

## ABSTRACT

**Background:** Autism Spectrum Disorders (ASDs) are common, heritable neurobiologic conditions of unknown etiology confounded by significant clinical and genetic heterogeneity. In recent years, array CGH technology has been used to screen the genome for pathogenic copy number variants (pCNVs) associated with ASDs and data from 6 studies suggests that pCNVs contribute to ASD pathogenesis in 6-27% of cases. However, the role of pCNVs in ASDs remains poorly understood, due to the absence of comprehensive phenotyping of ASD subjects.

**Methods:** To address this, we collected detailed clinical, medical, physical and morphologic information on all subjects and investigated whether these phenotypes would be good indicators of pCNV risk. We studied somatic phenotypes, as opposed to behavioural indices that change over time and with treatment, in an attempt to provide better evidence for the biological/embryological origin of ASDs and help define new syndromes.

**Results:** Seven disease-specific and potentially pathogenic CNVs were uncovered in 6/40 patients (15%). Two changes were *de novo* and 5 were inherited from normal parents, but had never been reported in normal populations before. All pCNVs were discovered in individuals without family history of autism, ranged in sizes from 175kb to 2.5Mb, and revealed 9 good candidate genes. Our results suggest that whilst no single phenotypic feature investigated associates with pCNV risk, there is an indication that the presence of phenotypic abnormalities involving multiple body areas may be a better indicator of pCNVs in ASDs than the presence or number of minor physical anomalies alone. In addition, our findings lend support to the idea that complex autism, involving significant dysmorphology, is etiologically distinct from essential autism, with an increased prevalence of ID, seizures and health problems, and a higher proportion of individuals without family history of ASDs.

**Conclusion:** We identified novel areas of chromosomal imbalance associated with ASDs and provide detailed phenotypic information for every subject for which these new pCNVs were detected. The extensive phenotyping of affected individuals carrying clinically relevant CNVs is needed in order to understand their role in the etiology of autism and ultimately provide earlier and more reliable means for diagnosis and treatment.

## BIOGRAPHICAL NOTES

Born: 12/21/82, Montréal, QC

Academic Studies: B. Sc. McGill University, 2005

Current Position: MSc candidate, UBC

(500 level and above):

Course	Course Title	Course Co-ordinator
MEDG 520	Advances in Human Molecular Genetics	Dr. Angela Brooks-Wilson
MEDG 530	Human Genetics	Dr. Lorne Clarke
MEDG 545	Current Topics in Medical Genetics Research	Dr. Carolyn Brown
MEDG 548	Directed Studies	Dr. Suzanne Lewis and Dr. Evica Rajcan-Separovic
MEDG 535	Genetics and Ethics	Dr. Michael Burgess
MEDG 549	M.Sc. Thesis	Dr. Suzanne Lewis and Dr. Evica Rajcan-Separovic

## AWARDS

2006-2007 UBC Graduate Entrance Scholarship

2006-2007 CIHR Canada Graduate Scholarship-Masters

2006-2009 CIHR/NAAR Inter-Institute Interdisciplinary Strategic Training Program in Autism Spectrum Disorders

2007-2009 Fondation pour la Recherche en Santé du Québec-Bourse de Maîtrise (Masters Scholarship)

2007-2009 Michael Smith Foundation for Health Research, Junior Graduate Studentship

## PUBLICATIONS

**Qiao Y., Harvard C., Riendeau N., Fawcett C., Liu X., Holden JJ., Lewis ME., Rajcan-Separovic E.** (2008) Putatively benign copy number variants in subjects with idiopathic autism spectrum disorder and/or intellectual disability. *Cytogenet Genome Res* **123(1-4)**: 79-87

**Qiao Y., Riendeau N., Koochek., Liu X., Harvard C., Hildebrand MJ., Holden JJ., Rajcan-Separovic E., Lewis ME.** (2009) Phenomic determinants of genomic variation in autism spectrum disorders. *J Med Genet* Jul. 21 (Epub ahead of print)

## SELECTED PRESENTATIONS

- October 2007 FISH confirmation of array-detected microduplications: an assessment of discrepancies with real-time qPCR findings
- November 2008 Phenomic determinants of genomic variation in autism spectrum disorders
- June 2009 Autism Spectrum disorders: Identification of novel microdeletions and microduplications and their associated phenotypes

## SUPERVISORY COMMITTEE

Dr. Suzanne Lewis  
Dr. Evica Rajcan-Separovic  
Dr. Wendy Robinson  
Dr. Margot Van Allen



## PROGRAMME

The Final Oral Examination  
For the Degree of

MASTER'S OF SCIENCE  
(Medical Genetics)

## NOÉMIE RIENDEAU

B.Sc., McGill University, 2005

Friday, September 4, 2009, 2:00 pm

Room D210, Children's and Women's Health Centre of BC  
4480 Oak Street, Vancouver

**"Autism Spectrum Disorders: Identification of Novel Microdeletions and Microduplications and their Associated Phenotypes"**

## EXAMINING COMMITTEE

Chair:

Dr. Marco Marra (Medical Genetics)

Supervisory Committee:

Dr. Suzanne Lewis, Research Supervisor (Medical Genetics)  
Dr. Evica Rajcan-Separovic, Research Co-Supervisor (Pathology)  
Dr. Wendy Robinson (Medical Genetics)

University Examiner:

Dr. Brett Casey (Diagnostic Molecular Genetics)

