# 39th Annual David W. Smith Workshop on Malformations and Morphogenesis

**August 24th – 29th, 2018**

**Banff Centre for Arts and Creativity, Banff, Alberta, Canada**

## Agenda

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| **Friday August 24, 2018** | |
| | Arrivals and Registration |
| **Saturday August 25, 2018** | |
| 7:00 AM – 8:15 AM | ***Breakfast***<br>*Venue: Vistas Dining Room* |
| **8:30 AM-8:45 AM** | **Introduction and Announcements**<br>**Micheil Innes and Kym Boycott**<br>**KC 101 & 103 (all sessions)** |
| **8:45 AM – 10:15 AM** | **Session I: Founding Fellows Lecture and Teratogens**<br>*Chair: Micheil Innes* |
| **8:45 AM** | |
| A retrospective look at 45 years of the fetal alcohol spectrum disorder: How did we get here from where we started<br>***Keynote speaker: Kenneth Lyons Jones - Department of Pediatrics, University of California, San Diego, USA*** | |
| **9:45 AM** | |
| Zika virus as a cause of birth defects: Were the teratogenic effects of Zika virus missed for decades?<br>***Sonja A. Rasmussen - Centers for Disease Control and Prevention, USA*** | |
| **10:00 AM** | |
| The pesticide synergist Piperonyl Butoxide inhibits sonic hedgehog signaling and causes holoprosencephaly in mice: Gene-environment interactions and subteratogenic effects<br>***Robert L Lipinski - University of Wisconsin-Madison, USA*** | |
| **10:15 AM – 10:45 AM** | ***Break*** |
| **10:45 AM – 11:45 AM** | **Session II: Placenta and Prenatal**<br>*Chair: Francois Bernier* |
| **10:45 AM** | |
| Stillbirth: Is the placenta the problem?<br>***Elspeth McPherson - Marshfield Clinic Research Institute, USA*** | |
| **11:00 AM** | |
| Beyond mesenchymal dysplasia: Clinical characterization of placental pathology in Beckwith-Wiedemann syndrome<br>***Rebecca Linn - Children's Hospital of Philadelphia, USA*** | |
| **11:15 AM** | |
| What not to expect when you're expecting: Unusual cases of placental mosaicism detected on non-invasive prenatal screening<br>***Amanda Barone* - Children's Hospital of Philadelphia, USA*** | |
| **11:30 AM** | |
| Prenatal profile of Pallister Killian syndrome: Retrospective analysis of 114 pregnancies, literature review and approach to prenatal diagnosis<br>***Ian Krantz - Children's Hospital of Philadelphia, USA*** | |
| **11:45 AM –1:15 PM** | ***Lunch***<br>*Venue: Vistas Dining Room* |

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| **1:15 PM –3:00 PM** | **Session III: Central Nervous System Diseases**<br>*Chair: David Dyment* |
| **1:15 PM** | |
| The patterns of brain malformations seen in discordant twins<br>***William B Dobyns - University of Washington and Seattle Children's Hospital, USA*** | |
| **1:30 PM** | |
| Pathogenic *DDX3X* mutations impair RNA metabolism and disrupt neuronal fate during fetal cortical development<br>***Elliot H. Sherr - University of California, USA*** | |
| **1:45 PM** | |
| POGZ-CHAMP1 are molecular partners associated with neurodevelopmental disorders and phenotypic ontology for olfactory bulb hypoplasia and intestinal malrotation<br>***Joseph T. Shieh - University of California San Francisco, USA*** | |
| **2:00 PM** | |
| Arthrogryposis – Genetic update<br>***Judith G. Hall - University of British Columbia, Canada*** | |
| **2:15 PM** | |
| Variants in *MAP4K4* cause a novel and potentially treatable form of neurologic dysfunction with cardiac anomalies<br>***Elizabeth J. Bhoj - Children's Hospital of Philadelphia, USA*** | |
| **2:30 PM** | |
| Variants of *NAA15*: Another newly recognized etiology for neurodevelopmental impairment as illustrated by 38 cases<br>***Alan F. Rope - Kaiser Permanente Northwest, USA*** | |
| **2:45 PM** | |
| *PIK3CB* causes a novel neurodevelopmental and overgrowth syndrome characterized by macrocephaly and polymicrogyria<br>***Priya T. Bhola* - Children's Hospital of Eastern Ontario, Canada*** | |
| **3:00 PM – 3:30 PM** | ***Break*** |
| **3:30 PM – 5:45 PM** | **Session IV: New Insights into Old Syndromes**<br>*Chair: Oana Caluseriu* |
| **3:30 PM** | |
| Kabuki syndrome: International consensus diagnostic criteria<br>***Margaret Adam - University of Washington, USA*** | |
| **3:45 PM** | |
| In depth phenotyping of Snyder-Robinson syndrome: Old and new findings<br>***Angela Peron* - University of Milan, Italy*** | |
| **4:00 PM** | |
| De novo truncating variants in *WHSC1* recapitulate the Wolf-Hirschhorn (4p16.3 microdeletion) syndrome phenotype<br>***Nada Derar - Medical College of Wisconsin, USA*** | |

