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# 1) Contact Information

Stephen E.P. Smith, PhD

JMB 1021, Center for Integrative Brain Research

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#### 2) Personal Data

Place of Birth: London, England

Citizenship: USA (naturalized) and United Kingdom

# 3) Education

1998-2002	BA, Cell and Molecular Biology, Occidental College, Los Angeles, CA
2002-2008	PhD, Biology, California Institute of Technology, Pasadena, CA

# 4) Postgraduate training

2008-2011	Harvard Medical School, Boston, M	ſΑ

Research Fellow, Neurology, Beth Israel Deaconess Medical Center

2011-2015 Mayo Clinic College of Medicine, Rochester, MN

Research Fellow, Immunology

### 5) Faculty Positions Held

2015-Present Assistant Professor, University of Washington School of Medicine, Department of

Pediatrics, (Division of Developmental Medicine) and Center for Integrative Brain

Research, Seattle Children's Research Institute

2015-Present Research Affiliate, Center for Human Development and Disease (CHDD)

2016-Present Faculty, Graduate Program in Neuroscience

# 6) Hospital Positions Held

N/A

#### 7) Honors

1999	Organic Chemistry Award, Occidental College
2002	Phi Beta Kappa Honors Society
2013	Mayo Fellows Association Poster Award
2013	American Association of Immunologists Trainee Travel Award
2015	Huntington's Disease Insights (HDI) "Insight of the Year in Imaging and Biomarkers"
2016	National Association for Research on Schizophrenia and Affective Disorders
	(NARSAD) Young Investigator Award

### 8) Board Certification

None

# 9) Current Licenses to Practice

None

# 10) Professional Organizations

2006-Present Member, Society for Neuroscience

2013-2014 Member, American Association of Immunologists2016-Present Member, International Society for Autism Research

# 11) Teaching Responsibilities

(a) Medical students and students in other health professions. UW Graduate Program in Neuroscience Graduate Students Devin Wehle 2018-, Emily Brown (co-Mentored with Horacio de la Iglesia) 2019-; UW Graduate Students Liza Severs rotated in the lab in 2017-2018. UW SOM student Mason Stillman completed his MSRTP summer project in the lab in 2018. UW undergraduates Andrew Chara, Andrew Ko, Pearl Woo, Ryan Mendel, Karen Immendorf, Noah Tashbook, Elizabeht Theirl and Shreya Patel have received credit for research conducted in my lab. Stanford undergraduate Kaleb Tsegay completed a URM Summer internship in 2019.

TABLE 1: UW SOM courses taught

Course	Title	Credits	Years	Students	Responsibility
MICROM 499A	Undergrad Lab Research	1-5	2016- 2017	2	Individual research advising (100%) – 13 credits total
PEDS 499A	Undergrad Lab Research	1-5	2016- 2020	4	Individual research advising (100%) – 25 credits total
MICROM 496B	Undergraduate Library Research	2	2016	1	Individual advising (100%) – 2 credits total
PBIO 508C	Physiology Lab	3	2017	1	Individual research advising (100%)
Neuro510	Neuroscience Seminar Series	0.5	2017	~20	Presented 1 seminar
PEDS 513	Scientific investigation in pediatric medicine	2	2018- 2020	~10	Present a seminar on lab's research focus
Oral Biology 575	Oral Biology Seminar Series	1	2018	~20	Presented 1 seminar on signal transduction
Path 558	Integrative Omics	1.5	2019- 2020	~20	Presented 1 seminar on Mass Spectrometry

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# (b) Pediatric residents:

None

# (c) Subspecialty fellows:

Mentorship for	Fellows (last 5 years)	
2015-2017	Alison Williams, PhD Role: Primary Research Mentor  Neurobiology/Neuroscience	
2017-	Jonathan Lautz, PhD Role: Primary Research Mentor	Neurobiology/Neuroscience
2018-	Devin Wehle Role: Primary PhD Mentor	UW Graduate Program in Neuroscience
2018-	Whitney Heavner, PhD Role: Primary Research Mentor	Neurobiology/Neuroscience
2019-	Emily Brown Role: Primary Research co- Mentor	UW Graduate Program in Neuroscience

### 12) Editorial Responsibilities

None

### 13) Special National Responsibilities

2016-Present Abstract reviewer for the Annual Meeting of the International Society for

