020	Shriner's Hospitals
2017	Scientific Officer, Canadian Institutes of Health Research, Genetics Panel
2018-2021	Canadian Institutes of Health Research, Genetics Panel
2019	Multiple Sclerosis Society of Canada, Biomedical Grants Review Panel

Ad Hoc Reviews

Medical Research Council of Canada, Muscular Dystrophy Association of Canada, NSERC, FRSQ, FCAR, Canadian Institutes of Health Research, National Science Foundation (USA), Alberta Heritage Medical Research Council, March of Dimes (USA), Muscular Dystrophy Association (USA).

External Promotion Reviews

2017	Dr. Barrington Burnett, Promotion to Associate Professor, USUHS
2017	Dr. Yongchao Ma, Promotion to Associate Professor, Northwestern University
2018	Dr. Allison Ebert, Promotion to Associate Professor, Medical College of Wisconsin
2020	Dr. Nasem Ghasemlou, Promotion to Associate Professor, Queen's University

Advisory Boards and Committees

2010-2018	Families of SMA (USA) (now Cure SMA), Scientific Advisory Board
2018-2020	CIHR Institute Advisory Board, IMHA
2020-2024	SMA Beyond (Europe) Advisory Board

Conference Organization

2011-2018	Organizing committee for the Families of SMA (Cure SMA) Research Conference, annual event
2017	4th Ottawa International Conference on Neuromuscular Disease and Biology, which hosted approximately 250 researchers and trainees in Ottawa
2019	5th Ottawa International Conference on Neuromuscular Disease and Biology

University Committees

2002-	Various recruitment committees, Faculty of Medicine, UO
2012-	Animal Care Users Committee, University of Ottawa
2018	External Review Committee, Vice-Dean, Graduate and Postdoctoral Studies, Faculty of Medicine, UO
2018	Selection Committee, CRC Tier 1in Rare Diseases, Faculty of Medicine, UO

Institute Committees

1999-	Chair, Internal Grant Review Committee, OHRI
2000-	Performance and Promotion Review Committee, OHRI
2001-	Senior Management Team, OHRI
2006-	Awards Committee, OHRI
2008-	Chair, Space and Equipment Committee, OHRI
2017-	Relationship Management Committee, OHRI
2014-	Clinical Departments Research Committee, OHRI

D. Current Trainee Supervision

TRAINEE	POSITION	DURATION
Yves De Repentigny	Senior Research Assistant	1990-present
Ariane Beauvais	Research Assistant	2003-2009, 2010-present
Sabrina Gagnon	Research Assistant	July 2011-present
Rebecca Yaworski	Research Assistant	July 2020-
Sarah Cummings	Ph.D.	Sept 2013-present
Lucia Chehade	M.D./Ph.D. student	June 2018-
Alexandra Beaudry-Richard	M.D./Ph.D. student	June 2018-
Aoife Reilly	M.Sc. Student	January 2018-
Kelsea McKay	M.Sc. Student	Sept 2019-
Morgan Donoghue	M.Sc. Student	Sept 2020-

