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The Actin-binding Protein Moesin and Memory Formation in *Drosophila*

A thesis presented to Massey University in partial fulfillment of
the requirements for the degree of Master of Science in
Biochemistry

2016

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Abstract

Moesin is a cytoskeletal adaptor protein that plays an important role in modification of the actin cytoskeleton and the formation of dendritic spines, which may be crucial to long-term potentiation. Moesin has also been found to be overexpressed in brains affected by Alzheimer's disease. Despite being identified as a potential memory gene and linked to several neurological diseases, its role in memory has not been evaluated. The role of Moesin in the *Drosophila melanogaster* brain was investigated by characterizing the impact of modulating Moesin expression on several aspects of development and behavior. Moesin is involved in both brain and eye development. Knockdown and overexpression of Moesin led to defects in the development of the mushroom body, a brain structure critical for memory formation and recall. Further, knockdown of Moesin throughout development resulted in a significant deficit in long-term memory. Additionally, knockdown of Moesin restricted to adulthood also resulted in a significant deficit in long-term memory, which suggests that Moesin also has a non-developmental role in memory. Further, this requirement for Moesin in long-term memory was traced to the alpha/beta and gamma neurons of the mushroom body. Through the use of a phosphomimetic Moesin mutant that mimics the phosphorylated, activated form of Moesin, the regulation of Moesin in the *Drosophila* brain was analyzed. Expression of this mutant in neurons disrupted photoreceptor development in the *Drosophila* eye and a novel sensorimotor phenotype attributed to its expression in the brain was identified resulting in a defect in stereotypical climbing behavior. These results suggest a critical role for Moesin in general neurological functioning and the molecular pathways involved in its activation require further investigation.

Acknowledgements

First and foremost I'd like thank my supervisor Dr Helen Fitzsimons for giving me this opportunity. I sincerely appreciate your thoughtful guidance. I'd also like to thank my labmates Silvia, Patrick #2, Sarah, Lance, Raoul and Tracy as well as the members of the Biomedical lab group for their comments, suggestions, and camaraderie.

Special thanks to Dr Matthew Savoian, Jordan Taylor, and Niki Murray from the Manawatu Microscopy and Imaging Centre for their assistance with SEM and confocal microscopy. I would also like to acknowledge the kind gift of a Drosophila Moesin antibody from Professor Dan Kiehart of Duke University. Finally, I'd like to thank Chay Fhun Low for her spectacular editing skills and never-ending patience.

Abbreviations

BDSC	Bloomington Drosophila Stock Center
CAMKII	Ca ²⁺ /calmodulin-dependent protein kinase II
cAMP	Cyclic adenosine monophosphate
Cdc42	Cell division control protein 42 homolog
CI	Courtship index
CRE	cAMP response element
CREB	cAMP response element binding protein
CPEB	Cytoplasmic polyadenylation element binding protein
ELAV	Embryonic lethal, abnormal vision
ERM	Ezrin, Radixin, Moesin
FasII	Fasciclin II
FERM	Four point one, Ezrin, Radixin, Moesin
GluRIIA	Glutamine receptor IIA
HDAC4	Histone deacetylase 4
IHC	Immunohistochemistry
KD	Knockdown
L1CAM	L1 cell adhesion molecule
LPTC	Lobula plate tangential cells
LRRK2	Leucine-rich repeat kinase-2
LTM	Long-term memory
MARCM	Mosaic analysis with a repressible cell marker
MI	Memory index
MOE	Moesin
NGF	Nerve growth factor
OE	Overexpression
PKA	cAMP-dependent protein kinase A
Rac1	Ras-related C3 botulinum toxin substrate 1

RhoA	Ras homolog gene family, member A
ROCK	Rho-associated protein kinase
SEM	Scanning electron microscopy
STM	Short-term memory
TARGET	Temporal and regional gene expression targeting
UAS	Upstream activating sequence
VDRC	Vienna Drosophila Resource Center
WB	Western Blot

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