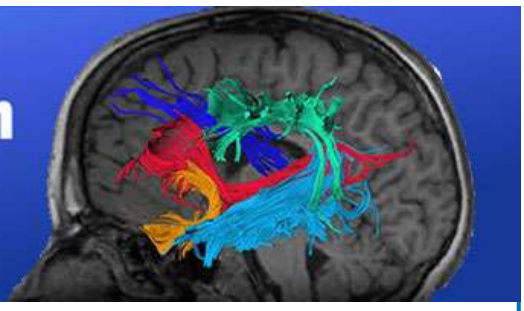
CCNA/CCNV Team 9 Bulletin

Biomarkers of Aging and Neurodegeneration
2020 Edition (Issue 2)



Greetings from CCNA/CCNV Team 9

This newsletter is a periodic publication from Team 9 of the Canadian Consortium on Neurodegeneration in Aging (CCNA). It is produced and distributed by the Biomarkers Team leads, Roger A. Dixon (Alberta) and Pierre Bellec (Montréal). In our previous newsletter we announced a new Team 9 partnership with Alberta Innovates and CIHR in the context of CCNA. The goal of this special 2020 issue is to announce a new opportunity for research collaborations related to this exciting new partnership. Specifically, we are building a network within Team 9 for development and application of a variety of neuroinformatics technologies in biomarker research. These quantitative modeling technologies include machine and deep learning, data-driven analytics, omics and multi-omics platforms, and selected artificial intelligence applications. This new network will share interests, compare data and approaches, and initiate new CCNA collaborations. Please see articles in this newsletter for more information. We thank Team 9 member Christian Beaulieu (Alberta) for the vivid diffusion MRI image in the banner.

Roger A. Dixon and Pierre Bellec

Salutations de l'équipe CCNA/CCNV 9

Ce bulletin est une publication périodique issue de l'équipe 9 du Consortium canadien sur la neurodégénérescence associée au vieillissement (CCNV). Celui-ci est produit et distribué par les directeurs de l'équipe de biomarqueurs, Roger A. Dixon (Alberta) et Pierre Bellec (Montréal). Dans notre publication précédente, nous avons annoncé un nouveau partenariat avec Alberta Innovates et les IRSC dans le cadre du CCNV. L'objectif de cette publication 2021 est d'annoncer une nouvelle opportunité pour des collaborations de recherche liées à ce nouveau partenariat. Plus précisément, nous construisons un réseau au sein de l'équipe 9 pour le développement et l'application d'une variété de technologies neuro-informatiques pour la recherche de biomarqueurs. Ces technologies de modélisation quantitative incluent l'apprentissage automatique et profond, l'analyse axée sur les données, les plateformes omiques et multi-omiques ainsi que certaines applications d'intelligence artificielle. Ce nouveau réseau nous permettra de partager des intérêts communs, de comparer les données et les approches et d'encourager de nouvelles collaborations CCNV. Veuillez consulter les articles dans ce bulletin pour de plus amples informations. Nous aimerions remercier Christian Beaulieu (Alberta), membre de l'équipe 9, pour nous avoir fourni l'image de l'IRM de diffusion affichée dans la bannière.

CIHR IRSC
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

ALBERTA INNOVATES

CCNA
Canadian Consortium on Neurodegeneration in Aging

CCNV
Consortium canadien en neurodégénérescence associée au vieillissement

Team 9: Developing a Network to Promote Neuroinformatics Applications to Biomarker Research in Aging and Neurodegenerative Disease

From its inception, the mission of the CCNA Biomarkers Team was to conduct multi-disciplinary research on aging and neurodegenerative disease that would accommodate a broad spectrum of biomarker domains and approaches. The team membership represents four major clusters of biomarker work: neuroimaging, neurobiological, neurocognitive, and neuroquantitative. Unlike some CCNA teams, we do not have a single theme or specific goal (such as an RCT or principal clinical cohort). Our diverse membership employs approaches such as preclinical, experimental (hypothesis-guided), and large-scale (data-driven, including untargeted omics and machine learning technologies). However, a key Phase I goal was to advance the latter approach, as data-driven modelling of multi-modal biomarker data sets (ADNI, CCNA) is a strength of a large subset of Team 9 members. Phase II began with the publication of a major Team 9 integrative review (connectomics, genomics, metabolomics) aimed at developing a machine-learning-based roadmap to biomarker detection and subtype discrimination.

