List of Figures

Chapter 1: Introduction 1-25

- Figure 1: Structure based classification of neurons 1
- Figure 2: Axonal transport 3
- Figure 3: Structure of motor proteins 6
- Figure 4: Mitochondrial transport machinery 11
- Figure 5: Life cycle of *C. elegans* 18
- Figure 6: 3D reconstruction of *C. elegans* neurons 20
- Figure 7: Touch receptor neurons (TRNs) in *C. elegans* 22

Chapter 2: Materials and Methods 25-41

- Figure 1: Gentle touch assay to test TRNs response 33

Chapter 3: Characterization of mutants show pleiotropic defects in Touch Receptor Neurons 41-82

- Figure a: Forward screening mutagenesis 41
- Figure 1: Mitochondria number in TRNs increases linearly with the development 44
- Figure 2: Mitochondrial distribution in *jsIs609* and mutants and their external appearance 46-47
- Figure 3: Mitochondrial distribution in the second set of mutants 48
- Figure 4: Mitochondrial flux in TRNs of wild type and mutants 50
- Figure 5: Mutants show fewer moving mitochondria 51
- Figure 6: Mutants do not show any gross change in mitochondrial size distribution 52
- Figure 7: Mutant phenotype is severe in PLM 53
- Figure 8: Mutants do not show mitochondrial distribution defects in DA9 neurons 54
- Figure 9: Mutants show disrupted RAB-3 presynaptic vesicles distribution in TRNs 56
Figure 10: Mutants show accumulation of synaptobrevin vesicles in proximal neuronal process

Figure 11: Mutants show defects in presynaptic vesicles trafficking in TRNs

Figure 12: Presynaptic vesicles flux reduced in mutants

Figure 13: Mutants show reduced defects in vesicle dynamics in TRNs with endogenous Rab-3 promoter

Figure 14: Mutants exclusively show defects in TRNs with endogenous vesicle promoter

Figure 15: Mutants do not show vesicles accumulation in cell body in other neurons

Figure 16: Mutants show neuron morphology defects in TRNs

Figure 17: Mutants show short neuronal process

Figure 18: Extent of Branching in mutants increase with the development

Figure 19: Mutants do not show neuron morphology defects in PVD

Figure 20: Other neurons do not show gross defect in mutant

Figure 21: Mutant show defects in microtubule stabilization in TRNs

Figure 22: Mutant show defects in microtubules end binding protein (EBP-1) distribution

Figure 23: Mutants show defects in microtubule dynamics in TRNs

Figure 24: Mutants are unresponsive to gentle touch

Figure 25: Mutants are sensitive to aldicarb

Figure 26: Mutants respond to harsh touch assay

Figure 27: TRNs have not changed fate to FLP or PVD

Figure 28: TRNs have not changed fate to PVD

Figure 29: Mutants did not show a reduction in mitochondria number in khc-1 mutant

Figure 30: Mitochondrial number in mutants is slightly affected in kinesin mutant
Figure 31: Overexpression of UNC-104 reduced the severity of neuronal morphology in mutants.

Chapter 4: Mapping of the mutants with pleiotropic defects in TRNs

Figure a: Non-complementation test process
Figure 1: Cross strategy to find if tb118 is linked to X chromosome
Figure 2: Three-point mapping of mutants
Figure 3: Position of the mutated gene on the genetic map
Figure 4: zig-3 and fis-2 complement the mutant phenotype
Figure 5: mec-7 non-complemented the mutants
Figure 6: Genomic DNA after Restriction digestion with Eco R1
Figure 7: Annotation of total SNPs in jsIs609
Figure 8: Histogram of the distribution of SNPs on X chromosome of jsIs609 and mutants as a result of whole genome sequencing
Figure 9: SNPs in region of interest among mutants and wild type
Figure 10: SNPs annotation in mapped region on X
Figure 11: SNPs annotation from sequencing data
Figure 12: Location of possible candidate genes with respect to visible markers on X chromosome
Figure 13: Graphical representation of position of novel SNPs in candidate
Figure 14: Homology of a conserved domain in K09F5.6
Figure 15: Gene ontology prediction for K09F5.6 protein
Figure 16: Conserved domains in MEC-7
Figure 17: Affected domain in MEC-7
Figure 18: Affected domains in alpha beta dimer
Chapter 5: Long-term growth and high-resolution Imaging of *C. elegans* in microfluidic device

Figure 1: Schematic of a microfluidic chip and membrane usage
Figure 2: Device grown animals have similar developmental characteristics
Figure 3: Synaptic size growth from L2 to adult
Figure 4: Graphical representation of synapse growth
Figure 5: Expression of the vulval (*zmp::gfp*) markers the lineage
Figure 6: PVD development in microfluidic device
Figure 7: PVD development in *wdIs51* grown on NGM plates
Figure 8: Growth of TRN in an individual animal
Figure 9: High-resolution imaging of mutant *tb118; tbIs222(pmec4:mcherry)* shows branching

Chapter 6: Mitochondrial pattern development in developing Touch Receptor Neurons

Figure a: microfluidic device set up during imaging hours
Figure 1: Mitochondrial distribution in L2 and L4
Figure 2: Mitochondrial distribution and size in TRNs with the development
Figure 3: Events contributing to turnover of stationary mitochondrial position
Figure 4: Flux across bleached mitochondria in *jsIs609*
Figure 5: Mitochondrial interactions across stationary mitochondria
Figure 6: Mitochondria entry rate is higher than exit in L2 and L4
Figure 7: Compression and expansion of neuronal process on immobilization
Figure 8: Mitochondria docking along the neurons could be visualized with bubble plot
Figure 9: Mitochondria move apart with the development 156

Figure 10: Representation of long-term imaging of mito:: GFP in the jsIs609 grown microfluidic device for 24 hours 157

Figure 11: Effect of photobleaching in long-term mitochondrial imaging 157

Figure 12: Low-frequency inter mitochondrial bin show large dip and mitochondria move apart with development 160

Figure 13: Mitochondrial number increase in proportion to increase in the neuronal process length 161

Figure 14: Long-term imaging of early developmental stage from L2 to early L4 162

Figure 15: Inter-mitochondrial distribution from long-term imaging of early developmental (L2) and late stages (early adult) 163

**Chapter 7: Conclusions and Discussion** 165-176

Figure 1: SNPs location in MEC-7 Protein 170

Figure 2: Proposed model for the mechanism through which MEC-7 could be giving mutant phenotype 175-176