



PROGRAMME

The Final Oral Examination
For the Degree of

MASTER'S OF SCIENCE
Medical Genetics

JANE RYAN

B. Sc. University of British Columbia, 2002

Monday, June 16, 2008, 10:00 am
Room 2108, Child and Family Research Institute, 950 West 28th Ave

**"A Genome-Wide Linkage Scan and Targeted Family-Based
Association Analysis of Dyslexia"**

EXAMINING COMMITTEE

Chair:
Dr. Angie Brooks-Wilson

Supervisory Committee:

Dr. Leigh Field, Research Supervisor (Medical Genetics)
Dr. Wendy Robinson (Medical Genetics)
Dr. Debbie Giaschi (Ophthalmology and Visual Science; Psychology)

University Examiners:

Dr. Debbie Giaschi (Ophthalmology and Visual Science; Psychology)

ABSTRACT

As a specific reading disability with a neurobiological origin, developmental dyslexia is distinct from reading difficulties due to sensory impairments in vision or hearing. The disability is commonly attributed to a core deficit in phonological processing, the understanding of how phonemes, syllables and words are used in a language. Dyslexia is a complex genetic disorder with a strong genetic component; nine susceptibility loci (DYX1-9) have been identified with eight other dyslexia linkages lacking gene symbols also reported.

The statistical methods of linkage and association were employed to investigate the genetic susceptibility for phonological coding dyslexia (PCD), a common form of dyslexia characterized by difficulties in single word decoding and resulting from deficits in phonological processing. An autosomal genome-wide non-parametric linkage (NPL) study and four targeted fine-mapping family-based association studies were performed to locate the genes predisposing to PCD in 101 Canadian families with multiple affected members.

The NPL scan identified suggestive evidence for linkage with PCD at the two novel regions 16p12 and 4q12-q13, and provided independent confirmation of linkage to the well-replicated DYX3 locus (at 2p21). Some support for linkage was noted at a further five regions previously linked to dyslexia, while no linkage was detected at five other reportedly-linked regions, in particular, no linkage to DYX2 (6p22.2). Four regions (16p12, 2p21, 4q12-q13 and 6p22.2) were tested for association with PCD in 83 trios, a subset of the 101 families, using the TDT (transmission disequilibrium test) and the AFBAC (affected family-based controls) test. Association was detected in each of the three PCD-linked regions in the NPL scan; none of the tested marker alleles was associated with PCD in the 6p22.2 region. Four candidate genes were identified, two of which belong to the same gene family, with a possible role in the neurodevelopmental mechanisms underlying reading.

BIOGRAPHICAL NOTES

Born: April 27, 1981, Ottawa, Canada
Academic Studies: B. Sc. University of British Columbia, 2003
Current Position: MSc candidate, UBC, Medical Genetics

GRADUATE STUDIES

Field of Study: Genetic mapping of complex traits

Courses

MEDG 505	Genome Analysis	Instructors	Drs. S. Jones & P. Hieter
MEDG 520	Advances in Human Molecular Genetics		Dr. A. Brooks-Wilson
MEDG 530	Human Genetics		Dr. L. Clarke
MEDG 545	Current Topics in Medical Genetics		Dr. J. Friedman
MEDG 548	Directed Studies		Dr. L.L. Field
HCEP 502	Epidemiological Methods 1		Dr. P. Janssen

AWARDS

2006 CFRI Research Methodology Training Grant
2005 UBC Medical Genetics Entrance Scholarship
2005 SFU Graduate Fellowship (Masters) Research Award (declined)

PRESENTATIONS

K. Shumansky, J. Ryan, D. Truong, L.L. Field. To Keep or Delete: How Many High-density-array SNPs Should We Use For Linkage Analysis? 3rd Annual Canadian Genetic Epidemiology & Statistical Genetics Meeting, Toronto, April 29-May 1, 2008.

J. Ryan. High-Density Genome-Wide Screen for Dyslexia Susceptibility Genes. 54th Wellcome Trust Advanced Course Human Genome Analysis: Genetic Analysis of Multifactorial Diseases. Hinxton, England, July 19-25, 2006.

S.H. Goh, J. Ryan, N. Sham, A. Haji, D. Chan, C. Shaw, J. Isaac-Renton, and G. Stephens. Profiling of Genomic Variation in Pertactin (prn) and Pertussis Toxin (ptx) Gene Alleles from Clinical Isolates of *Bordetella pertussis* Isolated in British Columbia Between 1981-2003. Conjoint Meeting of CACMID, Regina, SK, 2004.

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