

Pacific Parkinson's RESEARCH INSTITUTE

2021 IMPACT REPORT

Marg Meikle Professorship in Parkinson's Research



The Pacific Parkinson's Research Institute (PPRI) partners with the UBC Faculty of Medicine to fund the strategic research priorities of the Pacific Parkinson's Research Centre (PPRC), a Canadian Centre for Excellence for the diagnosis and management of Parkinson's disease and related disorders.

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The University of British Columbia Faculty of Medicine and the Pacific Parkinson's Research Centre (PPRC) thank the Pacific Parkinson's Research Institute (PPRI) for its visionary support of the leadership in discovering critical links between research into Parkinson's disease (PD) and clinical care for patients, inspiring exciting collaborations across UBC, the PPRC and their partners. In the spirit of Marg Meikle's contribution in building a grassroots community around PD, this research is essential to advancing our understanding of the disease, enabling innovation in shaping its progression, and to increasing the quality of life for patients, their families and carers.

Principal Investigator, Dr. Silke Cresswell, is pleased to present this report, which celebrates and reflects on her achievements over the last five years as the holder of the Marg Meikle Professorship in Parkinson's Research, with the support of the PPRI, and looks to the future of treatments and preventative strategies for PD during her next term.



THE UNIVERSITY OF BRITISH COLUMBIA

Notable Accomplishments of the Last Five Years

Nutrition

The recent publication on the association of a significantly later age of onset in individuals with PD who closely adhere to Mediterranean diet principles has fueled great interest into the role of diet in PD. Based on those findings, we are now applying for funding for a dedicated randomized controlled trial into the Mediterranean-DASH Intervention for Neurodegenerative Delay—the MIND diet—in PD.

Six of our papers on lifestyle interventions such as nutrition (Postuma et al., 2017, Metcalfe-Roach et al., 2021) and exercise (Sacheli et al., 2018, Sacheli et al., 2019, projected funded by PPRI, PI Dr. Jon Stoessl) as well as on the microbiome and brain disorders (Tremlett et al., 2017, Cirstea et al., 2020) had excellent Altmetric Attention Scores, which measure the attention that scholarly articles receive, illustrating major interest in these fields in general and our work specifically and the wide reach of those publications (see addendum).

The IMPACCT project, PPRI Database (“iCAPTURE PD”)

In parallel to the development of the database, we created and implemented a standardized, comprehensive assessment embedded into our electronic medical record system which serves as a most valuable educational tool for medical students and residents in the clinic, facilitates electronic research data capture in the clinic and which provides personalized, written summaries of their clinic visit for patients. In addition, the IMPACCT PD project funded by PPRI acted as an important catalyst for the building of the interdisciplinary clinical care team at our centre.

Canadian Parkinson's Guidelines

As a section lead, Dr. Cresswell was part of the team of Canadian Movement disorder specialists to update the Canadian guidelines for the management of Parkinson's disease. The guidelines are a key resource for clinicians across the country to guide the treatment of PD. Not surprisingly, the associated paper (Grimes et al., 2019) attracted high media attention with an excellent Altmetric Attention Score in the top 5% of all outlets (over 17 Million) scored.

Papers, Presentations & Collaboration Highlights

- **Published** 22 Peer-Reviewed Papers and 1 Medical textbook
- **Presented** at 18 Professional Conferences
- **Spoke** at 26 Public Talks (including 6 PPRI events)
- **Developed** 12 National and International Collaborations and numerous UBC collaborations
- **Founded** the BC Brain Wellness Program
- **Integrated** exercise, nutrition and other lifestyle interventions into the clinical care provided by the BC Brain Wellness Program
- **Collaborated** with movement disorder specialists across Canada as the President of the Canadian Movement Disorder Group, the national organization of movement disorder specialists (2018 to 2020)
- **Served** as the director of the annual National Canadian Residents' Course on Movement Disorders to educate the next generation of neurologists and pediatric neurologists in the field of movement disorders (since 2017)
- **Co-founded** the first Canadian course on ultrasound guidance of botulinum toxin injections in movement disorders
- **Collaborated** with colleagues in Germany to increase the accuracy of botulinum toxin injections using ultrasound technology, benefiting patients with dystonia including those with dystonia as part of PD
- **Collaborated** with movement disorder specialists across Canada on the updating of the Canadian Guidelines on the management of Parkinson's disease

