

ABSTRACT

Aniridia is a rare genetic panocular disorder which, for the majority of cases, is caused by mutations or chromosomal rearrangements involving paired box gene 6 (*PAX6*). Peters' anomaly (PA), also a genetic eye disorder, has also been found to be associated with mutations in *PAX6*, and also in *FOXC1*, *PITX2*, and *CYP1B1*. However, in approximately 20% of patients who have aniridia and 75% of patients with PA, no mutation has been found in *PAX6*, or other genes involved these eye disorders, and for these patients, their genetic mutation is unknown. This precludes these patients from genetic testing and thus, from gaining the benefits from genetic counseling and early medical interventions. My hypothesis was that patients who have aniridia, Peters' anomaly or related eye disorders, for which genetic cause is unknown, have mutations in *NR2E1*. The purpose of this thesis was to study patients with aniridia, Peters' anomaly, and related eye disorders in order to identify mutations in a novel candidate gene, *NR2E1*. Here, the first germline amino acid change was identified in the *NR2E1* gene in a patient with Peters' anomaly and his mother, and not found in 392 control subjects. The identification of an amino acid variant in *NR2E1* is significant as it supports the hypothesis that *NR2E1* is a regulator of eye development in humans and has implications for the gene in the development of eye disorders. If future analysis leads to the identification of *NR2E1* mutations in additional patients, it will allow patients with eye disorders of otherwise unknown genetic etiology to receive the benefits of modern genetic medicine and genetic counseling. This future work endeavors to provide the scientific and medical community with a greater depth of knowledge of the role of *NR2E1* in genetic eye disorders.

BIOGRAPHICAL NOTES

Born: December 16, 1984, Dunedin, New Zealand

Academic Studies: B.Sc. McMaster University, 2007

Current Position: MSc candidate, UBC

Course	Course Title	Course Co-ordinator
MEDG 520	Advances in Human Molecular Genetics	Dr. Matthew Lorincz
MEDG 530	Human Genetics	Dr. Lorne Clarke
MEDG 545	Current Topics in Medical Genetics Research	Dr. Michael Kobor
NRSC 501	Neuroscience II	Dr. Nicholas Swindale

AWARDS

Post Graduate Scholarship – Masters Award, NSERC for \$17,300 (2008)

Medical Genetics Graduate Entrance Scholarship, UBC for \$2,750 (2007)

PRESENTATIONS

The Centre for Molecular Medicine and Therapeutics TGIF Series, September 2009, Vancouver (Canada)

Seminar Presentation – “*A mutation screen of NR2E1 in patients with Aniridia and related eye disorders*”

The Child and Family Research Institute 2009 Student Research Forum, June 2009, Vancouver (Canada)

Poster Presentation – “*A mutation screen of NR2E1 in patients with Aniridia and related eye disorders*”

The Canadian Neuroscience Meeting, May 2009, Vancouver (Canada)

Poster Presentation – “*A mutation screen of NR2E1 in patients with Aniridia and related eye disorders*”

The Centre for Molecular Medicine and Therapeutics TGIF Series, September 2008, Vancouver (Canada)

Seminar Presentation – “*NR2E1: A Novel Candidate Gene Underlying Aniridia*”

The Medical Genetics Research Day, November 2007, Vancouver (Canada)

Poster Presentation – “*NR2E1: A Novel Candidate Gene for Aniridia*”

Aniridia International Medical Conference, July 2007, Memphis, TN (USA)

Poster Presentation and DNA collection – “*NR2E1: A Novel Candidate Gene for Aniridia*”

SUPERVISORY COMMITTEE

Dr. Elizabeth M. Simpson, Research Supervisor (Medical Genetics)

Dr. Angela Brooks-Wilson (Medical Genetics)

Dr. Deborah Giaschi (Ophthalmology and Visual Sciences)

Dr. Robert Molday (Ophthalmology and Visual Sciences)



PROGRAMME

The Final Oral Examination
For the Degree of

MASTER'S OF SCIENCE
(Medical Genetics)

ADRIENNE BORRIE

B.Sc., McMaster University, 2007

Date & time: Friday, December 11, 2009, 9:30 am

Exam location: Room 3113, Centre for Molecular Medicine and
Therapeutics, 980 West 28th Avenue, Vancouver, BC

**“A Mutational Screen of NR2E1 in Patients with Aniridia, Peters’
Anomaly, and Related Eye Disorders.”**

EXAMINING COMMITTEE

Chair:

Dr. Diana Juriloff (Medical Genetics)

Supervisory Committee:

Dr. Elizabeth M. Simpson, Research Supervisor (Medical Genetics)

Dr. Angela Brooks-Wilson (Medical Genetics)

University Examiner:

Dr. Blair Leavitt (Medical Genetics)