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| **4:15 PM** | |
| CHARGE syndrome in the era of molecular diagnosis: Need for higher clinical suspicion - findings in the CCHMC CHARGE center cohort<br>***Brittany Simpson* - Cincinnati Children's Hospital Medical Center, USA*** | |
| **4:30 PM** | |
| Chimeric versus mosaic genome-wide paternal uniparental isodisomy as etiologies for Beckwith-Wiedemann Syndrome<br>***Sarah Sheppard* - Children's Hospital of Philadelphia, USA*** | |
| **4:45 PM** | |
| Influence of molecular classes and growth hormone on dysmorphology features in Prader-Willi syndrome: A multicenter study<br>***Virginia Kimonis - University of California, Irvine, USA*** | |
| **5:00 PM** | |
| Further delineation of Temtamy syndrome of corpus callosum and ocular abnormalities<br>***Laila Ali Alrakaf*- Alfaisal University, Saudi Arabia*** | |
| **5:30 PM** | |
| *ASXL*-related disorders: The first year of our registry<br>***Bianca Russell* - Cincinnati Children's Hospital, USA*** | |
| **5:45 PM** | |
| Method of diagnosis relative to phenotype in Incontinentia Pigmenti<br>***Angela Scheuerle - UT Southwestern Medical Center, USA*** | |
| **6:00 PM – 7:30 PM** | ***Dinner***<br>*Venue: Vistas Dining Room* |
| **7:30 PM – 8:30 PM** | **Poster Session: Posters 1-36**<br>**KC 203/205** |
| **8:30 PM – 9:30 PM** | **Poster Session: Posters 37-71**<br>**KC 203/205** |
| **Sunday August 26, 2018** | |
| **7:00 AM – 8:15 AM** | ***Breakfast***<br>*Venue: Vistas Dining Room* |
| **8:30 AM – 10:30 AM** | **Session V: Gene Environment Interaction and Complex Disease**<br>*Chair: Joseph T. Shieh* |
| **8:30 AM** | |
| Genetic and environmental causes of congenital malformation<br>***Keynote speaker*: Sally Dunwoodie, University of New South Wales, Australia**<br>*Introduction: Kym Boycott* | |
| **9:30 AM** | |
| Variation in aortic disease in mice and humans with elastin insufficiency and Williams Beuren syndrome is modified by secondary changes in extracellular matrix and immune pathway genes<br>***Beth Kozel – National Heart, Blood, and Lung Institute of NIH, USA*** | |
| **9:45 AM** | |
| Pregestational diabetes and neural tube defects in Manitoba<br>***Jane Evans - University of Manitoba, Canada*** | |