- **Collaborates** internationally as a Member of the Educational Committee of the Pan American Section, International Parkinson and Movement Disorder Society. Membership is by invitation, term: 2019 to 2022.
- **Contributed** to key plenary sessions at the MDS Congress, the premier international congress in the field of movement disorders. With an audience of several thousand, she co-presented the Grand Rounds plenary session in Vancouver in 2017, won a bronze medal in a field of more than 80 entries in the Video Challenge competition for a case presented in Hong Kong in 2018, and has been invited as one of just ten international movement disorder experts for the Video Challenge in 2021's virtual congress.

Microbiome Analysis



Dr. Silke Cresswell

Thanks to the visionary funding from PPRI, the UBC microbiome in PD research program that is at the heart of the PPRI-funded longitudinal study leads the field in Canada, and it is currently one of the largest internationally. As a result of their innovative study, Dr. Cresswell and her team have demonstrated that the microbiome composition and function in PD differs from healthy controls of the same age. In PD, the microbiome shows differences in composition and function, is less diverse and produces less butyrate (which supports digestive health) as a key short-chain fatty acid; those changes along with other mechanisms increase

inflammation, weaken the protective mucine layer of the gut wall leading to a leaky gut and the migration of toxic bacterial metabolites into the bloodstream. The success of the program has led to further grant funding from the Weston Family Foundation, Parkinson Canada, Canadian Consortium on Neurodegeneration and Aging (CCNA) and Canadian Institutes of Health Research (CIHR), national and international collaborations and clinical trials with the goal to develop microbiome-based interventions for PD and its symptoms.

In the past year, Dr. Cresswell's publications on the role of the microbiome in PD have significantly contributed new insights to the rapidly expanding field of research into the microbiome in PD. To date, the study supported by PPRI is one of the most extensive published studies investigating the microbiome in PD. Insights from this research are now informing clinical trials which are currently underway or planned at the Centre. The microbiome project has provided training opportunities for more than ten trainees, including undergraduate, graduate and medical students as well as postgraduate trainees. A major project in collaboration with the University of Calgary is building on the foundation of our microbiome work towards developing the next generation of microbiome-based interventions.

Brain Wellness Program

Dr. Cresswell has significantly expanded the BC Brain Wellness Program, founded by her in collaboration with Dr. Jack Taunton, professor emeritus for Sports Medicine at UBC and former Chief Medical Officer for the Vancouver 2010 Olympic and Paralympic Winter Games, to improve care for individuals with chronic brain conditions including PD. The BC Brain Wellness Program is an interdisciplinary initiative to optimize brain health with lifestyle interventions both for the treatment of existing conditions and for prevention. These interventions include exercise, nutrition, sleep, mindfulness/stress reduction, coping skills, art (including music, visual arts and performing arts), time in nature, self-management/coping strategies and essentially, community building. The program spans clinical, research and educational realms and is a collaboration between numerous disciplines at UBC as well as Vancouver Coastal Health.



Celebrating the launch of the Brain Wellness Program

The program exists in clinical, research and educational realms and embodies a collaboration between many disciplines at UBC and Vancouver Coastal Health. Several research projects, focusing on exercise and other lifestyle interventions to capture the program's impact, are at the planning stage. Dr. Cresswell has received donor funding for a randomized controlled trial into a combined exercise, nutrition and mindfulness intervention in healthy agers as the backbone of the research program.

Since its inception in October 2019, the program has had significant outreach and in the past year has grown exponentially with 26 different classes currently on offer, over 1,200 hours of free classes delivered and over 1,100 active users, the majority of which live with PD. In response to the pandemic, Dr. Cresswell and her team pivoted to virtual programming within two weeks, providing a lifeline to many in times of physical and social distancing. In addition to classes, regular public educational events known as "Wellness Wednesdays," covered a variety of stimulating topics in the past year, including:

- Music for the Mind
- Improv and Theatre for Brain Health
- Social Connections and Your Community
- A Time for Care Partners
- Exploring Mindfulness
- Living Your Best in Times of COVID-19

The BC Brain Wellness Program will continue to seek feedback from its participants to improve as a learning healthcare system. These insights will help Dr. Cresswell's team shape its research projects into lifestyle interventions.