A Continued Commitment to Diversity in Approaches to Biomarker Research

Team 9 continues to adhere to our four original goals: **(1) Coordinate** biomarker discovery and validation for multiple approaches, including multi-site data-driven and omics teams and individualized hypothesis-guided and mechanism-linked programs; **(2) Contribute** to core biomarker development in both neuroimaging (Platform 3) and biofluid-based neurobiological (Platform 4) modalities; **(3) Initiate** new synergistic and leveraging collaborations within and across CCNA teams, platforms and programs; and **(4) Promote** visibility, productivity, and functional participation in CCNA. **We currently have potential or active collaborations with**: Teams 7, 8, 12, 13, and 14; Platforms 3 and 4; and CCNA Programs WGSD (Women, Sex, Gender and Dementia) and ELSI (Ethical, Legal and Social Implications).

Team 9, Bridging From CCNA Phase I to Phase II

Team 9 is now funded by a unique partnership amongst Alberta Innovates, CIHR and CCNA, with fiduciary responsibilities shared by Baycrest Hospital (Toronto) and University of Alberta. The purpose of a generous investment by Alberta Innovates is to promote innovations in biomarker and subtype discovery, validation and translation in the field of aging and neurodegeneration. These innovations will be driven, in part, through the application and integration of Artificial Intelligence approaches, machine learning technologies, neuroinformatics modeling, and omics-based platforms. In Phase II, Team 9 will engage in capacity building and network enhancement in Alberta, Quebec and other provinces with interested Team 9 researchers. We are very interested in identifying Team 9 members and trainees who would like to learn more about or participate in the exciting new initiatives.
Please see next page for more information about getting involved.

Phase II: A New Partner and New Opportunities

Team 9 has partnered with CCNA, CIHR, and Alberta Innovates to pursue continuing and new research opportunities in Phase II. We thank many individuals in these organizations for their contributions. Special acknowledgments go to Drs. Howard Chertkow (CCNA Scientific Director) and Nathalie Bélanger (CCNA Chief Operating Officer), as well as Dr. Rajah Mita (Executive Director, Health Innovation, Alberta Innovates). Team 9 looks forward to promoting networking and innovation in biomarker-related discovery, validation and translation in aging and neurodegenerative diseases. The full acknowledgment is to Alberta Innovates, Ministry of Economic Development, Trade, and Tourism, Government of Alberta.

If You are Interested in the CCNA Team 9 Neuroinformatics Network (T9 NiNet)….

The **T9 NiNet** is being developed in order to promote, support, and integrate "neuroinformatics" approaches to biomarker research in aging and neurodegeneration. These approaches include a cluster of related quantitative modeling methods or platforms, often characterized as data-driven, machine learning, deep learning, or omics (multi-omics). We welcome expressions of interest from a broad range of Team 9 members, including:

(1) Those members or trainees who have little or no experience with such approaches, but want to learn more and perhaps explore the applicability in their own data or research;

(2) Those members or trainees who are experienced in the application of such approaches in their research, but would like to learn more or participate in possible new collaborations; and

(3) Those members or trainees who are already skilled in development or application of such technologies but want to stay current in CCNA and perhaps develop new techniques or collaborations.

In other words, any interested Team 9 member (or trainee) is welcome!

If you would like to join in building the T9 NiNet, please send an email to: rdixon@ualberta.ca. To get us started, please describe your background and interests in terms of the three categories above. We will contact you.

Some Recent Examples of T9 NiNet Research

Badhwar, A., McFall, G.P., Sapkota, S., Black, S., Chertkow, H., Duchesne, S., Masellis, M., Li, L., Dixon, R.A., & Bellec, P. (2020). *A multiomics approach to heterogeneity in Alzheimer's disease: Focused review and roadmap*. Brain, 143(5), 1315–1331. doi:10.1093/brain/awz384

Boukhdhir, A., Zhang, Y., Mignotte, M., & Bellec, P. (in press). *Unraveling reproducible dynamic states of individual brain functional parcellation*. Network Neuroscience. doi:10.1162/netn_a_00168

Han, W., Sapkota, S., Camicioli, R., Dixon, R.A., & Li, L. (2017). *Profiling novel metabolic biomarkers for Parkinson's disease using in-depth metabolomic analysis*. Movement Disorders, 32(12), 1720–1728. doi:10.1002/mds.27173

Iturria-Medina, Y., Carbonell, F.M., Evans, A.C., & ADNI (2018). *Multimodal imaging-based therapeutic fingerprints for optimizing personalized interventions: Application to neurodegeneration*. NeuroImage, 179, 40–50. doi:10.1016/j.neuroimage.2018.06.028

Feature: New Team 9 Member Dr. Josefina Maranzano

Josefina Maranzano, MD, PhD, spent the first 10 years of her career as a radiologist in industry, specializing in MRI acquisition protocols used to quantify normal or pathological brain structures, as well as lesions developed in multiple sclerosis (MS) and Alzheimer's disease (AD). From 2014 to 2018, she conducted PhD work in McGill's integrated neuroscience program. Her focus was on the underlying physical principles of MRI that are central to selecting adequate pulse-sequences targeting the quantification of specific lesions. She developed standardized multi-contrast MRI quantification protocols to assess cortical lesions in MS in 3T and 7T scanners. Since December 2018, she has been an Assistant Professor in the Department of Anatomy at the Université du Québec à Trois-Rivières and, since March 2019, an Adjunct Professor in the McGill Faculty of Medicine. She has recently launched a novel ex vivo, in situ method for MRI and histological brain assessment that allows a translation to pre-mortem MRI findings. This new method has the potential to advance our understanding of changes happening in the normal and pathological aging brain. We welcome Josefina as an important new member of CCNA Team 9 and Platform 3.