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| **10:00 AM** | |
| Auriculocondylar syndrome: A Craniofacial disorder with a vasospastic complication?<br>***Matthew A. Deardorff - The Children's Hospital of Philadelphia, USA*** | |
| **10:15 PM** | |
| Mutations in the Epithelial Cadherin-P120-Catenin complex are significant contributors to non-syndromic cleft lip with or without cleft palate<br>***Timothy Cox - University of Washington, USA*** | |
| **10:30 AM – 11:00 AM** | ***Break* KC 203/205** |
| **11:00 AM – 12:15 PM** | **Session VI: Syndromes - Michael Cohen**<br>*Chair : John Carey* |
| **11:00 AM** | |
| Delineation and definition of the Carey-Fineman-Ziter-Syndrome (CFZS): A tale of (ten) cities<br>***John C. Carey - University of Utah, USA*** | |
| **11:15 AM** | |
| The many faces of *SOS1*: Exon 20 frameshift mutations are associated with multiple mucosal neuroma syndrome – A benign MEN2B phenocopy<br>***Micheil Innes - Alberta Children's Hospital Research Institute, Canada*** | |
| **11:30 AM** | |
| The full spectrum of post-zygotic *PIK3CA* mutations in non-syndromic lymphatic malformations<br>***James T. Bennett - University of Washington, USA*** | |
| **11:45 AM** | |
| *SUZ12*-related overgrowth: Expanding the phenotype<br>***William Gibson - University of British Columbia, Canada*** | |
| **12:15 PM – 1:30 PM** | ***Lunch***<br>*Venue: Vistas Dining Room* |
| **1:30 PM – 3:30 PM** | **Session VII: Next-Generation Phenotyping 1**<br>*Chair: Anne O'Donnell* |
| **1:30 PM** | |
| Phenotyping with and without typing: Capturing and structuring your patient data<br>***Keynote speaker*: Michael Brudno - Department of Computer Science, University of Toronto, Centre for Computational Medicine, The Hospital for Sick Children, Canada*** | |
| **2:30 PM** | |
| Deep phenotyping in the NIH undiagnosed diseases network<br>***John Mulvihill - National Human Genome Research Institute of NIH, USA*** | |
| **2:45 PM** | |
| Blended phenotypes: An interesting subset of the first 400 patients of the CAUSES research study<br>***Alison M. Elliott - University of British Columbia, Canada*** | |
| **3:00 PM** | |
| Confirming the candidacy of 46 disease genes and delineation of their phenotypic expression<br>***Fowzan S. Alkuraya - Alfaisal University, Saudi Arabia*** | |
| **3:15 PM** | |
| HARS syndrome: Expansion of the natural history of the disorder associated with homozygous Y454S mutations in the Histidyl-tRNA Synthetase (HARS) gene<br>***Victoria Mok Siu - University of Western Ontario, Canada*** | |

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| **3:30 PM – 4:00 PM** | ***Break* KC 203/205** |
| **4:00 PM – 6:00 PM** | **Session VIII: Next-Generation Phenotyping 2**<br>*Chair: Elizabeth Bhoj* |
| **4:00 PM** | |
| The impact of next generation sequencing on syndrome delineation<br>***Michael Bamshad - University of Washington, USA*** | |
| **4:15 PM** | |
| Alternative diagnoses for individuals referred for exome sequencing with a clinical diagnosis of Dubowitz syndrome<br>***David Dyment - Children's Hospital of Eastern Ontario Research Institute, Canada*** | |
| **4:30 PM** | |
| Cohort analysis reveals diverse genetic etiology underlying Dubowitz syndrome<br>***Anne O'Donnell - Broad Institute, USA*** | |
| **4:45 PM** | |
| Final demise of the lethal recessive acrofacial dysostosis syndrome Rodriguez type<br>***Elaine H. Zackai - Children's Hospital of Philadelphia, USA*** | |
| **5:00 PM** | |
| Deep phenotyping using 3D craniofacial morphometry<br>***Francois Bernier - Alberta Children's Hospital Research Institute, Canada*** | |
| **5:15 PM** | |
| The facial phenotype of Aymé-Gripp syndrome is recognizable by the next generation phenotyping software<br>***Karen W. Gripp - A. I. duPont Hospital for Children, USA*** | |
| **5:30 PM** | |
| Emerging phenotype of a *CREBBP*-Related disorder distinct from Rubinstein-Taybi syndrome<br>***Julie Kaplan - Nemours A.I. DuPont Hospital for Children, USA*** | |
| **5:45 PM** | |
| Diagnosis and Management of the phenotypic spectrum of twins with Beckwith-Wiedemann Syndrome<br>***Jennifer L. Cohen*- Children's Hospital of Philadelphia, USA*** | |
| **6:00 PM – 7:30 PM** | ***Dinner***<br>*Venue: Vistas Dining Room* |
| **8:00 PM – 10:00 PM** | Activity<br>GH 101&103 |
| **Monday August 27, 2018** | |
| **7:00 AM – 8:15 AM** | ***Breakfast***<br>*Venue: Vistas Dining room* |
| **8:30 AM – 10:30 AM** | **Session IX: Treatment 1**<br>*Chair: Sue White* |
| **8:30 AM** | |
| Emerging therapies in skeletal dysplasias: The journey from diagnosis to precision intervention<br>***Keynote speaker*: Ravi Savarirayan - Murdoch Children's Research Institute, and University of Melbourne, Australia*** | |

