BIOGRAPHICAL SKETCH

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NAME: V. WEE YONG

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: PROFESSOR

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Manchester, UK	B.Sc.(Hons)	1981	Pharmacology
University of British Columbia, Vancouver, Canada	PhD	1986	Pharmacology and Neurochemistry
University of British Columbia, Vancouver, Canada	Post-doctoral fellowship	1988	Glial cell biology

A. Personal Statement

My research projects have been guided by extremes of immune dysfunctions: MS with chronic inflammation, and glioblastoma where the brain tumor suppresses the immune system, as lessons learned from these extremes can help each condition. I also study intracerebral hemorrhage where secondary neuroinflammation drives injury and recovery. Indeed, I recently highlighted the invariant occurrence of neuroinflammation across neurology, emphasizing commonalities but also important differences across several neurological disorders, with implications for treatment (Shi and Yong, Science 388:eadx0043, 2025). I have published >435 peer-reviewed manuscripts (Pubmed: Yong VW or Wee Yong V) that have been cited >36,800 times with a h-index of 110 (Web of Science); >47,800 citations in Google Scholar (h-index 122). I have also written 12 reviews in Nature Reviews series. I am Clarivate Web of Science Highly Cited Researcher (top 0.1%) in 2023, 2024 and 2025. I am a Highly ranked Scholar of ScholarGPS (top 0.05% of all scholars worldwide). My articles are cited over 3000 times a year the past 5 years (~3500 in 2025).

I am considered a leader in translational medicine, having taken laboratory findings of generic drug repurposing into eight clinical trials, including a Phase 3 trial in clinically isolated syndrome of MS (Metz et al., New Engl J Med 2017) and a Phase 2 trial in primary progressive MS (Koch et al., Ann Neurol 2021). I have mentored many trainees, including 35 who are now in professorial positions worldwide. My commitment to MS is not only in the form of research and translational medicine, and training, but also in the leadership of activities related to the MS agenda (see below).

B. Positions and Honors

1989 – 1994: Assistant Professor, Department of Neurology and Neurosurgery, McGill University, Canada
1994 – 1996: Associate Professor, Department of Neurology and Neurosurgery, McGill University, Canada
1996 – 2001: Associate Professor, Department of Clinical Neurosciences, University of Calgary, Canada
2001 – present: Professor, Department of Clinical Neurosciences, University of Calgary, Canada

2013 – 2024: Head, Division of Translational Neurosciences, University of Calgary, Canada
2009 – present: Director, Alberta MS Network

Honors:
Awardee, Queen Elizabeth II's Golden Jubilee Year Medallion, 2002
Canada Research Chair (Tier I) in Neuroimmunology, 2004 – 2018
Fellow of the Canadian Academy of Health Sciences, 2010
Order (highest honor) of the University of Calgary, 2014
Fellow of the Royal Society of Canada, 2014
Recipient, Allyn Taylor International Prize in Medicine, 2017
Profiled in Lancet Neurology, issue of August 2021
Recipient, Association of Faculties of Medicine Canada, inaugural Scientist Award, 2023

National/international leadership positions in MS:
Member, Research Priority Advisory Committee, National MS Society of the USA, 2007-2011
Chair, Medical Advisory Committee, Multiple Sclerosis Society of Canada, 2007 – 2011
President, International Society of Neuroimmunology, 2014 – 2016
Member, Program Committee, Department of Defense Congressionally Directed Multiple Sclerosis Research Program, USA, 2016 – 2021
Co-Coordinator, Americas and Global Schools of Neuroimmunology for the International Society of Neuroimmunology, 2015 – present
Member, Partnership Committee, ACTRIMS, 2018 – present
Member, Scientific Advisory Committee, OCTOPUS (Efficient Clinical Trials Platform of the United Kingdom MS Society), 2020 - present. This committee selects the treatments for trials in progressive MS
Chair, Restore session, Pathways to Cures meeting, New York City, May 2023
Member, Executive Board, ACTRIMS, 2022 – present
I am proud to be one of 10 international authors who are publishing the 5th Edition of McAlpine's Multiple Sclerosis aimed for June 2026; this textbook used to be the classic text book for MS but has largely been forgotten since the 4th edition was published in 2005. I am the primary author of the chapters on Immunology of MS, and Disease Modifying Therapies for MS (each about 100 pages, single line spacing); and the secondary author of the chapters on Neuropathology of MS, and Remyelination. The 10 authors for this book intended as the new textbook of MS are Coles A, Compston A, Dobson R, Jacobs B, Lassmann H, Lubetzki C, Rocca MA, Vucic S, Weinshenker B and Yong VW.

