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TITLE: TSC Regulates Oligodendroglial Differentiation and Myelination in the CNS

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14. ABSTRACT The basis of the proposed research is to investigate a novel idea that some of the underlying cause of brain abnormalities in TSC is due to disruption of the oligodendrocytes and production of the myelin wrapping; this in turn leads to alterations in the neurons and their ability to signal properly to other neurons. Proper communication between the oligodendrocytes and the axons is necessary for normal brain development. The oligodendrocytes receive signals from the axons to initiate myelination and to wrap the axon properly. In turn, the formation of the myelin wrapping allows communication between neurons and refinement of neuronal and brain function during development. Data accumulating from these studies indicate that disruption of TSC in primary rat oligodendrocyte progenitors in vitro alters the differentiation and myelination program in these cells. The altered development of the myelin-producing cells may interfere with the ability of the neurons to develop and function normally.					
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INTRODUCTION:

Tuberous sclerosis complex (TSC) syndrome causes dysplastic and disorganized overgrowth within many organs including the brain. Most TSC patients exhibit various neurological disorders, however, the underlying mechanisms for these disorders in TSC remain largely unknown. The TSC1-TSC2 (hamartin-tuberin) complex is a critical negative regulator of the mammalian target of rapamycin (mTOR) signaling pathway through its GAP (GTPase-activating protein) activity towards the small G-protein Rheb. Our recent data strongly support the hypothesis that mTOR signaling is essential for differentiation of oligodendrocytes (OLs), the myelin producing cells of the central nervous system (CNS). To date, investigations of TSC syndrome in the CNS have focused on neuronal populations. Based on our new data, we hypothesize that TSC loss of function mutations also result in over-activation of mTOR in OLs leading to abnormal OL numbers and myelination. Dysregulation of mTOR in OLs could have a dramatic effect on neuronal function and could contribute to the neurological phenotypes observed in TSC. In support of this hypothesis, studies are emerging suggesting a role for abnormal myelination in a variety of neurological disorders including autism. *The goal of the proposed project is to test the novel hypothesis that dysregulation of OL differentiation and myelination contributes to the phenotype of TSC in the CNS.*

BODY: Progress Report according to SOW as proposed

Aim 1: Test whether knockdown of TSC in OPCs in vitro accelerates OL differentiation and myelination.

Task 1. Approval for IACUC protocols (timeframe, 0-1 months)

1a. IACUC approval for animal experiments with primary rat OPCs and DRGs in vitro for aim 1. Dr. Wood has written successful IACUC protocols in the past for primary rat neural cells including extensive studies on rat OPCs. This approval will be initiated prior to the award. Timeframe = months 0-1.

Milestone #1 Animal Use approval for in vitro studies on rat neural cells

Progress: Approval for animal use for in vitro studies on rat neural cells was obtained originally in September, 2009. The renewal for this protocol was obtained in September 2010.

1b. Institutional approval for use of lentiviral vectors in Wood laboratory for use in rat OPC cultures. The Wood laboratory currently has approval for use of adenoviral vectors in cultured rodent cells. This approval will be initiated prior to the award. Timeframe = months 0-1.

Milestone #2 Biohazard approval for use of lentiviral vectors in rat neural cells in vitro.

Progress: Approval for use of lentiviral vectors in rat neural cells in vitro was obtained originally in November, 2009 and renewed April, 2011.

Task 2. siRNA knockdown of TSC1 in primary rat OPCs (timeframe, 3-9 months)

2a. Test timecourse for efficient siRNA knockdown of TSC1 using siRNA knockdown. Perform electroporation of primary rat OPCs and test for reduction of siRNA target (TSC1) by Western immunoblotting at 24, 36, 48, 72 hrs. 4 litters (10-12 pups/litter) of postnatal day 1-2 rats. Timeframe = months 2-3.

Milestone #3 Establish time and level of siRNA knockdown.

Progress: Knockdown of TSC1 has been performed on primary rat OPCs in three separate experiments. In two of three experiments, we established that the knockdown of TSC is optimal at 24-48 hrs with recovery of TSC protein levels apparent by 72 hrs (Figure 1A,B). One representative experiment is shown in Figure 1. In the third experiment, the level of transfection of the siRNA appeared low due to reduced cell viability so knockdown of TSC was not observed. Thus, this experiment was not used for further analysis of targets.