Maranzano, J., et al. (2020). *A novel ex vivo, in situ method to study the human brain through MRI and histology*. Journal of Neuroscience Methods, 345, 108903. doi:10.1016/j.jneumeth.2020.108903

News: Two Team 9 Workshops at CCNA 2020 Partners Forum and Science Day

Roger A. Dixon (Alberta) moderated a panel presentation and discussion on the topic: ***New Directions in Biomarker Research and Application in Alzheimer's Disease***. Four stellar CCNA biomarker researchers served as panelists: (1) Pedro Rosa-Neto (McGill), speaking on ***Biomarkers for Staging Pathophysiological Progression in Alzheimer's Disease***; (2) Mari DeMarco (UBC), speaking on ***Alzheimer's Disease CSF Testing in the Wild: The IMPACT-AD Study***; (3) Cheryl Wellington (UBC) speaking on ***Progress in Fluid Biomarkers for Neurodegenerative Diseases of Aging***; and (4) Yasser Iturria-Medina (McGill), speaking on ***The Importance of Multifactorial Disease Progression Modeling in Neurodegeneration***. The concise and informative talks were followed by a synchronous (and lively!) Q&A session. Thanks to Inbal Itzhak (CCNA Central) for expertly organizing the logistics.

Team 9 member, AmanPreet Badhwar moderated a CCNA Trainee panel entitled ***What is a biomarker?*** The biomarker potential of **gait** and **retinal thickness** were discussed by Frederico Pieruccini-Faria (Team 12 trainee) and Amin Banihashemi (Team 9 trainee), respectively. Subsequently, two data-driven approaches to biomarker research were presented. Linzy Bohn (Team 9 trainee) discussed **machine learning applications for early identification of frailty profiles**, and Désirée Lussier (Team 9 trainee) presented on **increasing the robustness and scalability of multisite resting-state functional MRI data**. Panel talks were followed by an energetic and insightful live discussion session with the CCNA community.

Left to right:
(Top) AmanPreet Badhwar, Linzy Bohn, Désirée Lussier;
(Bottom) Frederico Pieruccini-Faria, Amin Banihashemi.
Image courtesy of CCNA trainee Lauren Bechard.

Team 9 Members: Roger A. **Dixon** (Alberta), Pierre **Bellec** (Montréal), AmanPreet **Badhwar** (Montréal), Robert **Bartha** (Western), Christian **Beaulieu** (Alberta), Sandra **Black** (Sunnybrook), Richard **Camicioli** (Alberta), Mallar **Chakravarty** (McGill), Ting-Huei **Chen** (Laval), Howard **Chertkow** (McGill), D. Louis **Collins** (McGill), Mari **DeMarco** (UBC), Simon **Duchesne** (Laval), Alan **Evans** (McGill), Esther **Fujiwara** (Alberta), Scott **Hofer** (Victoria), Zahinoor **Ismail** (Calgary), Yasser **Iturria-Medina** (McGill), Liang **Li** (Alberta), Nikolai **Malykhin** (Alberta), Josefina **Maranzano** (Québec à Trois-Rivières), Mario **Masellis** (Sunnybrook), Joanne A. **Matsubara** (UBC), G. Peggy **McFall** (Alberta), Douglas **Munoz** (Queen's), Sridar **Narayanan** (McGill), Jacqueline **Pettersen** (UNBC), Marc J. **Poulin** (Calgary), Hyman **Schipper** (McGill), Eric **Smith** (Calgary), Peter **Stys** (Calgary), Sylvia **Villeneuve** (McGill), David **Westaway** (Alberta), David **Wishart** (Alberta).

Acknowledgment: Team 9 (Dixon and Bellec) acknowledges the support of the CCNA/CCNV through funding from CIHR in partnership with Alberta Innovates (Ministry of Economic Development, Trade, and Tourism, Government of Alberta). Pierre acknowledges support from the Courtois Foundation. Roger acknowledges leveraging with the NIH-funded Victoria Longitudinal Study and contributions from the SynAD Program (funded through a partnership with Alzheimer Society of Alberta and Northwest Territories and University Hospital Foundation). Thanks to Jill Friesen for editorial and technological assistance.