Autism Research (INSAR)

2019-Present Member, INSAR programming committee

# 14) Special Local Responsibilities

2016-Present Mary Gates Scholarship reviewer

2016-2018 Thesis Committee Member: Phillip Silva (Neumeir lab); Rachel (YuChi) Chang

(Costa lab)

2017-Present Admissions Committee, UW Graduate Program in Neuroscience
2018-2019 PhD Quality of Life Committee, Seattle Children's Research Institute
2019-Present Capital Equipment Selection Committee, Seattle Children's Research

Institute

# 15) Research Funding

### **Current Support**

National Institute of Mental Health

R01 MH113545 (PI: Smith) 07/01/2017-06/30/2022 3 mos

\$2,933,139 Total Cost for Entire Project Period (including Indirect Costs)

\$268,158/yr Annual Direct Costs

Investigating the synaptic pathology of Autism

National Institute of Neurological Disorders and Stroke

R01 NS031224 (PI: Welsh) 09/30/2015-6/30/2020 1.5 mos

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\$3,386,090 Total Cost for Entire Project Period (including Indirect Costs)

\$351,072/yr Annual Direct Costs

Central Rhythmogenesis and Behavior

National Institute of Drug Abuse

R21 DA048632 (PI: Smith) 07/01/2019-06/30/2021

2.5 mos

\$514,854 Total Cost for Entire Project Period (including Indirect Costs)

\$150,000 (YR1)/\$125,000(YR2) Annual Direct Costs

Purification of cell-type specific synaptic material using virally-expressed tags

**National Cancer Institute** 

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1 R01 CA240985 (PI: Smith) 04/01/2020-03/31/2025

2.5 mos

\$3,168,260 Total Cost for Entire Project Period (including Indirect Costs)

\$321,821-388,095 Annual Direct Costs

Quantitative protein network profiling to improve CAR design and efficacy

National Institute of Mental Health

1 R01 MH121487 (PI: Smith) 07/09/2020-04/30/2022

2.5 mos

\$1,450,000 Total Cost for Entire Project Period (including Indirect Costs)

\$357,126-388,095 Annual Direct Costs

Subtyping the autisms using individualized protein network analysis

**Brotman Baty Institute** 

2019 Catalytic Collaborations granting program (PI: Yadev) 2/1/2020-1/21/2021 0.5 mos \$149,900 Total Cost for Entire Project Period (including Indirect Costs)

\$50,000 for Smith Lab

Unraveling mechanisms underlying brain overgrowth in 16p11.2CNV associated autism

Institute of Translational Health Services @ UW

2020 COVID Pilot Award (PI: Smith) 5/1/2020-11/30/2020

0.0 mos

0.0 mos

6.0 mos

\$2,500 Total Cost

Bead-based detection of SARS-COV-2 Antibodies and binding to ACE2

Seattle Children's Research Institute Integration Hub

2020 COVID Award (PI:Smith) 06/01/2020 - 5/31/2021

\$20,000 Total Cost

Repurposed drug screen for inhibiting SARS-COV-2 binding to ACE2

**Completed** 

Brain and Behavior Research Foundation (NARSAD Young investigator Award)

25037 (PI: Smith) 01/15/2017-01/14/2019 0.0 mos

\$70,000 Total Cost for Entire Project Period (including Indirect Costs)

\$35,000/yr Annual Direct Costs

Synaptic Homeostasis of the Homer1 Network in a Shank3 Model of Autism

National Institute of Mental Health

R00 MH102244-04 (PI: Smith) 08/01/2015-07/31/2018

\$733,611 Total Cost for Entire Project Period (including Indirect Costs)

\$126,784/yr Annual Direct Costs

Protein Interaction Network Analysis to Test the Synaptic Hypothesis of Autism

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Mayo Clinic Development Office

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Dana Center for Autism Research Award (PI: Smith) 7/1/2014-7/31/2015 0.0 mos

\$40,000 Total Cost for Entire Project Period (including Indirect Costs)

\$20,000/yr Annual Direct Costs

"Preclinical Investigation of Mouse Models of Autism and Autism with Self-Injury Behavior"

National Institute of Mental Health

F32 MH087085-01 (PI: Smith) 10/01/2009-10/01/2011 12.0 mos

\$100,000 Total Cost for Entire Project Period (including Indirect Costs)

\$50.000/vr Annual Direct Costs

"Characterization of Autism Susceptibility Genes on Chromosome 15q11-13."