Teaching and Leadership

Dr. Cresswell has continued to teach undergraduate, graduate and postgraduate students as well as movement disorder specialist peers. She has supervised 21 trainees in the past year, including undergraduate, masters, doctoral, postdoctoral and medical students. She is the co-director for the Canadian courses on ultrasound-guided botulinum toxin injections to treat cervical dystonia, alongside Dr. Sylvain Chouinard, Associate Professor, Department of Medicine, University of Montreal.

Dr. Cresswell has continued to serve as the director of the annual Canadian National Movement Disorders Residents Course as well as the President of the Canadian Movement Disorder Group.

Future Objectives

Dr. Cresswell's long-term objectives continue to be developing and optimizing of treatments and preventive strategies for Parkinson's disease and related disorders with a focus on the role of the microbiome, nutrition, exercise and other lifestyle interventions. Her approaches to research will include observational and mechanistic studies, clinical trials and implementation studies.

Dr. Cresswell's milestones for the next five-year term include:

- The completion of the five-year longitudinal microbiome project funded by PPRI and the publication of at least one to two papers annually based on microbiome-related research
- The completion of five clinical trials into nutrition and/or microbiome-based and combined lifestyle interventions (e.g. nutrition plus exercise plus mindfulness)
- The creation of a nutrition-microbiome-brain health Research Cluster at UBC
- Deepening of international collaborations on the theme of nutrition-microbiome-brain health and other lifestyle interventions for the prevention and treatment of PD and related disorders
- The incorporation of lifestyle interventions into the standard clinical care for Parkinson's disease and other brain disorders, leveraging the impact of the BC Brain Wellness Program.

A Personal Message from Dr. Cresswell

The past five years have been an incredible journey for me and have taught me valuable lessons on joy, resilience and positive capacity. A highlight has been how both the Brain Wellness and Microbiome Analysis programs have firmly taken root and flourished, despite the considerable challenges presented by the COVID-19 pandemic, and in turn, created new, synergistic possibilities. I deeply appreciate PPRI's visionary funding and support in increasing our understanding of PD and related disorders, bringing this new knowledge to the research community and the impact we make in the day-to-day lives of individuals living with Parkinson's, their families and care partners. As we have increased our understanding of the factors that have great potential to improve their quality of life, including nutrition, exercise, performative art and mindfulness, we experience more joy in empowering them to live their best times and create meaningful and long-lasting bonds with others in the PD community.



Dr. Silke Cresswell

As we look to the next five years, we are excited at what we may accomplish. Possessing the key data that nutrition is a crucial factor, we are eager to examine its impact on the related clinical mechanisms in the microbiome and the clinical course of PD. With your continuing support, we anticipate translating our newfound knowledge to build projects and communities, undertake robust research into lifestyle and microbiome interventions and connect patients and carers who otherwise may be isolated. Thank you!

Thank You

The UBC Faculty of Medicine and the PPRC are deeply grateful to the PPRI for supporting our investigations into the role of the microbiome in the development of Parkinson's disease and the development of a holistic approach to advance wellbeing for patients and care partners, especially during a year that has had an extraordinary impact on Parkinson's disease patients, their carers and families. Thank you for enabling our experts in neurology, microbiology, immunology, nutrition, exercise, metabolomics, psychiatry and other fields to proceed with this extensive research program to inform the development of much-needed therapies and interventions for Parkinson's disease.

Addendum

Peer-Reviewed Papers (2020-2021)

Kok JG, Leemans A, Teune AK, Leenders KL, McKeown MJ, Appel-Cresswell S, Kremer HPH, De Jong BM. Structural network analysis using diffusion MRI tractography in Parkinson's disease and correlations with motor impairment. *Front Neurol*. 2020 Sep 2;11:841. eCollection 2020. PMID: 32982909
Cited by one research paper (PubMed accessed June 6, 2021). Altmetric Attention Score: 7. 73rd percentile compared to outputs of the same age <https://frontiers.altmetric.com/details/89338822#score>, accessed June 6, 2021).