E. Selected Peer-reviewed publications (2017-present only)

153. *O'Meara, R.O.M., *Cummings, S.E., De Repentigny, Y., McFall, E., Michalski, J-P., Deguise, M-O., Gibeault, S., and **Kothary, R.** (2017). Oligodendrocyte development and CNS myelination are unaffected in a mouse model of severe spinal muscular atrophy. *Hum. Mol. Gen.* **26**(2), 282-292.
154. Deguise, M.O., De Repentigny, Y., McFall, E., Auclair, N., Sad, S., and **Kothary, R.** (2017). Immune dysregulation may contribute to disease pathogenesis in spinal muscular atrophy mice. *Hum. Mol. Genet.* **26**(4), 801-819.
155. Deguise, M.O., and **Kothary, R**. (2017). New insights into SMA pathogenesis: immune dysfunction and neuroinflammation. *Ann. Clin. Transl. Neurol.* **4**(7), 522-530.
156. Sutherland, L.C., Thibault, P., Durand, M., Lapointe, E., Knee, J.M., Beauvais, A., Kalatskaya, I., Hunt, S.C., Loiselle, J.J., Roy, J.G., Tessier, S.J., Ybazeta, G., Stein, L., **Kothary, R.**, Klinck, R., and Chabot, B. (2017). Splicing arrays reveal novel RBM10 targets, including SMN2 pre-mRNA. *BMC Mol. Biol.* **18**(1), 19.
157. Nash, L.A., McFall, E.R., Perozzo, A.M., Turner, M., Poulin, K.L., De Repentigny, Y., Burns, J.K., McMillan, H.J., Warman Chardon, J., Burger, D., **Kothary, R.**, Parks, R.J. (2017). Survival Motor Neuron protein is released from cells in exosomes: A potential biomarker for Spinal Muscular Atrophy. *Sci. Rep.* **7**(1), 13859. doi: 10.1038/s41598-017-14313-z.
158. Bowerman, M., Murray, L.M., Scamps, F., Schneider, B.L., **Kothary, R.**, and Raoul, C. (2018). Pathogenic commonalities between spinal muscular atrophy and amyotrophic lateral sclerosis: converging roads to therapeutic development. *Euro. J. Med. Gen* **61**:685-698.
159. Walter, L.M., Deguise, M.O., Meijboom, K.E., Betts, C.A., Ahlskog, N., van Westering, T.L., Hazell, G., McFall, E., Kordala, A., Hammond, S.M., Abendroth, F., Murray, L.M., Shorrock, H.K., Prosdocimo, D.A., Haldar, S.M., Jain, M.K., Gillingwater, T.H., Claus, P., **Kothary, R.**, Wood, M.J.A., and Bowerman, M. (2018). Interventions targeting glucocorticoid-Kruppel-like factor 15-branched-chain amino acid signaling improve disease phenotype in spinal muscular atrophy mice. *EBioMedicine* **31**, 226-242.
160. Lynch-Godrei, A., De Repentigny, Y., Gagnon, S., Trung, M.T., and **Kothary, R.** (2018). Dystonin-A3

upregulation is responsible for maintenance of tubulin acetylation in a less severe dystonia musculorum mouse model for hereditary sensory and autonomic neuropathy type VI. *Hum. Mol. Genet.* **27**, 3598-3611.

