## **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

#### NAME: Monica J Carson

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

### POSITION TITLE: Professor of Biomedical Sciences

#### EDUCATION/TRAINING

| INSTITUTION AND LOCATION                     | DEGREE<br>(if applicable) | Completion<br>Date<br>MM/YYYY | FIELD OF STUDY    |
|--|---------------------------|-------------------------------|-------------------|
| Bryn Mawr College, Bryn Mawr, PA             | AB                        | 05/1982                       | Biology           |
| University of Pennsylvania, Philadelphia, PA | PhD                       | 10/1990                       | Biology           |
| The Scripps Research Institute, La Jolla CA  | Post-doctoral             | 11/1991                       | Neuropharmacology |
| The Scripps Research Institute, La Jolla CA  | Post-doctoral             | 06/1996                       | Molecular Biology |

### A. Personal Statement

The focus of my lab is defining the roles of microglia and macrophages during central nervous system (CNS) development, homeostasis and neuroinflammatory/neurodegenerative disease: To define CNS-specific immune responses, we contrast models of CNS inflammation, injury and autoimmunity with similar models in peripheral (non-immune privileged) sites. My lab and I have substantial expertise with *in vivo*, *ex vivo* and *in vitro* analysis of neuroinflammation, synaptogenesis, neuronal degeneration, gliosis and demyelination/remyelination. Using these techniques, we have coupled hypothesis-driven and discovery-driven approaches to demonstrate that microglia are truly a CNS-specific tissue macrophage specialized to maintain CNS function throughout our lifespan. We have further demonstrated that defects in microglial function can lead to devastating effects on brain development, homeostasis as well as the propensity for and progression of neurodegenerative disease. Using human IPSC derived microglia, we are currently using both discovery-based and hypothesis-based approaches to determine specific microglial functions and pathways that contribute to neurodegenerative disease susceptibility, severity and progression and that are modulated by environmental exposures.

<u>I have had a long-standing involvement in scientific education and mentorship</u>: Since my first faculty position at The Scripps Research Institute (TSRI), I participated each year in several programs aimed at fostering research opportunities for groups traditionally underrepresented in the sciences, including MARCU\*, CAMP, UC LEADS, MYBEST, UCR Medical Scholar's Program (MSP) and UCR Mentoring Summer Research Internship Program (MSRIP). I have provided mentorship and additional funding so that students working in my lab from these programs have been able to attend international, national as well as regional scientific conferences. I have pursued similar priorities in education and mentorship in my roles locally as Director of the Center for Glial-Neuronal Interactions & Chair of the Division of Biomedical Sciences as an officer, nationally as a council member for the American Society for Neurochemistry (2001-2005, 2007-2009) and Internationally as Secretary (2011-2015) and most recently as President (2015-2017) of the International Society for Neurochemistry (ISN). Lastly, for UCR's U54 grant supporting the Center for Health Disparities Research (HDR@UCR), I am the Director for the Investigator Development Core. I am responsible for guiding: (a) formation and function of multidisciplinary mentoring teams for Center Trainees, (b) work in progress seminar series fostering research related skills and interaction between multidisciplinary teams (trainees and mentors) (c) review and implementation of seed grants for trainees.

## B. Positions, Scientific Appointments and Honors Academic Appointments

Jun 1996 - Jul 1999: Senior Research Associate, Dept of Molecular Biology, The Scripps Research Institute Aug 1999 - April 2004: Assistant Professor, Dept of Molecular Biology, The Scripps Research Institute May 2004-Oct 2004: Associate Professor, Dept of Molecular Biology, The Scripps Research Institute Oct 2004 – June 2014: Associate Professor, Division of Biomedical Sciences, UC Riverside July 2014 - present: Full Professor, Division of Biomedical Sciences, UC Riverside School of Medicine July 2007 – June 2013: Director, Graduate Program in Biomed. Sci & Grad Advisor for Enrolled Students Jan 2007- present: Co-founder and Director, UC Riverside Center for Glial-Neuronal Interactions. July 2013-2014: UC Riverside School of Medicine, Interim Senior Associate Dean for Research July 2013-present: Chair, Division of Biomedical Sciences, UC Riverside School of Medicine February 2018-November 2019: Interim Chair, Dept of Social Medicine, Population and Public Health

## Honors and Awards:

Sigma Xi, Scientific Research Honor Society- 1982 (Associate Member) and current (Regular Full Member) National Multiple Sclerosis Society postdoctoral fellowship award, 1990-1993.