Cirstea M, Sundvick K, Golz E, Yu A, Boutin RCT, Kliger D, Finlay BB, Appel-Cresswell S. The gut mycobiome in Parkinson's disease. *J Parkinsons Dis*. 2020 Oct 31. doi: 10.3233/JPD-202237. Online ahead of print. PMID: 33164944.

Cited by three research papers (PubMed accessed June 6, 2021). Altmetric Attention Score not available.

Rodin I, Sung JH, Appel-Cresswell S, Chauhan H, Smith K, Vila-Rodriguez F, Ainsworth NJ. Psychiatric, motor, and autonomic effects of bifrontal ECT in depressed Parkinson's disease patients. *J Neuropsychiatry Clin Neurosci* 2021 Feb 25. doi:10.1176/appi.neuropsych.20050133. Online ahead of print. PMID: 33626885

Cited by 0 research papers (PubMed accessed June 6, 2021). Altmetric Attention Score: 6, in top 25% of all research outputs scored by Altmetric, 70th percentile compared to outputs of the same age (<https://psychiatryonline.altmetric.com/details/100822544>, accessed June 6, 2021).

Metcalfe-Roach A, Yu AC, Golz E, Cirstea M, Sundvick K, Kliger D, Foulger LH, Mackenzie M, Finlay BB, Appel-Cresswell S. MIND and Mediterranean diets associated with later onset of Parkinson's Disease. *Mov Disord*. 2021 Apr;36(4):977-984. doi: 10.1002/mds.28464. Epub 2021 Jan 6. PMID: 33404118.

Cited by 1 academic paper (PubMed accessed June 6, 2021). **Attention Score 223, in top 5% of all research outputs scored, one of the highest-scoring outputs from this source (#10 of 3,806), high attention score compared to outputs of the same age (99th percentile) and high Attention Score compared to outputs of the same age and source (99th percentile, #1 out of 132 outputs) by Altmetric (<https://wiley.altmetric.com/details/97258054>, accessed June 6, 2021)**

Fietzek, UM, Nene D, Schramm A, Appel-Cresswell S, Kosutzka Z, Walter U, Wissel J, Berweck S, Chouinard S, Bäumer T. The Role of Ultrasound for the Personalized Treatment of Cervical Dystonia. *Toxins*, 2021 May 20;13(5):365. doi: 10.3390/toxins13050365. PMID 34065541.

Cited by 0 academic papers (PubMed accessed June 6, 2021). Altmetric Attention Score: not available

MacLellan AD, Finlay BB, Appel-Cresswell S. Age-Matching in Pediatric Fecal Matter Transplants. Accepted for publication by *Frontiers in Pediatrics* June 2021.

Lee DG, Lindsay A, Yu A, Neilson S, Sundvick K, Golz E, Folger L, Mirian M*, Appel-Cresswell S*. Data-driven prediction of fatigue in Parkinson's disease patients. Accepted for publication by *Frontiers Artificial Intelligence – Medicine and Public Health*, August 2021. *joint senior authors.

Papers Submitted/Under Review

Toh TS, BSc, Chong CW, Lim SY, Bowman J, Cirstea M, Lin CH, Chen CC, Appel-Cresswell S, Finlay BB, Tan AH. Meta-analysis of Gut Microbiome in Parkinson's disease: Impact of Geographical and Methodological Differences. Submitted to *Park Rel Dis*. June 2021.