National Alliance for Autism Research

Pre-doctoral fellowship (PI: Patterson) 1/1/2007-6/1/2008 12.0 mos

\$52,000 Total Cost for Entire Project Period (including Indirect Costs)

\$26,000/yr Annual Direct Costs

"The role of cytokines in mediating the effects of maternal immune activation on the fetal brain."

# 16) Bibliography

- a) Manuscripts in Refereed Journals
- \*1) **Smith SEP**, Li J, Garbett K, Mirnics K, Patterson PH. (2007) Maternal immune activation alters fetal brain development through interleukin-6. *J Neurosci* 27(40):10695-702. PMCID: PMC2387067
- 2) Shi L, **Smith SEP**, Malkova N, Tsu D, Patterson PH. (2009) Activation of the maternal immune system alters cerebellar development in the offspring. *Brain Behav Immun* 23(1):116-23. PMCID: PMC2614890
- 3) Zhou Y, Lee S, Jin Z, Wright M, **Smith SEP**, Anderson MP. (2009) Arrested maturation of excitatory synapses in autosomal dominant lateral temporal lobe epilepsy. *Nat Med* 15(10):1208-14. PMCID: PMC2759408
- 4) Ito HT, **Smith SEP**, Hsaio E, Patterson PH. (2010) Maternal immune activation alters nonspatial information processing in the hippocampus of the adult offspring. *Brain Behav Immun* 24(6):930-41. PMCID: PMC2897971
- \*5) **Smith SEP**, Zhou YD, Zhang G, Jin Z, Stoppel DC, Anderson MP. (2011) Increased gene dosage of Ube3a results in autism traits and decreased glutamate synaptic transmission in mice. *Sci Transl Med* 3(103):103RA97. PMCID: PMC3356696
- 6) **Smith SEP**, Xu L, Kasten M, Anderson MP. (2012) Mutant LGI1 inhibits seizure-induced trafficking of KV4.2 potassium channels. *J Neurochem* 120(4):611-21. PMCID: PMC3261618
- 7) **Smith SEP**, Elliott R, Anderson MP. (2012) Maternal immune activation causes increased thickness and increased cell density in the cortex of neonatal offspring. *J Neuroimmune Pharmacol* 7(3):529-32. PMCID: PMC3672058