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| **9:30 AM** | |
| Transformation of clinical care for plexiform neurofibromas in Neurofibromatosis type 1 (NF1) with the advent of MEK inhibitors<br>***David Viskochil - University of Utah, USA*** | |
| **9:45 AM** | |
| One-year pilot treatment trial oral nitisinone in Oculocutaneous Albinism, type 1B<br>***Brian Brooks - National Eye Institute and National Human Genome Research Institute of NIH, USA*** | |
| **10:00 AM** | |
| A child with an advanced lymphatic anomaly due to a novel gain-of-function mutation in *ARAF* has remission following treatment with a MEK inhibitor<br>***Dong Li* - The Children's Hospital of Philadelphia, USA*** | |
| **10:15 AM** | |
| Landscape of treatable rare disease in a founder population<br>***Alison Eaton* - University of Calgary, Canada*** | |
| **10:30 AM – 11:00 AM** | ***Break* KC 203/205** |
| **11:00 AM – 12:30 PM** | **Session X: Treatment 2**<br>*Chair: Wen-Hann Tan* |
| **11:00 AM** | |
| Cantu syndrome: Treatment of a mouse model with the sulfonylurea glibenclamide and potential for human therapy<br>***Dorothy K. Grange - Washington University School of Medicine, St. Louis Children's Hospital, USA*** | |
| **11:15 AM** | |
| Role of Leptin and Adiponectin in *PIK3CA*-Related Overgrowth Spectrum (PROS) – Implications for Phenotype and Response to Sirolimus Therapy<br>***Kim M Keppler-Noreuil - National Human Genome Research Institute of NIH, USA*** | |
| **11:30 AM** | |
| *FASTKD2* mutations associated with developmental delay, tremor, and chronic kidney disease responsive to Coenzyme Q10<br>***Michael J. Lyons - Greenwood Genetic Center, USA*** | |
| **11:45 AM** | |
| Impact of molecular diagnosis on management, treatment, and long term outcomes in congenital diarrheal disorders<br>***Rachel Lombardo* - Cincinnati Children's Hospital and Medical Center, USA*** | |
| **12:00 PM** | |
| Dietary treatment for Neurofibromatosis type 1<br>***David Stevenson - Stanford University, USA*** | |
| **12:15 PM** | |
| Nonsense suppression therapy can rescue *BMP4* nonsense mutation in vitro and the bmp4st72 allele in vivo in zebrafish<br>***Anne Slavotinek - University of California, San Francisco, USA*** | |
| **12:30 PM – 05:30 PM** | Lunch: Vistas Dining Room (until 1:30)<br>Free Time |

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| **12:30 PM -2:00 PM** | Fellows session |
| **5:30 PM – 7:30 PM** | ***Dinner***<br>*Venue: Vistas Dining Room* |
| **8:00 PM – 10:00 PM** | **Unknowns Session**<br>**GH 101&103**<br>*Chairs: Marilyn Jones and Micheil Innes* |
| **Tuesday August 28, 2018** | |
| **7:00 AM – 8:15 AM** | ***Breakfast:***<br>*Venue: Vistas Dining Room* |
| **8:30 AM – 10:30 AM** | **Session XI: Epigenetics**<br>*Chair: Matthew A. Deardorff* |
| **8:30 AM** | |
| Functional molecular diagnostic opportunities created by cross–talk between histone modifications and DNA methylation<br>***Keynote speaker*: Rosanna Weksberg - Department of Pediatrics, University of Toronto, Genetics and Genome Biology Program, Hospital for Sick Children, Canada** | |
| **9:30 AM** | |
| ADNP syndrome has a unique genomic DNA methylation signature that suggests *PACSIN1* may contribute to the disease mechanism<br>***Eric Bend* - Greenwood Genetic Center, USA*** | |
| **9:45 AM** | |
| Identification of a unique DNA methylation signature associated with Nicolaides-Baraitser syndrome<br>***Resham Ejaz* - University of Toronto, Canada*** | |
| **10:00 AM** | |
| Why do *FMR1* full mutations become methylated? An outstanding question<br>***Giovanni Neri - Institute of Genomic Medicine, Catholic University School of Medicine, Italy*** | |
| **10:15 AM** | |
| The phenotype spectrum of Beckwith-Wiedemann syndrome due to loss of methylation at imprinting center 2<br>***Jennifer M. Kalish - The Children's Hospital of Philadelphia, USA*** | |
| **10:30 AM – 11:00 AM** | ***Break* KC 203/205** |
| **11:00 AM – 12:30 PM** | **Session XII: New and Emerging Syndromes 1**<br>*Chair: Fowzan Alkuraya* |
| **11:00 AM** | |
| Examination of the landscape of Histone Lysine Methylases and Demethylases in human developmental disorders leads to the identification of novel syndromes<br>***Victor Faundes*- University of Manchester*** | |
| **11:15 AM** | |
| Mutations in the BAF-complex subunit *DPF2* associated with Coffin-Siris syndrome<br>***André Reis - Institute of Human Genetics, FAU Erlangen-Nürnberg, Germany*** | |

