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EDITORIAL

Cerebellum: from Development to Disease—the 8th International Symposium of the Society for Research on the Cerebellum and Ataxias

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Abstract
In recent years, there has been tremendous growth in research on cerebellar motor and non-motor functions. Cerebellum is particularly involved in the spectrum of neurodevelopmental diseases. The 8th International Symposium of the Society for Research on the Cerebellum and Ataxia (SRCA) was held in Winnipeg, Manitoba, (Canada) on May 24–26, 2017. The main theme of the 8th International Symposium was "Development of the Cerebellum and Neurodevelopmental Disorders." Advances in genetics, epigenetic, cerebellar neurogenesis, axonogenesis and gliogenesis, cerebellar developmental disorders including autism spectrum disorders (ASD), neuroimaging, cerebellar ataxias, medulloblastoma, and clinical investigation of cerebellar diseases were presented. The goal of this symposium was to provide a platform to discuss cutting-edge knowledge while allowing researchers and trainees the opportunity to share and discuss their front-line research and ideas with others in the field, make connections, and strengthen international collaborations. The Ferdinando Rossi lecture was delivered by Dr. Richard Hawkes on the topic of patterning of the cerebellar cortex. This symposium emphasized the major importance of the involvement of the cerebellum in neurodevelopmental diseases from the clinical, radiological, biological, and genetic standpoint.

Keywords Cerebellar development · Neurogenesis · Gliogenesis · Neurodevelopmental disorders · Ataxias · ASD · Medulloblastoma

The 8th International Symposium of the Society for Research on the Cerebellum and Ataxia (SRCA) was held in Winnipeg, at the University of Manitoba, Rady Faculty of Health Sciences, on May 24–26, 2017. Manitoba is located in central Canada. Winnipeg is one of the "cultural cradles of Canada" and Manitoba's cosmopolitan capital city. The Winnipeg symposium focused on the broad field of cerebellar development ranging from normal and abnormal neurogenesis/axonogenesis, morphogenesis, and synapse formation, which underlie ataxia, autism spectrum disorder, and cerebellar tumors (medulloblastoma). During the 3 days' meeting, principal investigators, clinicians, graduate students, and trainees from Canada and around the world discussed their cutting-edge research in the field. The 8th SRCA symposium received approval for Continuing Medical Education (CME) credits.

The organizing and program committees of the 8th International Symposium and the executive committee of the SRCA express appreciation to all attendees, the chairpersons, and speakers who made this highly successful symposium happen in Canada. We would like to extend our appreciation to the sponsors for their financial support, which made this symposium possible: the Health Sciences Centre Foundation, the Department of Human Anatomy and Cell Science, the University of Manitoba (including the Rady Faculty of Health Sciences, Max Rady College of Medicine, and Faculty of Graduate Studies), the Children's Hospital Research Institute of Manitoba, the Department of

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Physiology and Pathophysiology (Peter A. Cattini, Henry G. Friesen Chair in Endocrine & Metabolic Disorders), the Department of Biochemistry & Medical Genetics, the Regenerative Medicine Program, Canad Inns Winnipeg, the Department of Pharmacology and Therapeutics, St. Boniface Research Centre, the Research Manitoba, Springer Publishing, and Tourism Winnipeg for their support in helping to organize this significant event.

The theme of the 8th SRCA Symposium was devoted to investigate cerebellar development and neurodevelopmental disorders. The first thematic session was held on May 24 and the Keynote address was dedicated as the Ferdinando Rossi Memorial Lecture. This Keynote lecture was delivered by Richard Hawkes, in which he discussed the molecular patterning of the adult cerebellar cortex, pattern formation during embryonic development, and the mechanisms that lead to pattern formation during cerebellar development [1].

The second session began on May 25 with a focus on current knowledge regarding neurogenesis and morphogenesis during cerebellar development. Mikio Hoshino discussed the multiple functions of myeloid ectopic viral integration site 1 homolog (Meis1) in coordinating granule cells differentiation and development. Richard Wingate explained the development of cerebellar output with a focus on the origins of projection glutamatergic cerebellar nuclei neurons and inhibitory output neurons and factors that regulate their specification. Alexander Joyner discussed cellular interactions underlying proportional scaling of cell types during cerebellar development and repair by analyzing the phenotypes of mouse engrailed gene (En1/2) condition mutants. Joanna Yeung explained the cerebellar rhombic lip development with focus on a novel rhombic lip marker, Wntless (Wls), relative to its interaction with other rhombic lip markers (Atoh1, Pax6, and Lmx1a).

The third session addressed current knowledge regarding normal and abnormal differentiation during cerebellar development. Azad Bonni discussed the role of the epigenetics in cerebellar circuit assembly and function with a focus on the nucleosome remodeling and deacetylase (NuRD) complex in parallel fiber presynaptic differentiation as well as granule neuron dendrite pruning in vivo. James Li presented on Bergmann glia development with emphasis on the FGF-ERK-ETV axis, Bergmann glia induction, and the role of Bergmann glia in organizing cerebellar foliation [2]. David Solecki's talk was entitled "Granule Cell Migration-Polarity, Link to Medulloblastoma." He discussed the upstream regulator of the Pard complex and Seven in Absentia in controlling granule cells from tangential migration to radial migration. Martine Roussel discussed epigenetic drivers in pediatric medulloblastoma with focus on the role of the EZH2, PRC2, and histone 3 lysine 27 trimethylation (H3K27me3) in group3 medulloblastomas [3].