161. De Repentigny, Y., and **Kothary, R.** (2018). Surgical artificial insemination in mice. *Cold. Spring Harb. Protoc.* 2018 Sep 4; 2018(9) doi: 10.1101/pdb.prot092734.
162. Chardon, J.W., Jasmin, B.J., **Kothary, R**., and Parks, R. (2018). Report on the 4th Ottawa International Conference on Neuromuscular Disease and Biology – September 5–7, 2017, Ottawa, Canada. *Journal of Neuromuscular Diseases*. **5**, 539-552.
163. Deguise, M.O., and **Kothary, R.** (2019). Into the unknown: Chromatin signaling in Spinal Muscular Atrophy. In: Binda, O., ed., Chromatin Signaling and Neurological Disorders. Academic Press. 27-52.
164. Nery, F.C., Siranpsian, J.J., Rosales, I., Deguise, M.O., Sharma, A., Muhtaseb, A.W., New, P., Hohnstone, A.J., Zhang, R., Fatouraei, M., Huemer, N., Alves, C.R.R., **Kothary, R**., and Swoboda, K.J. (2019). Impaired kidney structure and function in spinal muscular atrophy. *Neurology Genetics* **5**, e353.
165. Eshraghi, M., Gombar, R., De Repentigny, Y., Vacratsis, P., and **Kothary, R**. (2019). Pathologic alterations in the proteome of synaptosomes from a mouse model of spinal muscular atrophy. *J. Proteome Res.* **18**, 3042-3051.
166. Deguise, M.O., Baranello, G., Mastella, C., Beauvais, A., Micahud, J., Leone, A., De Amicis, R., Battezzati, A., Dunham, C., Selby, K., Chardon, J.W., McMillan, H.J., Huang, Y.T., Courtney, N.L., Mole, A.J., Kubinski, S., Calus, P., Murray, L.M., Bowerman, M., Gillingwater, T.H., Bertoli, S., Parson, S.H., and **Kothary, R.** (2019). Abnormal fatty acid metabolism is a core component of spinal muscular atrophy. *Ann. Clin. Transl. Neurol.* **6**, 1519-1532.
167. Galloway, D.A., Gowing, E., Setayeshgar, S., and **Kothary, R**. (2019). Inhibitory milieu at the multiple sclerosis lesion site and the challenges for remyelination. *Glia* **68**, 859-877.
168. Deguise, M.O., Chehade, L., Tierney, A., Beauvais, A., and **Kothary, R.** (2019). Low fat diets increase survival of a mouse model of spinal muscular atrophy. *Ann. Clin. Transl. Neurol.* **6**, 2340-2346.
169. Alvarez-Saavedra, M., Yan, K., Chaudary, N., Hashem, L.E., Yang, D., De Repentigny, Y., Ioshikhes, I., **Kothary, R.,** Hirayama, T., Yagi, T., and Picketts, D.J. (2019). Snfh2 drives chromatin remodeling to prime upper layer cortical neuron development. *Frontiers in Molecular Neuroscience* **12**, 243.
170. Lynch-Godrei, A., De Repentigny, Y., Yaworski, R.A., Gagnon, S., Butcher, J., Manoogian, J., Stintzi, A., and **Kothary, R**. (2020). Characterization of gastrointestinal pathologies in the dystonia musculorum mouse model for hereditary sensory and autonomic neuropathy type VI. *Neurogastroenterol. Motil.* **32**, e13773.
171. Lynch-Godrei, A., and **Kothary, R.** (2020). HSAN-VI: a spectrum disorder based on dystonin isoform expression. *Neurology Genetics* **6**, e389.
172. Deguise, M.O., De Repentigny, Y., Tierney, A., Beauvais, A., Michaud, J., Chehade, L., Thabet, M., Paul, B., Reilly, A., Gagnon, S., Renaud, J-M., and **Kothary, R.** (2020). Motor transmission defects with sex differences in a new mouse model of mild spinal muscular atrophy. *EBioMedicine* **55**, 102750.
173. Deguise, M.O., Beauvais, A., Schneider, B.L., and **Kothary, R.** (2020). Blood flow to the spleen is altered in a mouse model of spinal muscular atrophy. *J. Neuromusc. Dis.* **7**, 315-322.
174. Kornfeld, S>F., Cummings, S.E., Fathi, S., Bonin, S.R., and **Kothary, R.** (2020). MiRNA-145-5p prevents differentiation of oligodendrocyte progenitor cells by regulating expression of myelin gene regulatory factor. *J. Cell Physiol.* doi: 10.1002/jcp.29910. Online ahead of print.
175. Wassmer, S.J., De Repentigny, Y., Sheppard, D., Lagali, P.S., Fang, L., Coupland, S.G., **Kothary, R.**, Guy, J., Hauswirth, W.W., and Tsilfidis, C. (2020). XIAP protects retinal ganglion cells in the mutant ND4 mouse nodel of Leber hereditary optic neuropathy. *Invest. Ophthalmol. Vis. Sci.* **61**, 49.
176. Kosaraju, J., Seegobin, M., Gouveia, A., Syal, C., Sarma, S.N., Lu, K.J., Ilin, J., He, L., Wondisford, F., Lagace, D., De Repentigny, Y., **Kothary, R**., and Wang, J. (2020). Metformin promotes CNS remyelination and improves social interaction following focal demyelination through CBP Ser436 phosphorylation. *Exp Neurol.* **334**, 113454.
177. Pringle, E.C., Nelson, R., Miller, W., **Kothary, R.,** and Michaud, J. (2020). Spinal Muscular Atrophy Type III complicated by spinal superficial siderosis: a case report with molecular and neuropathological findings. *Acta Neuropathologica Communications* in press.
178. Lynch-Godrei, A., De Repentigny, Y., Gagnon, S., and **Kothary, R.** (2020). Dystonin loss-of-function leads to impaired autophagy-endolysosomal pathway dynamics. *Biochem. Cell Biol.* under review.
179. Deguise, M.O., Pileggi, C., Beauvais, A., Tierney, A., Chehade, L., De Repentigny, Y., Michaud, J.,

Llavero-Hurtado, M., Lamont, D., Atrih, A., Wishart, T.M., Gillingwater, T.H., Schneider, B.L., Harper, M-E.., Parson, S.H., and **Kothary, R.** (2020). A mouse model for spinal muscular atrophy provides insights into non-alcoholic fatty liver disease pathogenesis. *Cellular and Molecular Gastroenterology and Hepatology* under revision.

