

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/35805> holds various files of this Leiden University dissertation

Author: Lahaye, Liza

Title: Drosophila Ryks and their roles in axon and muscle guidance

Issue Date: 2015-10-14

ABBREVIATION LIST

aa	amino acids
AC	Anterior Commissure
AEL	After Egg Laying
AL	Antennal Lobe
APC	Adenomatous Polyposis Coli
APF	After Puparium Formation
BDB	Brachdactyly type B
CAMKII	Ca ²⁺ /calmodulin-dependent protein kinase II
CAT	Chloramphenicol AcetylTransferase
CE	Convergent Extension
CK1 α	Casein Kinase 1 α
Cn	Calcineurin
CNS	Central Nervous System
CRD	Cysteine Rich Domain
CREB	cAMP response element-binding protein
CRISPR/Cas	Clustered regularly interspaced short palindromic repeat/CRISPR-associated
CST	Corticospinal Tract
DAAM1	Dishevelled Associated Activator of Morphogenesis
DAG	Diacylglycerol
Dlg1	Disc large tumor suppressor
Dll	Distalless
DM	Dorsomedial
Dnt	Doughnut
Dpp	Decapentaplegic
DRL	Derailed
DRL-2	Derailed-2
DSB	Double stranded breaks
Dsh	Dishevelled
ECD	Extracellular Domain
ECL	Enhanced-Chemiluminescence
ECM	Extracellular Matrix
EGF	Epidermal Growth Factor
Egr	Early Growth Response
EphB2	Ephrin receptor B2
EphB3	Ephrin receptor B3
FasII	Fasciclin II
FCM	Fusion Competent Myoblasts
FGFR	Fibroblast growth factor Receptor
FLNa	Filamin A
FMI	Flamingo
FRA	Frazzled
FZD	Frizzled
GAL4	Yeast transcription activator protein
Gpa	Glycophorin A
GSK3	Glycogen Synthase Kinase 3

HA	Hemagglutinin
HRP	Horseradish Peroxidase
ICD	Intracellular Domain
Ig	Immunoglobulin
IP ₃	Inositol triphosphate
IRK	Insulin kinase receptor
JNK	c-Jun N-terminal Kinase
Kr	Kringle
Lam	Laminin
LDL	Low Density Lipoprotein
LH	Lateral Horn
LRP	LDL receptor Related Protein
mAb	mouse Anti-body
MAPK	Mitogen-Activated Protein Kinases
MAS	Muscle Attachment Site
MB	Mushroom Body
Mew	Multiple edematous wing
MTJ	Myotendinous Junction
NFAT	Nuclear Factor of Activated T-cells
NF-KB	Nuclear transcription factor kappa-light-chain-enhancer of activated B-cells
NGF	Nerve Growth Factor
NMJ	Neuromuscular Junction
ORF	Open Reading Frame
ORN	Olfactory Receptor Neuron
PC	Posterior Commissure
PCP	Planar Cell Polarity
PDE6	Phosphodiesterase 6
PDZ-BD	zonula occludens 1 protein binding domain
PKC	Protein Kinase C
PLC	Phospholipase C
PM	Plasma Membrane
PN	Projection Neurons
PNETs	Primitive neuroectodermal tumors
PNS	Peripheral Nervous System
PRD	Proline Rich Domain
PSD95	Postsynaptic density protein
PTK	Phosphotyrosine Kinase
RGD	Arg-Gly-Asp
ROBO	Roundabout
ROCK/ROK	Rho associated Kinase
ROR	Receptor tyrosine kinase-like Orphan Receptor
RRS	Robinow syndrome
RTK	Receptor Tyrosine Kinase
RYK	Receptor Related to Tyrosine Kinase
Ser	Serine
SFK	Src family kinases
sFRPs	secreted Frizzled-Related Proteins

SH2	Src Homology 2
SH3	Src Homology 3
Slp	Sloppy-paired
Smo	Smoothened
Sr	Stripe
STAR	Signal Transduction and Activation of RNA
TBC	Tetra-Basic protease Cleavage
TCF/LEF	T cell-Specific transcription Factor/Lymphoid Enhancer-binding Factor
Thr	Threonine
TMD	Transmembrane domain
UAS	Upstream Activating Sequence
Vang	Van Gogh
VNC	Ventral Nerve Cord
WCE	Whole Cell Extracts
Wg	Wingless
WIF	Wnt Inhibitory Factor
ZO-1	zonula occludens 1

CURRICULUM VITAE

On December 20th 1976 Liza Lucia Lahaye was born in Gouda, The Netherlands. She studied Biomedical Sciences at the University of Utrecht and obtained the Bachelor as well as Master diploma. The Master internships were taken at the department of Cell Biology, Utrecht University and the Department of Pediatrics, Cell Biology and Physiology Washington University School of Medicine in St. Louis, USA. In Utrecht she worked in the lab of Prof. Dr. G.J.A.M. Strous and worked on the Growth Hormone Receptor and its dimerization capacity and maturation. In the USA, the amino acids that are responsible for the endocytosis rate of another receptor, LRP1B, were studied in the lab of Dr. G. Bu. To complete the Master's, the Master thesis was written at the Erasmus Medical Center at Rotterdam at the Department of Molecular Immunology in the lab of Dr. F.J.T. Staal and concerned the possible involvement of Wnt-signalling in abnormal haematopoietic development that results in B-cell Leukaemogenesis. The subsequent PhD project was executed in the lab of Prof. Dr. J.N. Noordermeer and Dr. L.G. Fradkin at the department of Molecular Cell Biology at the Leiden University Medical Center. Currently, she is holding a position as a postdoctoral researcher at the department of Cell Biology at the University Medical Center Groningen in the lab of Prof. Dr. O. Sibon.