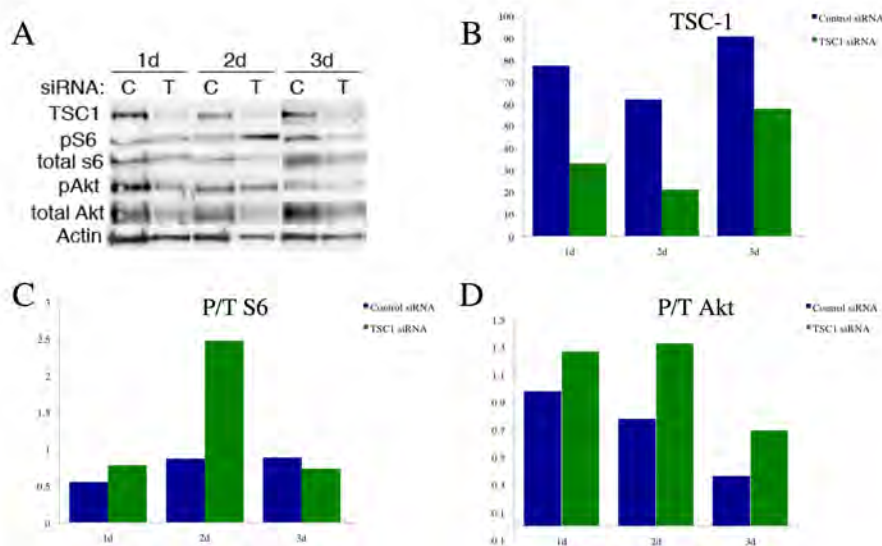


Figure 1. siRNA mediated knockdown of TSC1. **A.** Western immunoblot analysis of siRNA knockdown of TSC1, phospho-S6, total S6, phospho-Akt, total Akt, and β-actin during differentiation of primary oligodendrocytes. **B.** Quantification of TSC-1 normalized to β-actin. TSC-1 protein levels are reduced in TSC-1 siRNA treated OPCs relative to control at 1-3d. **C.** Quantification of phospho/total S6. Phospho-S6 levels are increased relative to total levels in TSC-1 siRNA treated samples at 2d. **D.** Quantification of phospho/total Akt. Phospho-Akt levels are increased relative to control at 1-3d in TSC-1 siRNA treated samples.

2b. Test effect of siRNA knockdown of TSC1 on phosphorylation of the TORC1 targets, S6K and/or 4EBP and TORC2 target, Akt (Ser 473) as well as expression of cleaved caspase-3 and Ki67 by Western blot analysis. OPCs will be electroporated, after 24 hr transferred to differentiation media and analyzed at 12, 24, 48 and 72 hr. 8 litters of postnatal day 1-2 rats. Timeframe = months 3-6.

Milestone #4 Determine whether knockdown of TSC alters activation of TORC1 and TORC2 targets and whether it alters proliferation or survival of OPCs.

Progress: Using samples from experiments where we verified knockdown of TSC1, we analyzed phosphorylation of mTORC1 or mTORC2 targets. We found that P/total-S6 was increased at day 2 consistent with TSC acting as an inhibitor of mTORC1 (Figure 1A,C). We also observed increased P/Total levels of Akt(ser473), a readout of mTORC2 activity (Figure 1A,D). This finding suggests that TSC acts to negatively inhibit both complexes. However, we also note that total levels of Akt are significantly decreased in the TSC knockdown cells which contributes to the increased ratio of P/total Akt levels. We are unclear at this time how this finding alters our model of TSC function in oligodendrocyte progenitors but will continue to monitor Akt levels in future experiments. Cleaved caspase 3 and Ki67 have not yet been analyzed in the TSC knockdown experiments.

2c. Test effect of siRNA knockdown of TSC1 on mTOR targets involved in OL differentiation and regulated at mRNA level, Id2, Id4, TCF4, MBP, PLP, by qPCR analysis. OPCs will be electroporated, after 24 hr transferred to differentiation media and analyzed at 24, 48, 72 and 96 hr. 8 litters of postnatal day 1-2 rats. Timeframe = months 6-9.

Milestone #5 Determine whether knockdown of TSC alters mRNA expression of genes involved in OL differentiation.

Progress: These experiments are planned for the next 2 months.