Dana Foundation Award in Neuroimmunology, 2007.

Outstanding Graduate Advisor and Mentor, 2010.

Faculty Mentor of the Year, UC Riverside Honors Program - 2015-2016

Distinguished Mentor, UCR MSRIP program (Inaugural Cohort of Faculty so named), 2019

S. Sue Johnson Presidential Endowed Chair in Glial-Neuronal Interactions, 2019

American Society for Neurochemistry - Bernard Haber Award, 2020

## Selected scientific service positions:

- American Society for Neurochemistry (ASN) Councilor, 2001-2005; ASN Program committee, 2002, 2003, 2005, 2006, 2008, 2009, 2016; ASN Scientific Program Chair for the 37th Annual ASN Meeting, 2006; Chair, ASN's Public policy, publicity and education committee, 2003-2006; ASN President 2007-2009, Chair of ASN Journal Liaison/Oversight committee 2009-2011;
- International Society for Neurochemistry (ISN), Councilor 2009-2011; ISN Secretary 2011-2015, ISN President 2015-2017; ISN Past-President 2017-2018, 2019-2021; Interim ISN President 2018-2019, Company Secretary (2021-present)

Member: Advisory Board, International Society for Neuroimmunology (ISNI), 2012-2016; Co-Chair & Co-Organizer: FASEB Summer Conference – "Translational Neuroimmunology", 2016 and 2018.

**Review boards:** Member: NIH CMBG study section 2007-2011. Member: NIH F03A fellowship review committee, 2003-2007; Member: National Multiple Sclerosis Society (NMSS) Fellowship advisory committee, 2004-2009; Member: AFAR's National Scientific Advisory Council, 2005-2009; Member: Neurobiology Keystone Symposia Study Group for the 2008 season; Member, NMSS Fast Forward Program, 2010-2011; Chair, NMSS pilot project review board, 2012-2014; Member: Race to Erase MS Scientific Advisory Board 2014-2020; Member, Brain Research Foundation, 2018-present.

## ad hoc reviewer (2000-current):

Multiple NIH study sections including BBBP, BDCN-5, DBD, IFCN-2; NINDS R15, RFA, ARRA, and SEP study sections. Alzheimer's Association, American Heart Association, Australian MS Society, Canadian Multiple Sclerosis Society; US Department of Veterans Affairs, Fondazione Telethon, Irish Scientific Review Board, Israel National Science foundation, Italian Multiple Sclerosis Society, Neuronal Ceroid Lipofuscinosis (Batten's Disease) foundation; UK Medical Research Council (MRC).

*Editorial boards:* Brain, Behavior and Immunity 2013-present; GLIA 2005-2019; Journal of Neuroinflammation 2007-present; Journal of Neuroscience Research 2008-2011; NeuronGliaBiology 2008-2012; Neurotherapeutics 2010-present;

<u>Associate Editor</u>, Journal of Immunology, 2011-2015, <u>Associate Editor</u>, Journal of Neuroscience, 2012-2018; <u>Associate Editor</u>, Journal of Neuroscience Research, 2011-2013; <u>Associate Editor</u> NCI 2007-2014 <u>Guest Editor</u>, Neurochemistry International (NCI), Special Issue on Cerebral inflammation, 2005; <u>Guest Editor</u>, NCI, Special Issue on Glia, Inflammation and Epilepsy, 2013; <u>Founding Senior Editor</u>, ASN Neuro 2008-2013; <u>Editor-in-Chief</u>, ASN Neuro 2013-2018; <u>Editor-in-chief</u>, Journal of Neuroinflammation 2018-present Co-Editor-in-Chief, Basic Neurochemistry: Principles of Molecular Cellular and Medical Neurobiology, 9<sup>th</sup> edition (2021-present)