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| **11:30 AM** | |
| Missense mutations disrupting the helicase domain of chromatin remodeller CHD3 cause a novel neurodevelopmental syndrome with intellectual disability, macrocephaly and impaired speech and language<br>***Philippe M. Campeau - CHU Sainte-Justine Research Center Canada*** | |
| **11:45 AM** | |
| Clinical and molecular characterization of *TFE3* mutation-related neurocutaneous syndrome<br>***Daphné Lehalle - Université de Bourgogne Franche-Comté, France*** | |
| **12:00 PM** | |
| Characterization of novel X-linked, *IGSF1*-associated human and canine overgrowth<br>***Thoa K. Ha* - University of California San Francisco, USA*** | |
| **12:15 PM** | |
| Craniofacial anomalies, ptosis, agenesis of the corpus callosum, and developmental delay associated with loss of function variants in *ZNF462*: Humans and zebrafish<br>***Paul Kruszka - National Human Genome Research Institute of NIH, USA*** | |
| **12:30 PM – 1:45 PM** | ***Lunch***<br>*Venue: Vistas Dining Room* |
| **1:45 PM – 4:30 PM** | **Session XIII: New and Emerging Syndromes 2**<br>*Chair: Alison M. Elliott* |
| **1:45 PM** | |
| The human engrailed-1 (*EN1*) locus: Two different types of mutations resulting in limb and brain malformation phenotypes<br>***Andrea Superti-Furga - Lausanne University Hospital, Switzerland*** | |
| **2:00 PM** | |
| Do heterozygous loss-of-function variants in *MTOR* cause a treatable neurodevelopmental phenotype?<br>***Susan White - Victorian Clinical Genetics Services, Australia*** | |
| **2:15 PM** | |
| Missense mutation in actin-building protein plastin 3 cause X-linked multiple congenital anomalies with diaphragmatic hernia<br>***Robin D. Clark - Loma Linda University School of Medicine, USA*** | |
| **2:30 PM** | |
| Phenotypic spectrum of Au-Kline syndrome: 12 new cases and review of the literature<br>***P.Y. Billie Au - University of Calgary, Canada*** | |
| **2:45 PM** | |
| Expansion of the *GTPBP2*-Associated Neuro-ectodermal Syndrome Phenotype<br>***Melissa Carter - Children's Hospital of Eastern Ontario, Canada*** | |
| **3:00 PM** ***Break KC 203/205*** | |
| **3:15 PM** | |
| *UBE2A*- related XLID – a recognizable X-linked intellectual disability syndrome<br>***Roger Stevenson - Greenwood Genetic Center, USA*** | |

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| **3:30 PM** | |
| A novel neuromuscular disorder linked to *STX4*<br>***Carlos E. Prada - Cincinnati Children's Hospital Medical Center, USA*** | |
| **3:45 PM** | |
| Truncating variants in *PPMID* case a recognizable dysmorphic and behavioral phenotype with similarities to Williams syndrome<br>***Cynthia J. Curry - University of California, San Francisco/Fresno, USA*** | |
| **4:00 PM** | |
| Armfield XLID syndrome has a distinct phenotype (short stature, small hands/feet, ocular anomalies, seizures), results from mutations in *FAM50A*, and is a spliceosomopathy<br>***Charles E. Schwartz - Greenwood Genetic Center, USA*** | |
| **4:15 PM** | |
| 10 Faces You Should Know<br>***Charles E. Schwartz - Greenwood Genetic Center, USA*** | |
| **4:30 PM** Presentation of Fellows/Trainee Awards | |
| **6:30 PM – 1:00 AM** | ***Dinner Reception and Dance***<br>*Venue: KC 201/203* |
| **Wednesday August 29, 2018** | |
| **7:00 AM – 9:00 AM** | ***Breakfast***<br>*Venue: Vistas Dining Room* |