LIST OF PUBLICATIONS

- Reynaud E , Lahaye LL , Boulanger A , Petrova IM , Marquilly C , Flandre A , Martiáñez T , Privat M , Noordermeer JN , Fradkin LG* and Dura JM* **Guidance of *Drosophila* mushroom body axons depends upon DRL-Wnt receptor cleavage in an adjacent brain structure.** Cell Rep. 2015
- Petrova IM*, Lahaye LL*, Martiáñez T, de Jong AW, Malessy MJ, Verhaagen J, Noordermeer JN, Fradkin LG. **Homodimerization of the Wnt receptor Derailed recruits the Src family kinase SRC64B.** Mol Cell Biol. 2013
- Lahaye LL, Wouda RR, de Jong AW, Fradkin LG, Noordermeer JN. **WNT5 interacts with the Ryk receptors doughnut and derailed to mediate muscle attachment site selection in *Drosophila melanogaster*.** PLoS One. 2012
- van den Eijnden MJ, Lahaye LL, Strous GJ. **Disulfide bonds determine growth hormone receptor folding, dimerisation and ligand binding.** J Cell Sci. 2006

ACKNOWLEDGEMENTS

Na een spectaculaire les scheikunde op de middelbare school besloot ik dat ik later 'onderzoeker' wilde worden. Ik wilde begrijpen wat ik voor mijn neus zag gebeuren en mij zo deed verwonderen. Nu is het gevoel dat destijds ontstond gekristalliseerd in dit boekje. Ik heb met buitengewoon veel plezier geschreven, geschaafd en gewerkt aan de totstandkoming hiervan. Ik heb deze jaren niet alleen op een zolderkamertje doorgebracht. Daarom gaat mijn dank allereerst uit naar Jasprien en Lee voor de input en kritische blik gedurende de afgelopen jaren. De vrijheid en faciliteiten die het lab en de afdeling boden om te kunnen experimenteren waren geweldig. Ik wens jullie veel succes met de uitdaging om het lab weer opnieuw vorm te geven in de Verenigde Staten.

My gratitude extends to the members of the reading committee that invested time to review this thesis: Dr. Rabouille, Prof. Dr. Tanke, Prof. Dr. Staal and Prof. Dr. Verhaagen.

I am really happy we started our PhD adventure almost simultaneously, Iveta, and I cherish the lunches we had almost every day, discussing science and whatever was on our mind. Anja and of course also Bert, without you the fly lab would not have been in such good shape, thank you for introducing me into the fly world. During my last months at the lab, Tania joined the Wnt women team and I really enjoyed having you around. My thanks also goes out to Gonneke and Pui for sharing more than just an office. The microscopy shepherd, Annelies, you showed me the ropes on the confocal microscope which I would like to thank you for, besides alle gezelligheid and your infectious good mood. Put in random order I would also like to thank Job, Suzanne, David, Willem, AG, Guy, Joop, Hans, Roelant, Alfred, Bram, Carolina, Karoly, Martijn, Peter, Ton, Hans and Hans, who were always there for either a critical view, a quick talk and some fun. Ody, jou wil ik graag bedanken voor het vertrouwen mij aan te nemen zonder mijn proefschrift verdedigd te hebben.

De vele uren die ik met jullie doorbracht, Mirjam en Koek had ik voor geen goud willen missen. Hoewel in eerste instantie de omstandigheden iets te wensen overlieten, ben ik erg blij dat ik Yolanda en Marieke heb leren kennen en jullie vriendschap waardeer ik zeer. Ook wil ik graag mijn schoonfamilie bedanken: Klaas, Martijn, Sisi, Hilde, Hans, Judith en Maarten, jullie niet aflatende interesse en steun waren zeer waardevol en ik voel mij op mijn plek bij jullie. Mijn 'kleine' broer, Max, ik verstond je al voordat je kon praten en gelukkig versta je mij ook. Jij en Henrike hebben allebei een goed voorbeeld gegeven met jullie beider promotie en nu kan ik jullie bedanken in mijn proefschrift. Pap en mam, jullie opvoeding heeft natuurlijk bijgedragen aan het werk dat aan dit boekje vooraf gegaan is. Jullie interesse in wat er nou gebeurde in verschillende laboratoria leidde weleens tot uitgebreide tekeningen die uiteindelijk misschien beter voor kunst kunnen doorgaan. Lieve Saskia, jouw steun en aandacht waren onontbeerlijk en ik ben je dankbaar voor alle ruimte die je gecreëerd hebt om mijn thesis af te kunnen ronden. Met jou naast me prijs ik mij gelukkig.

