

ABSTRACT

Emergence of the higher eukaryotic organisms from their prokaryotic ancestors has been closely associated with an increase of the genetic material. This progression has been dependant on machineries that can package the DNA to various extents, from the levels seen in the 30 nm fibers of interphase nuclei to that of metaphase chromosomes. These evolutionary changes in genome organization have correlated with advancements in regulation of gene expression during development. In eukaryotes, cellular differentiation is partly dependent on the mechanisms that would silence the correct genes in a particular tissue and maintain this silenced state throughout subsequent stages of development. To understand the factors involved in such mechanisms many labs, including ours, have used position effect variegation (PEV) to identify proteins that form or remodel the chromatin fiber. Genetic screens have identified *S2214*, and *puckered* as genes coding for putative modifiers of PEV. The aim of this thesis, is to characterize *S2214*, and *puckered* by addressing two main questions: i) do the mutations in each of these genes modify the phenotype observed in PEV? And ii) do their products localize to the nucleus, and if so to the chromatin? Results show that *P* element mutations in these genes cause dominant and strong suppression of PEV in *w^{m4}* and *Sb^V*. Moreover, the observed *Su(var)* activity is reverted upon mobilization of the *P* elements. I developed and purified an antibody for each gene. Puc, the product of *puckered*, localized to the nucleus of S2 and KC1 cells (which are late embryonic *Drosophila* cell lines), as well as the nuclei of salivary gland cells of *Drosophila melanogaster*, but could not be detected on the polytene chromosomes. In addition, *S2214*, the product of *S2214*, was found in the nuclear fraction of S2 cells, and could be observed within the nuclei of S2 and KC1 cells as well as those of the salivary glands of *Drosophila melanogaster*. Furthermore, *S2214* was found at several interbands of the polytene chromosomes of these salivary glands. It is our conclusion that gene products of both *S2214* and *puckered* are involved in mechanisms that affect chromatin structure.

BIOGRAPHICAL NOTES

Born: 09, 23, 1977

Academic Studies: B. Sc. University of British Columbia, 2002

Current Position: MSc candidate, UBC

Course	Course Title	Course Co-ordinator
Zool 500A	Directed studies in Zoology	Dr. Tom Grigliatti
MEDG 520	Advances in Human Molecular Genetics	Dr. Matthew Lorincz
MEDG 530	Human Genetics	Dr. Jan Friedman
MEDG 545	Current Topics in Medical Genetics Research	Dr. Carolyn Brown
MEDG 548	Directed Studies-Protein Biochemistry	Dr. Tom Grigliatti
Gene 502	Genetics	Dr. Hugh Brock
Biol 548	Advanced topics in biologicalmicroscopy	DR. Geoff Wasteneys

AWARDS

Winner of a Graduate TA Teaching Award (2005/2006)

PRESENTATIONS

- Medical Genetics research day poster presentation (Nov 2005): Initial characterization of *S2214* and *puckered* as suppressors of position effect variegation in *Drosophila melanogaster*.
- Medical Genetics research day poster presentation (Nov 2006): *Puckered*'s role in position effect variegation may be separate from its role in the JNK pathway.
- Canadian Society of biochemistry and molecular and cellular biology "Epigenetics and Chromatin Dynamics" conference at Banff (march 2008): *S2214* is a strong suppressor of Position Effect Variegation and directly interacts with chromatin. Omid Toub¹ and Thomas A. Grigliatti²

SUPERVISORY COMMITTEE

Dr. Thomas A. Grigliatti (supervisor)

Dr. Hugh W. Brock

Dr. Carolyn J. Brown



PROGRAMME

The Final Oral Examination
For the Degree of

MASTER'S OF SCIENCE
(Medical Genetics)

OMID TOUB

B.Sc., University of British Columbia, 2002

Date & time: Tuesday, Nov. 24, 2009, 9:00 am

Exam location: Life Sciences Center, Rm 1516, 2350 Health Sciences
Mall, UBC

**“Initial characterization and Intracellular localization of two
suppressors of position effect variegation in *Drosophila
melanogaster*, *S2214* and *puckered*”**

EXAMINING COMMITTEE

Chair:

Dr. Carolyn J. Brown (Department of Medical Genetics)

Supervisory Committee:

Dr. Thomas A. Grigliatti (Department of Zoology)

Dr. Hugh W. Brock (Department of Zoology)

University Examiner:

Dr. Cornelius Boerkoel (Department of Medical Genetics)