Consultancies for companies with strong portfolio in MS:
Roche, 2020 - current
Novartis, 2020 - current
EMD Serono, 2019 - 2023
Sanofi-Genzyme, 2019 - current
Teva Pharmaceuticals, 2005 - 2018

C. Contributions to Science

Basic science discoveries: I have contributed to many areas in the field of MS. My early work was on the neurobiology of the matrix metalloproteinases (MMPs) where we detailed not only their neurotoxic consequences, but also that discretely expressed MMPs serve important roles in remyelination. My collective MMP reviews helped to propel the field of MMPs in the CNS forward during its infancy (collective citations of >2500 for Yong et al., Trends Neuroscience 1998; Yong et al., Nature Reviews Neuroscience 2001; Yong, Nature Reviews Neuroscience 2005). Aligned with MMPs remodeling matrix, I took on the field of the neural extracellular matrix (ECM) in MS. This has generated new discoveries of a particular class of ECM, the chondroitin sulfate proteoglycans (CSPGs), as fibrotic inhibitors of myelin repair (Annals Neurology 2012; Nature Comm 2016; Nature Comm 2022; J Clin Invest 2024) and as drivers of cytotoxic neuroinflammation (Brain 2021, Nature Comm 2022; J Neuroinflammation 2025). These discoveries have led to the design of a

potential new class of therapeutics to reduce the production of CSPGs after injury, with outcomes of improved remyelination and functional recovery in models of MS and intracerebral hemorrhage (described in this proposal).

While I have contributed to the neurotoxicity of an uncontrolled inflammatory response in brain, my research also involves the opposite spectrum of harnessing the benefits of a properly controlled neuroinflammation for regeneration. I pioneered the use of niacin (vitamin B3) to promote microglia phagocytosis to remove debris and provide a CNS lesion microenvironment conducive for repair (Acta Neuropathologica 2020). I have also highlighted the niacin-rejuvenation of compromised microglia to block glioblastoma growth in mice (Science Translational Medicine 2020), a result that is now in human clinical trial (see below). Another group cites my lead in its recent description of niacin to promote microglial removal of amyloid beta to reduce plaque burden in Alzheimer's disease (Moutinho et al., Science Translational Medicine 14:eabl7634,March 2022).

My lab has continued to publish what we consider to be important basic science fundamentals, as highlighted by our recent identification of oxidized phosphatidylcholines as a novel class of neurotoxins in MS (Nature Neuroscience 2021), and the mechanisms by which the normally protective microglia go awry in MS and in aging (Neuron 2022, Nature Aging 2022). Ongoing basic science work includes defining the entire ECM proteome and functions in the consequential chronic active lesions in MS, the predominance of NOX2 amongst oxidative pathways in chronic active MS lesions and countering that with novel drugs, and overcoming iron-induced neurotoxicity that is increasingly recognized in MS.

Bench-to-bedside translation: I have the privilege of taking my lab findings into 8 clinical trials in collaboration with neurologists, neurosurgeons or oncologists. I have been the lead or co-lead in the successful grant applications to fund these trials. The items below list the publication(s) describing the original bench work from my lab, the resultant clinical trial, and the primary result if available.