*NIH Advisory Workshops:* Invited participant for the NINDS workshop on "Glial inflammation in HIV-1 Dementia and other chronic neurodegenerative diseases" 2003; Invited speaker: NIEHS advisory workshop

on: "The interplay between neurotoxins, CNS inflammation and CNS pan-developmental disorders with an emphasis on autism spectrum disorders" 2005; Invited speaker: NIDA advisory workshop on "HIV/neuroAIDS, glial inflammation, and drug abuse interactions" 2006; Invited Speaker: NIDA sponsored workshop on glial neuronal interactions in drug addiction, 2007; Ad Hoc Member "invited expert on neuroinflammation" for the NIAAA External Advisory Board, focus on Stress and Alcohol Relapse, 2009. Invited speaker: NEI sponsored workshop on "Immunity and Inflammation in the Anterior Segment of the Eye", 2021

# C. Contribution to Science

Since graduate school, my research has focused on the role of glia in brain development, healthy aging and neuroinflammatory disease (Highlights selected from >70 peer reviewed publications with google calculated H-index=41, i10-index=57, total citations >10,250)

- 1. Regulation of myelination and gliosis during injury and neuroinflammatory disease. Glial cells are highly plastic in their biology. Thus, many key in vivo functions are not fully replicated in vitro. At times when glia were primarily examined with in vitro model systems, we were early adopters of in vivo technologies and open profiling methods for quantifying ex vivo and in vivo glial gene expression. Using these approaches, we defined (a) specific in vivo roles of IGF-1 promoting myelination, (b) revealed that in vivo TNF by itself was NOT toxic to oligodendrocytes and myelin in several in vivo models of neuroinflammation and (c) revealed that infiltrating antigen-presenting cells upregulated myelin family molecules during myelin directed autoimmunity exacerbating disease progression.
  - **Carson MJ**, Behringer RR, Brinster RL, McMorris FA (1993) IGF-I increases brain growth and myelination in transgenic mice. *Neuron* 10:729-740. PMID:8386530
  - Stalder AK, Carson MJ, Pagenstecher A, Asenio VC, Kincaid C, Benedict M, Powell HC, Masliah E, Campbell IL (1998) Late onset chronic inflammatory encephalopathy in immunecompetent and severe combined immune-deficient (SCID) mice with astrocyte targeted expression of tumor necrosis factor-alpha. *Am. J. Pathol.* 153:767-783. PMCID: PMC1852999
  - Papenfuss TL, Thrash JC, Danielson PE, Foye PE, Hillbush BS, Sutcliffe JG, Whitacre CC, Carson, M.J. (2007) Induction of golli-MBP expression in CNS macrophages during acute LPSinduced CNS inflammation and experimental autoimmune encephalomyelitis (EAE). *The Scientific World Journal*. 7:112-120. PMCID: PMC2626137
  - Heneka M.T., **Carson M.J.**, et al. (2015) Neuroinflammation in Alzheimer's Disease. *Lancet Neurology* 14:388-405. PMCID: PMC5909703
- Microglia as a central nervous system (CNS) specific tissue macrophage. At the time, we initiated our studies, most groups used cell lines and/or cultured primary cells from neonates as model systems for in adult and aged microglial due to limitations in technology and models then available. By focusing on in vivo and ex vivo model systems at the launch of our studies, we found that microglia:
  → are molecularly and functionally distinct from CNS infiltrating macrophages (first to report microglia were the CNS resident cells expressing TREM2, mutations associated with cognitive disorders).
  → display heterogeneous phenotypes dependent on age, brain region and environmental cues that can be both adaptive and maladaptive in context dependent mechanisms. We also have used phenotypes identified in vivo to further develop human IPSC model systems predictive of in vivo biology.
  - **Carson MJ**, Reilly CR, Sutcliffe JG, Lo D (1998) Mature microglia resemble immature antigen presenting cells. *GLIA* 22:72-85. PMID:9436789
  - Schmid CD, Sautkulis LN, Danielson PE, Cooper J, Hasel KW, Hilbush BS, Sutcliffe JG and Carson MJ (2002) Heterogeneous expression of the Triggering Receptor Expressed on Myeloid cells-2 (TREM-2) on adult murine microglia. *J. Neurochem.* 83:1309-1320.PMCID:PMC2637869
  - Schmid CD, Melchior B, Masek K, Puntambeker SS, Danielson PE, Lo DD, Sutcliffe JG, Carson MJ (2009) Differential gene expression in LPS/IFNgamma activated microglia and macrophages: in vitro versus in vivo. *J Neurochem*. 109(s1):117-125. PMCID:PMC2766614
  - Abud EM, Ramirez RN, Martinez ES, Healy LM, Nguyen CHH, Newman SA, Yeromin AV, Scarfone VM, Marsh SE, Fimbres C, Caraway CA, Fote GM, Madany AM, Agrawal A, Kayed R, Gylys KH, Cahalan MD, Cummings BJ, Antel JP, Mortazavi A, **Carson MJ**, Poon WW, Blurton-Jones M (2017) IPSC-Derived Human Microglia-like Cells to Study Neurological Diseases. *Neuron* 94:278-293. PMCID: PMC5482419