- 8) **Smith SEP**, Bida AT, Davis TR, Sicotte H, Patterson SE, Gil D, Schrum AG. (2012) IP-FCM measures physiologic protein-protein interactions modulated by signal transduction and small-molecule drug inhibition. *PLoS ONE* 7(9): e45722. PMCID: PMC3448684
- 9) Neier S, **Smith SEP**, Davis T, Gil D, Schrum A. (2013) Toward T cell protein-protein interaction activity relevant to alopecia areata. *J Investig Dermatol Symp Proc* 2013 Dec; 16(1):S31-3. PMCID: PMC4109688
- 10) Bauman MD, Iosif A, **Smith SEP**, Bregere C, Amaral DG, Patterson PH. (2014) Activation of the maternal immune system during pregnancy alters behavioral development of rhesus monkey offspring. *Biol Psychiatry* Feb 15; 75(4):332-41. PMID: 24011823
- 11) **Smith SEP**, Neier S, Davis T, Pittelkow M, Gil D, Schrum A. (2014) Signaling protein complexes isolated from primary human skin-resident T cells can be analyzed by Multiplex IP-FCM. *Exp Dermatol* March 28; 23(4):272-3. PMCID: PMC4003868
- 12) Machado CJ, Whitaker A, **Smith SEP**, Patterson PH, Bauman MD. (2015) Maternal immune activation in nonhuman primates alters social attention in juvenile offspring. *Biol Psychiatry* May 1; 77(9):823-32. PMID: 25442006
- 13) Weir RK, Forghany R, **Smith SEP**, Patterson PH, McAllister AK, Schumann CM, Bauman MD. (2015) Preliminary evidence of neuropathology in nonhuman primates prenatally exposed to maternal immune activation. *Brain Behav Immun* 48:139-46. PMID: 25816799
- 14) Southwell AL\*\*, **Smith SEP\*\***, Davis TR, Caron NS, Villanueva EB, Xie Y, Collins JA, Li Ye M, Sturrock A1, Leavitt BR, Schrum AG, Hayden MR. (2015) Ultrasensitive measurement of huntingtin protein in cerebrospinal fluid demonstrates increase with Huntington disease stage and decrease following brain huntingtin suppression. *Sci Rep* 5:12166. doi: 10.1038/srep12166. \*\*Co-first and co-corresponding authorship
- 15) **Smith SEP,** Maus RLG, Davis TR, Sundberg JP, Gil D and Schrum AG. (2016) Maternal IL-6 can cause T cell-mediated juvenile alopecia by non-scarring follicular dystrophy in mice. *Exp Derm* 25(3):223-8. DOI: 10.1111/exd.12914
- \*16) **Smith SEP**, Neier SC, Reed BK, Davis TR, Sinnwell JP, Eckel-Passow JE, Sciallis GF, Wieland CN, Torgerson RR, Gil D, Neuhauser C, Schrum AG. (2016) Multiplex matrix network analysis of protein complexes in the human TCR signalosome. *Sci Signal* 9(439):rs7. PMID: 27485017
- \*17) Lautz JD, Brown EA, VanSchoiack AAW, **Smith SEP**. (2018) Synaptic activity induces input-specific rearrangements in a targeted synaptic protein interaction network. *J Neurochem* 146: 540-559. PMID: 29804286
- \*18) Brown, EA, Lautz JD, Davis TR, Gniffke EP, VanSchoiack AAW, Neier SC, Tashbook N, Nicolini C, Fahnestock M, Schrum AG, **Smith SEP**. (2018) Clustering the autisms using glutamate synapse protein interaction networks from cortical and hippocampal tissue of seven animal models. *Mol Autism* 9:48. PMID: 30237867
- 19) Stratiievska A, Nelson S, Senning EN, Lautz JD, **Smith SEP**, Gordon SE. (2018) Reciprocal regulation among TRPV1 channels and phosphoinositide 3-kinase in response to nerve growth factor. eLife 7:e38869. PMID: 30560783

- 21) Neier SC\*\*, Wilton KM\*\*, Ferrer A\*\*, **Smith SEP\*\***, Kelcher AMH, Davis TR, Stiles RJ, Chen Z, McCluskey J, Burrows SR, Rossjohn J, Hebrink DM, Carmona EM, Limper AH, Kappes DJ, Wettstein PJ, Johnson AJ, Daniels MA, Neuhauser C, Gil D, and Schrum AG. (2019) The proximal  $\alpha\beta$  TCR signalosome instructs thymic selection through a quantitative protein interaction network. *Sci Immunol* 4(29):eaal2201, 15 February 2019. \*\*co-co-co-first authorship. PMID: 30770409
- 21) Li F, **Smith SEP**, Kim W. (2018) VIA-QMI: A visualized data analytic tool for Quantitative Multiplex Co-Immunoprecipitation (QMI) Platform. *IEEE BIBM 2018 Workshop Papers*. November 2018, DOI: 10.1109/BIBM.2018.8621312
- 22) Lautz JD, Gniffke EP, Brown EA, Immendorf KB, Mendel RD, **Smith SEP.** (2019). Activity-dependent changes in synaptic protein complex composition are consistent in different detergents despite differential solubility. *Sci Rep* 9:10890. doi:10.1038/s41598-019-46690-y. PMID: 31350430
- 23) Brown EA, Neier SC, Neuhauser C, Schrum AG, **Smith SEP.** (2019). Quantification of Protein Interaction Network Dynamics using Multiplexed Co-Immunoprecipitation. *J Vis Exp* (150): e60029. doi: 10.3791/60029 PMID: 31498315
- 24) Heavner WE and **SEP Smith**. (2020) Resolving the Synaptic vs. Developmental Dichotomy among Autism Risk Genes. *Trends in Neuroscience,* Apr;43(4):227-241. doi: 10.1016/j.tins.2020.01.009. PMID: 32209454
- 25) Gniffke EP, Harrington WE, Dambrauskas N, Jiang Y, Trakhimets O, VigdorovichV, Frenkel L, Sather DN, **Smith SEP** (2020) Plasma from recovered COVID19 subjects inhibits spike protein binding to ACE2 in a microsphere-based inhibition assay. *Journal of Infectious Disease*. Online preprint.