Vollstedt EJ, Schaake S, Lohmann K, Padmanabhan S, Brice A, Lesage S, Tesson C, Vidailhet M, Wurster I, Mirelman A, Giladi N, Orr-Urtreger A, Marder K, Waters C, Fahn S, Kasten M, Brüggemann N, Borsche M, Foroud T, Tolosa E, Garrido A, Annesi G, Bozi M, Stefanis L, Morris H, Correia Guedes L, Ferreira JJ, Avenali M, Petrucci S, Ruiz Martinez J, Clark L, Fedotova E, Abramychева N, Alvarez V, Jesús Maestre S, Gómez-Garre P, Mir P, Carmine Belin A, Crosiers D, Wszolek Z, Jankovic J, Nishioka K, Funayama M, Clarimon J, Albanese A, Williams-Gray CH, Cornejo-Olivas M, Wu YR, Januario C, Pulkes T, Berg D, Kühn A, Borngreber F, de Michele G, Zimprich A, Puschmann A, Mellick GD, Dorszewska J, Carr J, Bardien S, Ferese R, Chase B, Markopoulou K, Satake W, Rossi M, Merello M, Lynch T, Olszewska DA, Ahmad-Annuar A, Tan AH, Dieguez E, Al-Mubarak B, Hanagasi H, Kozirowski D, Genc G, de Carvalho Aguiar R, Barkhuizen M, van de Warrenburg B, Bloem B, Pimentel MMG, Saunders-Pullman R, Bressman S, Toft M, Appel-Cresswell S, Lang AE, Skorvanek M, Bonifati V, Krüger R, Sammler EM, Tumas V, Zhang B, Garraux G, Chung SJ, Kim YJ, Winkelmann J, Fung V, Sue CM, Tan EK, Damasio J, Klivényi P, Kostic SV, Arkadir D, Martikainen MH, Borges V, Hertz JM, Brighina L, Spitz M, Barrett MJ, Suchowersky O, Riess O, Das P, Mollenhauer B, Gatto EM, Kataoka H, Skaalum Petersen M, Hattori N, Wu RM, Illarioshkin S, Valente EM, Aasly JO, Alcalay R, Thaler A, Farrer MJ, Brockmann K, Corvol JC, Klein C on behalf of the MJFF Global Genetic Parkinson's Disease Study Group. The MJFF Global Genetic Parkinson's Disease Cohort. Submitted to Lancet Neurology June 2021.

Professional Conferences

Mini Med School 2020. Exploring the brain-gut-microbiome connection: the example of Parkinson's disease. Invited talk for several hundred high school students selected to participate in the Mini Med School online event, theme 2020: microbiome. October 2020.

"Investigating the role of the microbiome and nutrition in Parkinson's", invited speaker at the Neurodegenerative Disease Awareness Association at the University of California San Diego (UCSD) (student organization), November 2020

Wellness Wednesday. "Recent advances in Nutrition and Microbiome Research - Parkinson's research at UBC". Vancouver, online, January 2021.

"The BC Brain wellness program - a virtual transformation". Talk at "The 21st Century House Call - Is Virtual Health Here to Stay?", part of the "Transforming Health for Everyone" webinar series, UBC Faculty of Medicine. February 2021.

Neuroscience Colloquium, Djavad Mowafaghian Centre for Brain Health, The BC Brain Wellness Program, a research update. June 2021.

Public Talks and Presentations

Celebration of World Brain Day, BC Brain Wellness Program. "The impact of wellness activities on the brain". Vancouver, online, July 2020.

World PD Coalition: wellness approaches beyond medication. Presentation and Q&A on lifestyle interventions for wellbeing. Virtual event for patients and care partners (US and Canada), December 2020

Wellness Wednesday. "Recent advances in Nutrition and Microbiome Research - Parkinson's research at UBC." Vancouver, online, January 2021.

PPRI-Related Talks

"From microbes to movement - a systems approach to brain health." PPRI organized online event. September 2020.

Conference Presentations (National or International)

Metcalfe-Roach A, Cirstea M, Yu A, Golz E, Sundvick K, Kliger D, Finlay B, Appel-Cresswell S. Pet ownership associated with lower apathy and motor severity in female participants with PD. Virtual poster presentation. 24th International Congress of Parkinson's disease and Movement Disorders, September 2020

Metcalfe-Roach A, Cirstea M, Yu A, Golz E, Sundvick K, Kliger D, Finlay B, Appel-Cresswell S. Higher adherence to MIND diet associated with later onset of Parkinson's disease. Virtual poster presentation. 24th International Congress of Parkinson's disease and Movement Disorders, September 2020.

Dungate B, Yu A, Appel-Cresswell S. Sex differences in non-motor features of Parkinson's disease. Neuroscience Undergraduate Research Conference at UBC, Vancouver, January 2021.