- 3. **Microglia as Biosensors and Bioeffectors of CNS Health and Disease**. Using multiple models of brain injury and inflammation, we demonstrate how microglia serve as both biosensors and bioeffectors of brain function and brain disease.
  - Melchior B, Garcia AE, Hsiung B, Lo KM, Doose JM, Thrash JC, Stalder AK, Staufenbiel M, Neumann H, Carson MJ (2010). Dual induction of TREM2 and tolerance-related transcript, Tmem176b, in amyloid transgenic mice: implications for vaccine-based therapies for Alzheimer's disease. ASN NEURO. 2:157-170. PMCID: PMC2905103
  - Hernandez A, Donovan V, Grinberg YY, Obenaus A, Carson MJ (2016) Differential detection of impact site versus rotational site injury by MRI and microglial morphology in an unrestrained mild closed head injury model. *J. Neurochemistry* 136(s1) 18-28. PMID: 26806371 (recommended by Faculty of 1000) PMCID: PMC5047732
  - Peng E, Madany AM, Jang JC, Valdez JM, Rivas Z, Burr AC, Grinberg YY, Nordgren TM, Nair MG, Cocker D, Carson MJ\*, Lo DD (2018) Continuous inhalation exposure to fungal allergen particulates induces lung inflammation while reducing innate immune molecule expression in the brainstem. ASN NEURO 10:1-17 (\*corresponding author) PMCID: PMC6053578
  - Lainez NM, Jonak CF, Nair MG, Ethell IM, Wilson EH, Carson MJ, Coss D (2018) Diet-Induced Obesity Elicits Macrophage Infiltration and Reduction in Spine Density in the Hypothalami of Male but Not Female Mice. Frontiers in Immunology 9:1992 PMCID: PMC6141693
- 4. **Blood-Brain Interactions**. Using transgenic, knock-out and tissue specific/conditional expression in vivo models, we defined CNS-specific antigen-presentation, CCL21 and polyamine functions in regulating immune cell activation and influx from perivascular locations into the CNS parenchyma itself.
  - Carson MJ, Reilly CR, Sutcliffe JG, Lo D (1999) Disproportionate recruitment of CD8+ T cells into the CNS by professional antigen presenting cells. Am J Path 154:481-494. PMCID:PMC1850005
  - Ploix CC, Noor S, Crane J, Masek K, Carter W, Lo DD, Wilson EH, **Carson MJ**, (2011) CNSderived CCL21 is both sufficient to drive homeostatic T cell proliferation and necessary for efficient T cell migration into the CNS parenchyma following Toxoplasma gondii infection. *Brain, Behavior, and Immunity* **25**:883-96. PMCID:PMC3032828
  - Puntambekar SS, Davis DS, Hawel L, Crane J, Byus CV, **Carson MJ** (2011) LPS-induced CCL2 expression and macrophage influx into the murine central nervous system is polyamine-dependent. *Brain Behavior and Immunity* 25:629-639. PMCID:PMC3081407
  - McGovern KE, Nance JP, David CN, Harrison RES, Noor S, Worth D, Landrith TA, Obenaus A, Carson MJ, Morikis D, Wilson EH (2021) SPARC coordinates extracellular matrix remodeling and efficient recruitment and migration of antigen-specific T cells in the brain following infection. Scientific Reports 11: 1-11. PMCID: PMC7907143.

URL of Published Work: <u>https://scholar.google.com/citations?user=JTwlZCUAAAAJ&hl=en</u>