2d. Test effect of siRNA knockdown of TSC1 on mTOR targets involved in OL differentiation and regulated at protein level, Sirt2, beta4 tubulin, MBP, PLP, CNPase, by Western blot analysis. OPCs will be electroporated, after 24 hr transferred to differentiation media and analyzed at 24, 48, 72 and 96 hr. 8 litters of postnatal day 1-2 rats. Timeframe = months 6-9.

Milestone #6 Determine whether knockdown of TSC alters proteins induced during OL differentiation and regulated by mTOR.

Progress: We have initiated these studies using protein from experiments where we have verified sufficient TSC knockdown in OPCs. Analyses of MBP and Sirt2 protein levels indicate that both MBP and Sirt2 are decreased in TSC knockdown cells compared to control siRNA transfected cells (Figure 2). This result is very surprising and contradicts our model that knocking down TSC will promote oligodendrocyte differentiation and the myelination program. However, what is interesting is there is a significant response of the cells in terms of a differentiation program to knockdown of TSC supporting our hypothesis that TSC actions in the oligodendrocyte lineage may contribute to brain phenotypes in TSC mutations.

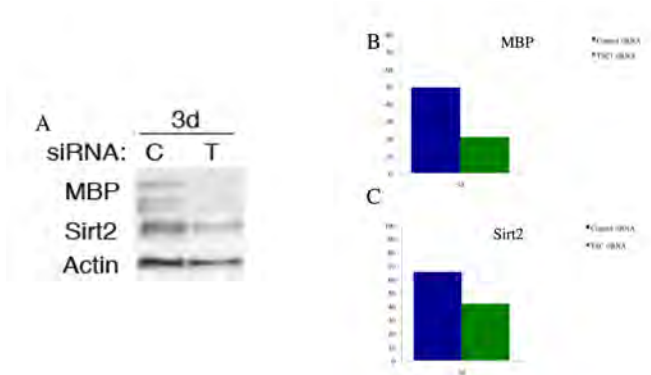


Figure 2. Effects of TSC-1 siRNA knockdown on MBP and Sirt2 protein expression. **A.** Western immunoblot analysis of MBP and Sirt2 at 3d of differentiation of primary oligodendrocytes. **B.** Quantification of MBP after TSC-1 knockdown at 3d. MBP is reduced in TSC-1 knockdown relative to control. **C.** Quantification of Sirt2 after TSC-1 knockdown at 3d. Sirt2 is reduced after TSC-1 knockdown relative to control.

2e. Test effect of siRNA knockdown of TSC1 on cellular markers of OL differentiation, A2B5, O4, GalC and PLP, by fluorescent immunostaining and morphologically for process outgrowth. OPCs will be electroporated, after 24 hr transferred to differentiation media and analyzed at 24, 48, 72 and 96 hr. 1 litter of postnatal day 1-2 rats. Timeframe = months 6-9.

Milestone #7 Determine whether knockdown of TSC alters cellular expression of markers of OL differentiation and of OL morphology.

Progress: These experiments are planned for the next period.

Task 3. Establish DRG-OPC co-cultures in the Wood laboratory (timeframe, 6-9 months)

3a. Establish isolation and culture of rat DRGs. We will work in collaboration with Dr. Kim, our collaborator at Rutgers University, Newark to establish the rat DRG cultures in our laboratory. 4 litters of prenatal rat pups. Timeframe = months 6-9.

Milestone #8 Establish technique to culture rat DRG neurons.

Progress: We have established isolation and culture of rat DRGs in the laboratory.

3b. Establish DRG-OPC co-cultures. We will work in collaboration with Dr. Kim, our collaborator at Rutgers University, Newark to establish the DRG-OPC myelinating co-cultures in our laboratory. Myelin will be analyzed by MBP and Dapi immunostaining. 2 litters of prenatal rat pups and 2 litters of postnatal rat pups. Timeframe = months 6-9.

Milestone #9 Establish myelination of DRG neurons by OPCs in vitro.

Progress: We have put these experiments as second priority and have focused on the in vivo mouse models as the best functional tests of TSC in oligodendroglia.

Task 4. Establish lentiviral shRNA knockdown of TSC1 in OPC (timeframe 9-12 months).

4a. Establish that lentiviral infection of OPCs results in knockdown of TSC1 and parameters of differentiation by Western blot analysis of TSC1, MBP at 24, 28, 72 and 96 hr after transduction. 4 litters of postnatal rat pups. Timeframe = months 9-12.

Milestone #10 Establish technique to knockdown TSC1 using lentiviral expression of shRNA.