#### b) Book Chapters

- 1) Patterson PH, Xu W, **Smith SEP** and Deverman BE. (2007) Maternal immune activation, cytokines and autism. In "Autism: Current Theories and Evidence", Zimmerman AW (ed), Humana Press, Totowa, NJ.
- 2) **Smith SEP**, Patterson PH. (2008) Immune challenge, neurodevelopment and behavior. In "The Neuroimmunological Basis of Behavior and Mental Disorders", Siegel A and Zalcman SS (eds), Springer, Norwell, MA.
- 3) **Smith SEP**, Hsiao E and Patterson PH. (2010) Activation of the Maternal Immune System as a Risk Factor for Neuropsychiatric Disorders. In "Maternal Influences on Fetal Neurodevelopment", Zimmerman AW and Connors SL (eds), Springer, Norwell, MA.
- c) Published Books, Videos, Software, ect. None
- <u>d) Other Publications</u> None
- e) Manuscripts Submitted

- 1) Heavner WE, Speed H, Lautz JD, Gniffke EP, Immendorf KB, Welsh JP, **Smith SEP** (2020) Homeostatic Plasticity Requires Remodeling of the Homer-Shank Interactome. *BioArxiv pre-print*, currently undergoing peer review. doi: https://doi.org/10.1101/2020.03.26.010314
- f) Abstracts (for the last 5 years only)

# **Symposium Presentations**

- 1) Williams AA, Brown EA, **Smith SE**. (2016) Activity-dependent interactions among Autism candidate-gene products at glutamatergic synapses. Society for Neuroscience Meeting, San Diego, CA. Presenter: A Williams. Nov 11-16, 2016
- 2) Lautz JD, **Smith SEP**. (2018) Synaptic activity induces input-specific rearrangements in a targeted synaptic protein interaction network. Meeting of the International and American Societies for Neurochemistry (ASN/ISN), Montreal, Canada. Presenter: J Lautz. August 4-8, 2019. Note: Award talk for the 2018 Mark A Smith prize for best paper in *J Neurochem* (Lautz 2018)
- 3) **Smith SEP** (2020) Gene and Protein Networks in Autism and Schizophrenia. Winter Brain Meeting, Big Sky, MO. Session Chair and Presenter: S Smith. Jan 25-30, 2020

#### **Poster Presentations**

- 1) **Smith SEP**, Neier SC, Davis TR, Schrum AG. (2015) Synaptic Protein Interaction Network Disruptions Suggest Convergence Among Autism Mouse Models. International Meeting for Autism Research, Salt Lake City, UT. Presenter: SEP Smith. May 13-16, 2015
- 2) Williams AA, Brown EA, Neier SC, Schrum AG, **Smith SEP**. (2016) Synaptic protein interaction network analysis of seven autism mouse models. Society for Neuroscience Meeting, San Diego, CA. Presenter: A Williams. Nov 11-16, 2016
- 3) **Smith SEP.** (2017) Autism-Linked Gene Products Form an Activity-Dependent Signaling Network at the Synapse. International meeting for Autism Research, San Francisco, CA. Presenter: S Smith. May 10-13, 2017
- 4) **Smith SEP,** Schrum AG. (2018) Quantitative Multiplex co-Immunoprecipitation of the T cell Receptor Signalosome: Translation to the CAR T cell system. Keystone Meeting on Emerging Cellular Therapies: T Cells and Beyond. Presenter: S Smith. Feb 11-15, 2018
- 5) Lautz J, Brown E, **Smith SEP**. (2018) Quantitative Multiplex co-Immunoprecipitation reveals basic principals of glutamate signaling in cultured cortical neurons. Winter Quantitative Biology Meeting, Maui, HI. Presenter: S Smith. Feb 22-25, 2018
- 6) **Smith SEP.** (2018) An Autism-Associated Signaling Network Differentiates Glutamate Receptor Inputs at Cortical Glutamatergic Synapses. International meeting for Autism Research, Rotterdam, Netherlands. Presenter: S Smith. May 9-12, 2018
- 7) Lautz JD, Brown EA, Williams AA, **Smith SEP.** (2018) Synaptically localized autism-linked gene products constitute an activity-dependent signalosome. Gordon Research Conference of Convergence in Autism and Fragile X, Tuscany, Italy. Presenter: S Smith. June 10-15, 2018