180. Kornfeld, S.F., Cummings, S.E., Dr Repentigny, Y., Gagnon, S., Zandee, S., Fathi, S., Yaworski, R., Prat, A., and **Kothary, R.** (2020). Loss of miR-145 promotes remyelination and functional recovery in a model of chronic central demyelination. *Communications Biology* under review.

Current Research Support (last 3 years)

1. **CIHR ($765,000 total) 2018-2023**
   Immune system dysfunction in spinal muscular atrophy
2. **MDA (USA) (US$300,000 total) 2018-2021**
   Abnormal fatty acid metabolism is a feature of SMA
3. **CIHR ($918,000 total) 2019-2024**
   MicroRNA-145 as a key regulator of oligodendrocyte differentiation and CNS myelination
4. **CIHR ($1,119,985 total) 2020-2023**
   NMD4C: An integrated research network for patients, scientists, and clinicians to improve outcomes and access to therapies for patients with neuromuscular disorders in Canada (PI – Dr. Hanns Lochmuller)
5. **Cure Spinal Muscular Atrophy ($100,000) 2020-2021**
   Characterization of Canonical Disease Features in a Novel Mouse Model of SMA Type III and IV
6. **Muscular Dystrophy Canada ($100,000 total) 2020-2022**
   Canonical disease features in a novel mouse model of SMA type III and IV
7. **CIHR ($1,119,985 total) 2020-2023**
   NMD4C: An integrated research network for patients, scientists, and clinicians to improve outcomes and access to therapies for patients with neuromuscular disorders in Canada (PI – Dr. Hanns Lochmuller)
8. **MS Society of Canada ($366,600 total), 2020-2023**
   Therapeutic effects of mir-145-5p antagonism in a mouse model of multiple sclerosis

Past Research Support (last 3 years)

1. MS Society of Canada ($301,920 total) April 2017-March 2020
   MicroRNA-145 is a key regulator of oligodendrocyte maturation and CNS myelination
2. MDA (US$253,800 total) May 2014-April 2017
   Modulating actin dynamics as a therapeutic strategy for SMA
3. MS Society of Canada ($347,310 total) April 2014-March 2017
   MicroRNAs as key regulators of oligodendrocyte maturation and CNS myelination
4. CIHR ($600,000 total) April 2014-March 2017
   The Canadian Neuromuscular Network (CAN-NMD) Catalyst Grant: Skeletal Muscle Research
   PI – Dr. Lawrence Korngut
5. CIHR ($734,540 total) 2013-2018
   Dystonin – A cytoskeletal linker protein critical for neuronal function
6. CIHR ($753,790 total) 2013-2018
   The molecular pathogenesis of spinal muscular atrophy
7. CIHR/e-Rare 6th Joint Call for European Research Projects on Rare Diseases ($390,150) 2015-2018 (Kothary component)
   Common Pathogenic Pathways and Therapeutics for SMA and ALS motoneuron diseases
   PIs: Dr. Cédric Raoul, Dr. Patrick Abischer, Dr. Rashmi Kothary
8. Cure SMA ($140,000 total) 2016-2018
   Muscle satellite cell biology and muscle regeneration in SMN depleted mice
9. CIHR ($714,391 total) 2014-2019
   Development of novel therapeutics for the treatment of the genetic disorder SMA
   PI – Dr. Robin Parks

10. Department of Medicine ($48,000 total) 2017-2018
    Filling a knowledge gap in Multiple System Atrophy, a lethal disease of oligodendrocytes (co-PI: Dr. Michael Schlossmacher)
11. University of Ottawa ($25,000 total) 2018-2019
    CNMD-INMG Joint Collaboration Research Program on Epigenetic mechanisms in SMA pathology
12. Cure SMA (US$50,000 total) 2018-2019
    The shifting landscape of SMA research: towards a better understanding for a role for SMN during aging