1. **Minocycline in MS**: Lab primary data: *Brundula et al., Brain 125:1297, 2002.* Resultant clinical trials: *Metz et al., Ann Neurol 55:756, 2004 (Phase 1); Metz et al., New England J Medicine 376:2122, 2017 (Phase 3).* Primary outcome: Minocycline reduces relapses in early MS.
2. **Minocycline plus glatiramer acetate in MS**: Lab primary data: *Giuliani et al., J Neuroimmunol 165:83, 2005.* Resultant clinical trial: *Metz et al., Multiple Sclerosis J 15:1183, 2009 (Phase 2).* Primary result: Minocycline adds to the benefits of the leading medication for MS at the time, glatiramer acetate.
3. **Minocycline in traumatic spinal cord injury**: Lab primary data: *Wells et al., Brain 126:1628, 2003.* Resultant clinical trial: *Casha et al., Brain 135:1224, 2012 (Phase 2).* Primary result: Patients with cervical spinal cord injury regained significant improvement in motor outcomes over a one year assessment period when given high dose IV minocycline compared to placebo.
4. **Domperidone in secondary progressive MS**: Lab primary data (with the Sam Weiss lab): *Gregg et al., J Neurosci 27:1812, 2007*. Resultant clinical trial: *Koch et al., Neurol 96:e2313, 2021 (Phase 2).* Primary result: Domperidone is not useful in secondary progressive MS.
5. **Hydroxychloroquine in primary progressive MS**: Lab primary data: *Koch et al., J Neurol Sci 358:131, 2015.* Resultant clinical trial: *Koch et al., Neurol 90:940, 2021 (Phase 2).* Primary outcome: Hydroxychloroquine slows the expected progression of disability in the unmet need of primary progressive MS; this is currently short-listed by OCTOPUS UK to enter a Phase 3 trial.
6. **Combination of hydroxychloroquine and indapamide in non-relapsing secondary progressive MS**. Lab primary data: *Faissner et al., Nature Comm 8:1990, 2017* and *Brown et al., Neurotherapeutics 18:387, 2021.* Resultant clinical trial: Phase 2, NCT05013463, led by Dr. Marcus Koch (neurologist collaborator). The trial is stopped prematurely due to high rate of loss to followup.
7. **Domperidone in a randomized controlled pilot clinical trial to assess potential lesion repair in relapsing MS**. Lab primary data: *Gregg et al., J Neuroscience 27:1812, 2007.* Resultant clinical trial: NCT02493049, led by Dr. Luanne Metz. Primary result: The enrolled patients have better MRI indices suggestive of lesion repair with drug *(Zhang et al., MS Related Disorders 85:105525, 2024).*
8. **Niacin in glioblastoma**: Lab primary data: *Sarkar et al., Nature Neurosci 17:46, 2014* and *Science Translational Med 12 pii: eaay9924, 2020.* Resultant clinical trial: Ongoing (Phase 2, NCT04677049), led by Dr.

Gloria Urgoiti (oncologist collaborator). Interim results of 24 patients show that niacin on top of standard of care has increased the number of individuals with 6-month progression-free survival to 82.3%, compared to standard of care alone of 53.9% (*Roldan Urgoiti et al., J Neurooncol 176:101, 2025*).

D. Education: My top honor is the mentorship of the next generation of academic leaders. I have directly supervised and graduated 116 trainees from the lab, with 35 of them now in professorial positions worldwide. I currently mentor 4 fellows, 4 PhD students, 2 BSc thesis students and 3 technicians. Outside of my lab, I direct the Alberta MS Network that provides a rich training and collaboration environment on MS across Alberta. The network has ~80 researchers/clinicians and ~120 trainees at all levels (graduate students, residents, fellows).

I also mentor internationally. When President (2014-2016) of the International Society of Neuroimmunology (ISNI), and to ensure that the learnings of neuroimmunology reach a worldwide audience (then available only as the European School of Neuroimmunology), I started the Americas School of Neuroimmunology (ASNI) in 2015. I have co-directed and raised funds for all the biennial ASNIs: the first in 2015 (Calgary), the 2nd ASNI in 2017 (Charlottesville), the 3rd in 2019 (Montreal), the 4th in 2022 (Columbus), and the most recent ASNI in Toronto in July 2024. I collaborated (led ISNI) with the Japanese Society of Neuroimmunology to start the inaugural Asia-Pacific School of Neuroimmunology (APSNI) in Tokyo, Aug 2015; with the Korean MS and Encephalitis Societies to host the 2nd APSNI in Seoul, Nov 2019; with the Australian Neuroimmunology Society for the 3rd APSNI in Sydney in February 2023; and with Chinese Society of Immunology for the 4th APSNI in Beijing in Nov 2024. I am organizing the 5th APSNI in Fuzhou, China for Dec 3-6, 2026. As well, I inaugurated and have led the Global Schools of Neuroimmunology (GSNI) that occurs on the first day of the biennial ISNI Congress. The first GSNI was in Jerusalem (September 2016), the second in Brisbane (August 2018), the 3rd (originally scheduled to be held in Nice) was held virtually in Nov 2021, the 4th was in Quebec City (Aug 2023), and the recent 5th GSNI was in Chiba, Japan (October 2025). Information on these schools can be found at https://www.isniweb.org/schools. I consider mentorship my highest honor and achievement.