- 8) Lautz JD, Brown EA, Gniffke E, **Smith SEP.** (2018) Multiprotein complexes containing synapse-associated proteins are differentially sensitive to lysis buffer detergent. Society for Neuroscience Annual Meeting, San Diego, CA. Presenter: S Smith. November 3-7, 2018
- 9) Lautz JD, **Smith SEP.** (2019) Synaptic protein interaction networks states following in vitro stimulation with receptor agonists or chemical LTP/LTD. Gordon Research Conference on Excitatory Synapses and Brain Function, Manchester, NH. Presenter: S Smith. June 9-14, 2019
- 10) Bjelajac J, Wilson A, Gustafson J, Matthaei J, Jensen M, **Smith SEP.** (2020) Comparing signal transduction downstream of TCR vs. CAR engagement. Keystone meeting on Emerging Cellular Therapies: Cancer and Beyond, Banff, Canada. Presenter: S Smith. Feb 8-12, 2020.

# 17) Other

#### <u>Invited lectures</u>

<u>Local</u>	
4/29/16	Invited Speaker, "Clustering the Autisms using synaptic protein interaction networks", The CHDD Biology of Autism Collaborative Research Area (CRA) Special Event, Seattle, WA
8/4/16	Grand Rounds, "Autism and the Molecular Biology of the Social Brain", UW Dept of Pediatrics, Seattle, WA
9/26/16	Invited Speaker, "Modeling an Autism-linked intracellular signal transduction network", 2016 UW Neuroscience Retreat, Seattle, WA
12/4/16	Grand Rounds, "Autism as a Signalopathy", Seattle Children's Hospital Autism Center, Seattle, WA
10/9/17	Invited Speaker, "Synaptic Signal Transduction and Autism", 2017-2018 Neuroscience Seminar Series: Neuro 510, Seattle, WA
10/15/18	Invited Speaker, "A Protein Network Approach to Modeling Complex Biological Processes", 2018 Oral Biology Seminar Series, Seattle, WA
11/29/18	Invited Speaker, "Subtyping the Autisms using Protein Networks at the Glutamate Synapse". Science Insights at the Institute series, Seattle Children's Research Institute, Seattle, WA
8/8/19	Invited Speaker, "Clustering the Autisms: Can iPS cells provide biologically relevant material for a bioassay?". Stem Cell Interest Group, Institute for Stem Cell and Regenerative Medicine (ISCRM), University of Washington, Seattle, WA
<u>National</u>	
10/23/15	Invited Speaker, "Immunoprecipitation-Flow Cytometry measures huntingtin protein in human CSF", Huntington Study Group, Tampa, FL, USA.
2/16/16	Invited Speaker, "Clustering the Autisms using synaptic protein interaction networks",

Psychiatric Research Society, Park City, UT, USA.

2/19/19 Plenary Speaker, "The Thought Process of Cells: Direct measurement of signal transduction network states demonstrate mechanisms by which cells encode stimulus-specific information", Winter Quantitative Biology, Honolulu, HI, USA.

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- 3/16/19 Invited Speaker, "Convergence Among the Autisms: Characterizing a synaptic signal transduction network composed of the protein products of autism-linked genes", World Congress of Society for Brain Mapping and Therapeutics 16th Annual Conference, Los Angeles, CA, USA.
- 2/20/20 Plenary Speaker, "Sorting Signal from Noise in Signal Transduction Networks", Winter Quantitative Biology, Kailua-Kona, HI, USA.

# <u>International</u>

- 3/27/14 Invited speaker, "Towards biochemical analysis of primary T cell signaling in Alopecia areata using multiplex IP-FCM" 9th International Congress on Autoimmunity, Nice, France.
- 10/2/15 Invited Speaker, "Signal Transduction Networks at the Immune and Neuronal Synapse", UBC "TGIF" Lecture Series, Victoria, BC, Canada