

BIOCHEMICAL AND BIOPHYSICAL CHARACTERIZATIONS  
OF IMMUNOGLOBULIN SUPERFAMILY RECEPTORS  
NEOGENIN AND L1

Thesis by

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## ABSTRACT

Immunoglobulin (Ig) superfamily receptors function in a wide variety of developmental and metabolic processes. We are particularly interested in characterizing two Ig superfamily receptors neogenin and L1. The first chapter of the thesis gives a brief review of the biological significance of neogenin and L1 and what has been learned in their functions. In Chapter 2, we describe the localization of the hemojuvelin-binding epitope of neogenin to the membrane proximal fifth and sixth fibronectin type III (FNIII) domains, with the sixth FNIII domain contributing the majority of the binding. Chapter 3 presents the crystal structure of this hemojuvelin-binding fragment at 1.8 Å, revealing a nearly linear domain arrangement. Hemojuvelin binding sites have been mapped to one face of the sixth FNIII domain based on sequence alignment between neogenin and DCC (Deleted in Colorectal Cancer), a molecule related to neogenin but does not bind to hemojuvelin. These results should also be informative in understanding the interaction between neogenin and repulsive guidance molecule (RGM), the closest homologue of hemojuvelin. The interaction between neogenin and RGM is known to regulate neuronal survival. Chapter 4, the second part of the thesis, describes our studies of L1-mediated homophilic adhesion using biophysical approaches. We built a basis shape model to describe L1-mediated homophilic adhesion between L1-coated giant unilamellar vesicles and flat substrate. Using confocal microscopy techniques, we were able to reconstruct the three-dimensional shape of an adhered vesicle. We developed an algorithm in order to derive adhesion strength from the configurations of adhered vesicles based on our basis shape model using energy minimization approach.

## TABLE OF CONTENTS

ACKNOWLEDGEMENT .....	iii
ABSTRACT .....	v
CHAPTER 1: Introduction.....	1
CHAPTER 2: Published as Yang F, West AP Jr, Allendorph GP, Choe S, Bjorkman PJ. (2008) Neogenin Interacts with Hemojuvelin through its Two Membrane-Proximal Fibronectin Type III Domains. <i>Biochemistry</i> <b>47</b> (14):4237-45 .....	29
CHAPTER 3: Published as Yang F, West AP Jr, Bjorkman PJ. (2010) Crystal structure of a hemojuvelin-binding fragment of neogenin at 1.8 Å ( <i>J. Struct. Biol. in press</i> ).....	41
CHAPTER 4: Biophysical studies of L1-mediated homophilic adhesion .....	62
APPENDIX A: Published as Zhang AS, Yang F, Meyer K, Hernandez C, Chapman-Arvedson T, Bjorkman PJ, Enns CA. (2008) Neogenin-mediated Hemojuvelin Shedding Occurs after Hemojuvelin Traffics to the Plasma Membrane. <i>Journal of Biological Chemistry</i> <b>283</b> (25):17494-502 .....	90
APPENDIX B: Published as Zhang AS, Yang F, Wang J, Tsukamoto H, Enns CA. (2009) Hemojuvelin-Neogenin Interaction Is Required for Bone Morphogenic Protein-4- induced Heparin Expression. <i>Journal of Biological Chemistry</i> <b>284</b> (34):22580-9.....	100
APPENDIX C: Matlab scripts for the L1 project.....	116

## LIST OF FIGURES AND TABLES

### CHAPTER 1:

- Figure 1. Ribbon and topology diagrams of typical Ig folds and FNIII fold..... 3-4
- Figure 2. Neural adhesion molecule of the Ig superfamily..... 6
- Figure 3. Molecular network of hemojuvelin-induced hepcidin expression ..... 14

### CHAPTER 2:

- Figure 1. Characterizations of HJV and neogenin proteins. .... 33
- Figure 2. Representative SPR data for neogenin proteins binding to immobilized wild-type HJV ..... 34
- Figure 3. Multiangle light scattering and sedimentation velocity analytical ultracentrifugation experiments to determine the oligomeric states of sFNIII 5-6 and HJV ..... 35
- Figure 4. Neogenin FNIII 5-6 and BMP-2 do not compete for HJV binding..... 36
- Figure S1. Proteolytic digests of the neogenin ectodomain and identification of the endoproteinase Glu-C digested products by western blot and pull-down ..... 39
- Figure S2. Determination of the oligomeric state of neogenin FNIII 1-6 using gel filtration chromatography with in-line light scattering ..... 40
- Table 1. SPR analysis of the binding of neogenin proteins to immobilized HJV 34

### CHAPTER 3:

- Figure 1. Crystal structure of neogenin FN5-6 ..... 59
- Figure 2. Structure-based sequence alignment of the FN5-6 regions of human neogenin and DCC ..... 59

- Figure 3. Hypothetical model for how interactions between neogenin FN5 and negatively-charged phospholipids on the surface of the neogenin-expressing cell could facilitate interactions between hemojuvelin on the surface of another cell and the hemojuvelin-binding site on neogenin FN6 ..... 60
- Table 1. Data collection and refinement statistics ..... 56
- Table 2. Interdomain tilt, rotation angles and buried surface area..... 57
- Supplementary Figure 1. Comparison of neogenin FN5-6 and other tandem FNIII domains in ribbon diagram (panel A) and electrostatic potential surface (panel B) representations ..... 61

#### CHAPTER 4:

- Figure 1. Three models of L1-mediated homophilic adhesion ..... 65
- Figure 2. Flow chart showing how the confocal images were processed ..... 73
- Figure 3. Schematic view of a vesicle adhering to a flat surface with the geometric parameters defined ..... 73
- Figure 4. Representative simulation results based on energy minimization shows how the shape changes as adhesion strength increases ..... 77
- Figure 5. L1 induces significant deformation in adhering GUVs ..... 79
- Figure 6. L1-mediated adhesion imaged by confocal microscopy ..... 81
- Figure 7. Typical evolution of a vesicle adhered to a flat substrate ..... 83
- Figure 8. Comparison of numerical results by Surface Evolver and best fitting using basic shape model ..... 83
- Figure 9. Recombinant L1-GFP is fluorescent and is able to induce vesicle deformation during adhesion ..... 85



- Figure 10. Successful production of GUVs from different lipid composition ..... 85
- Table 1. Summary of information during data processing ..... 80