E. Presentations: I have been an invited keynote, seminar or workshop speaker at 150 **international conferences**. Examples from 2025 include:
Keynote Speaker, 2nd Meeting Latin America Glia Club, University of Buenos Aires, Argentina, April 7-9, 2025, on: The neural extracellular matrix as a modifier of neuroinflammation and remyelination
Chair and speaker, Consortium of MS Clinics, Phoenix, May 28-31, 2025, on: Biology of remyelination
Rita Levi-Montalcini Neurobiology lecturer, 17th International Congress of Neuroimmunology, Chiba, Japan, Oct 5-8 2025, on: The extracellular matrix of the brain
Speaker, 33rd European Charcot Foundation, Bovena Italy, November 13 - 15 2025, on: TREM2 modulation in neurology

I have also delivered **296 seminars at 250 top institutions** worldwide (not including several in Calgary). I have also been a featured speaker at **72 lay public events** on 'Advances in MS research and treatment', at 42 cities/towns in Canada and USA over the years

F. Selected senior-authored publications from 2020, from 137 published or in press (trainees underlined)

Rawji KS, Young A, Ghosh T, Michaels NJ, Mirzaei R, Mishra MK, Kappen J, Kohlemainen K, Pu A, Tang W, Zein S, Kaushik DK, Keough MB, Plemel J, Calvert F, Knights A, Gaffney D, Tetzlaff W, Franklin RJM, Yong VW, Niacin-mediated rejuvenation of macrophage/microglia enhances remyelination of the aging central nervous system, **Acta Neuropathol** 139:893-909, 2020

Dong Y, D'Mello C, Moezzi D, Lozinski B, Kaushik D, Ghorbanigazar S, Brown D, Melo FC, Vo T, Yong VW, Oxidized phosphatidylcholines in multiple sclerosis lesions mediate neurodegeneration and are neutralized by microglia, **Nature Neuroscience** 24:489-503, 2021

Ghorbani S, Yong VW, The extracellular matrix of lesions as modifier of neuroinflammation and remyelination in multiple sclerosis, **Brain** April 23:awab059, 2021

Koch MW, Kaur S, Sage K, Kim J, Levesque-Roy M, Cerchiaro G, Yong VW, Cutter GR, Metz LM, Hydroxychloroquine for Primary Progressive Multiple Sclerosis, **Annals Neurol** 90:940-948, 2021

Yong HYF, Yong VW, Mechanism-based criteria to improve therapeutic outcomes in progressive multiple sclerosis, **Nature Rev Neurol** 18:40-55, 2022

Ghorbani S, Jelinek E, Jain R, Buehner B, Li C, Lozinski B, Sarkar S, Kaushik DK, Dong Y, Wight TN, Karimi-Abdolrezaee S, Schenk GJ, Strijbis EM, Geurts J, Zhang P, Ling CC, Yong VW, Versican promotes T helper 17 cell cytotoxic inflammation and impedes oligodendrocyte precursor cell remyelination, **Nature Communications** 13:2445, 2022

Dong Y, Jain RW, D'Mello C, Lozinski B, Visser F, Ghorbani S, Zandee S, Brown DI, Prat A, Xue M, Yong VW, Single cell and spatial RNA sequencing identify perturbators of microglia functions with ageing, **Nature Aging** 2:508-525, 2022