The fourth session was dedicated to circuitry and functional development of the cerebellum. Izumi Sugihara focused on the ansiform lobule (crus I in the rodent cerebellum) as a unique conformation, axonal connection, striped pattern, evolution, and development in the mammalian cerebellum [4]. Alanna Watt explained the transient developmental Purkinje cell axonal torpedoes in healthy and ataxic mouse cerebellum and revealed that torpedoes during the second postnatal week is a normal morphological feature in the mouse cerebellum. Karl Schilling discussed developmental migration of cerebellar basket and stellate cells using quantitative approaches to address how molecular layer interneurons navigate through the nascent cerebellar cortex [5]. Keiko Muguruma was scheduled to speak on disease modeling with patient-derived iPS cells. Unfortunately, she could not attend to the meeting and a summary of her talk was published in this special issue of the journal [6].

The fifth session was devoted to aberrations of cerebellar development and function: genetics and imaging. Michael Salman explained the epidemiology of cerebellar diseases, examination, and therapeutic approaches that are currently used in clinical practice [7]. Williams Dobyns' talk was entitled "Canary in the coal mine: the cerebellum as a sentinel for developmental brain disorders." He presented data from recent SNP microarrays in 250 children and whole exome sequencing data in 100 children (and parents) with cerebellar malformations. Catherine Limperopoulos discussed the use of quantitative MRI (qMRI) during development of the human cerebellum in utero. Christopher Gomez underlined the importance of the P/Q-type voltage-gated Ca^{2+} channel (VGCC) gene and CACNA1A in spinocerebellar ataxia type 6 (SCA6) [8].

The sixth session, on May 26, addressed the question of synaptogenesis during cerebellar development. Keiji Ibata explained Cbln1 release from granule cell axons and its accumulation on Purkinje cell dendrites based on activity-dependent and activity-independent manner using time-lapse imaging. Naofumi Uesaka discussed Semaphorin7A and Semaphorin3A in relation to retrograde signals from postsynaptic Purkinje cells to presynaptic climbing fibers and the role of regulatory pathways in elimination and maintenance of the climbing fibers [9]. Fabrice Ango spoke on the role of the axon guidance receptor neuropilin-1 that is expressed by GABAergic interneurons. His work suggested that neuropilin-1 orchestrate both guidance and subcellular synapse targeting through timely interactions with local cues. Laurence Cathala's talk was dedicated to the cellular mechanisms of interneuron synaptic integration in the developing cerebellum, and compared processing of immature stellate cells and adult stellate cell.

The seventh session was designed for poster presentations. The Winnipeg SRCA symposium received 64 abstracts that were posted on boards for 2 days and presented during the seventh session poster presentation. The Masao Ito awards for

the best posters were announced by our President Jean Mariani. There were three recipients: Lauren Watson (University of Oxford, UK) for a poster dedicated to using induced pluripotent stem cells to investigate the disease mechanisms of spinocerebellar ataxia; Parthiv Haldipur (Seattle Children's Research Institute, USA) for research on disrupted rhombic lip development caused by aberrant mesenchymal signaling that likely represents a unifying developmental mechanism for human Dandy-Walker malformation; and Hirofumi Fijita (Johns Hopkins University, USA) for a study on molecularly and anatomically distinct types of projection neurons in the medial cerebellar nucleus in relation to the cerebellar vermis.

The eighth session was focused on novel knowledge regarding aberrations of cerebellar development and function. This session included talks on motor and treatment models of cerebellar disease. Hirokazu Hirai discussed the role of protein kinase C in developing cerebellar function with an emphasis on PKCα and PKCγ and the role of the PKCγ in the adult cerebellum [10]. Lauren Nicole Miterko discussed motor dysfunction using a Car8wdl mouse model of hereditary cerebellar ataxia and CAR8 (carbonic anhydrase 8), a regulator of IP3R1 Ca^{2+} signaling [11]. Roger Reeves discussed the Shh pathway in the developing cerebellum of trisomic mice by investigating a mouse models of Down syndrome, the Ts65Dn model, which is trisomic for orthologs of more than half of the genes conserved with human chromosome 21 (Hsa21).

The ninth and final session was dedicated to discussing the role of cerebellum in autism spectrum disorder (ASD). Peter Tsai explained the cerebellar contribution to ASD and investigated sensitive periods of treatment and mechanisms by which the cerebellum regulates autistic behaviors. Christian Hansel talk was focused on Purkinje cell function in mouse models of ASD, and he discussed the cause of motor deficits in Dup15q syndrome/ASD and characterized synaptic and behavioral phenotypes in CYFIP1 overexpressing mice. John Welsh discussed ASD and eyeblink conditioning and analyzed the influence of the upward modulation of subthreshold oscillation (STO) amplitude and synchrony by NMDA-receptor mediated plasticity of electrical synapses for motor and associative learning, and its possible relevance to childhood autism. Aleksandra Badura discussed lobule-specific contribution to executive functions in mouse cerebellum with an emphasis on social choice/behavioral inhibition and cognitive flexibility after disruption of the reciprocal connection between lobules VI/VII and crus I/II with cerebral neocortex.

At the end, the president of the SRCA concluded that the Winnipeg symposium was very successful. We now look forward to meeting you all again at the next SRCA meeting in Taipei, Taiwan, from May 16 to 19, 2018 and hope you will continue to enjoy our next platform of cerebellar research and meet cerebellar investigators while visiting in a friendly atmosphere of our symposia!

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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