Jain RW, Yong VW, B cells in central nervous system disease: Diversity, locations and pathophysiology, **Nature Rev Immunology** 22:513-524, 2022

Yong VW, Microglia in multiple sclerosis: Protectors turn destroyers, **Neuron** 110:3534, 2022

Kuhlmann T, Moccia M, Coetzee T, Cohen JA, Correale J, Graves J, Marrie RA, Montalban X, Yong VW, Thompson AJ, Reich DS, Time for a new mechanism-driven framework toward defining multiple sclerosis progression, **Lancet Neurol** 22:78-88, 2023

Ghorbani S, Li C, Lozinski BM, Moezzi D, D'Mello C, Dong Y, Visser F, Li H, Silva C, Xue M, Yong VW, Fibulin-2 is an extracellular matrix inhibitor of oligodendrocytes relevant to multiple sclerosis, **J Clinical Investigation** 134:e176910, 2024

Beddows CA, Shi F, Horton A, Dalal S, Zhang P Ling CC, Yong VW, Loh K, Cho E, Rose AJ, Montgomery MK, Packer N, Watt N, Parker BL, Brown R, Moh ESX, Dodd GT, Pathogenic hypothalamic extracellular matrix promotes metabolic disease, **Nature** 633:914-922, 2024

Li H, Ghorbani S, Oladosu O, Zhang P, Visser F, Dunn J, Zhang Y, Ling CC, Yong VW*, Xue M*, Therapeutic reduction of neurocan in murine intracerebral hemorrhage lesions promotes oligodendrogenesis and functional recovery, **J Neuroinflammation** 22:2, 2025 (*co-senior authors)

Wuerch E, Yong VW, Cholesterol in the CNS: Functions, recycling and remyelination, **J Neuroinflammation** 22:180, 2025

Shi FD, Yong VW, Neuroinflammation across neurological diseases, **Science** 388(6753):eadx0043, 2025

G. Selected pre-2020 manuscripts

Lau L, Keough MB, Haylock-Jacobs S, Cua R, Doring A, Sloka S, Stirling DP, Rivest S, Yong VW, Chondroitin sulfate proteoglycans in demyelinated lesions impair remyelination, **Annals Neurology** 72:419-432, 2012

Lau L, Cua R, Keough MB, Haylock-Jacob S, Yong VW, Pathophysiology of the brain extracellular matrix: A new target for remyelination, **Nature Rev Neuroscience** 14:722-729, 2013

Keough MB, Rogers JA, Zhang P, Jensen SK, Robertson E, Chen T, Hurlbert MG, Lau LW, Rawji KS, Plemel JR, Koch M, Ling CC, Yong VW, An inhibitor of chondroitin sulfate proteoglycan synthesis promotes central nervous system remyelination, **Nature Communications** 7:11312, 2016

Mishra MK, Yong VW, Myeloid cells: targets of medications in multiple sclerosis, **Nature Rev Neurology** 12:539-551, 2016

Plemel JR, Liu WQ, Yong VW, Remyelination therapies: a new direction and challenge in multiple sclerosis, **Nature Rev Drug Discovery** 16:617-634, 2017

Faissner S, Mishra M, Wang J, Fan Y, Silva C, Rauw G, Metz L, Koch M, Yong VW, Systematic screening of generic drugs for progressive multiple sclerosis: Clomipramine as a promising therapeutic, **Nature Communications** 8:1990, 2017

Stephenson E, Mishra M, Moussienko D, Yong VW, Chondroitin sulfate proteoglycans as novel drivers of leukocyte infiltration in multiple sclerosis, **Brain** 141:1094-1110, 2018

Faissner S, Plemel JR, Gold R, Yong VW, Progressive multiple sclerosis: from pathophysiology to therapeutic strategies, **Nature Rev Drug Discovery** 18:905-922, 2019

Kaushik DK, Bhattacharya A, Rawji KS, Mirzaei R, Ann Y, Rho JM, Yong VW, Enhanced glycolytic metabolism supports transmigration of brain-infiltrating macrophages in multiple sclerosis model, **J Clinical Investigation** 129:3277-3292, 2019