Task 5. Test TSC1 knockdown on differentiation and myelination of OPCs co-cultured with DRGs (timeframe 12-15 months).

5a. Seed OPCs that carry the control or shRNA virus for TSC1. Numbers of O4+, MBP+ cells, myelin segments, and total cells (Dapi-positive) will be quantified by immunostaining on day 7 and day 18. These numbers will be obtained for the viral transduced (containing TurboRFP) or non-transduced cells. The ratio of O4+/Dapi+ cells and MBP+/Dapi+ cells for each group will be determined to assess OL differentiation. The ratio of myelin segments/ Dapi+ cells will be determined to assess the extent of myelination per field. 2 litters of prenatal rat pups, 2 litters of postnatal rat pups. Timeframe = months 12-15.

Milestone #11 Determine whether knockdown of TSC1 alters differentiation and myelination of OPCs co-cultured with DRGs.

5b. Determine cell survival and cell proliferation of OPCs in DRG co-cultures after transduction with control or TSC1 shRNA lentivirus. Co-cultures will be assayed at 7, 10, 14 and 18 d by IHC for active caspase 3 or Ki67, and co-stained for O4 or MBP to detect OPCs/OLs. 2 litters of prenatal rat pups and 2 litters of postnatal rat pups. Timeframe = months 12-15.

Milestone #12 Determine whether TSC1 knockdown alters proliferation of OPCs or survival of OPCs or OLs in co-cultures.

5c. Analyze myelination in co-cultures with knockdown of TSC1 in OPCs. Seed OPCs that carry the control or shRNA virus for TSC1. Cultures will be fixed, dehydrated, embedded in epon and semi-thin sections will be obtained and stained with toluidine blue on day 7 and day 18. The percentage of myelinated axons and the g-ratio will be determined. 2 litters of prenatal rat pups, 2 litters of postnatal rat pups. Timeframe = months 12-15.

Milestone #13 Determine whether knockdown of TSC1 alters amount and thickness of myelin in OPC-DRG co-cultures.

Progress Tasks 4-5: We have had some difficulty with growing lentiviruses in the laboratory and in infecting OPC cultures to maintain their viability. The standard reagents used for infection are toxic to the OPCs. We are currently consulting with colleagues who are experts in both viral vectors and primary OPC culturing. We have put these experiments as second priority and have focused on the in vivo mouse models as the best functional tests of TSC in oligodendroglia.

Aim 2: Test whether deletion of TSC in the OL lineage in vivo accelerates OL differentiation/myelination.

Task 6. Obtain IACUC approval, order mice and establish mouse lines for animal experiments with Aim 2 (timeframe 0-15 months).

6a. IACUC approval for transgenic mouse experiments for aim 2. Dr. Wood has written successful IACUC protocols in the past for primary rat neural cells including extensive studies on rat OPCs. This approval will be initiated prior to the award. Timeframe = months 0-3.

Milestone #14 Obtain IACUC approval for transgenic mouse experiments.

Progress: Approval for animal use for in vivo studies on transgenic mouse lines was obtained initially in September, 2009. The renewal for this protocol was obtained in September 2010.

6b. Order $Tsc1^{tm1Djk}/J$ and PLP-CreER^T mouse lines from Jax Laboratories and establish breeding colonies. Timeframe = months 3-12.

Milestone #15 Establish breeding colonies for experiments.

Progress: Both mouse lines were obtained and we have established breeding colonies.

6c. Test PLP-CreER^T-induced recombination in oligodendroglia in corpus callosum. Mate PLP-CreER^T and ROSA26 mouse lines, treat with tamoxifen by IP injection (1 mg tamoxifen in 100 μ l sunflower oil, daily for 5 days to the nursing dams or pups for post-weaning timepoints). We will administer tamoxifen at postnatal days 6-10, 11-15 and 16-20 in initial studies in order to delete mTOR at early, mid- or late stages of differentiation. Brains will be analyzed for LacZ and OL lineage by co-labeling for oligodendroglial markers (PDGFRA and NG2 for progenitors, CC1 for mature OLs). 3 animals per timepoint x 3 timepoints = 9 animals. Timeframe = months 9-15.

Milestone #16 Establish Cre-loxP deletion in oligodendroglia.

Progress: Initial analyses of bigenic lines following tamoxifen injection are planned for the next 2-3 months.

Task 7. Test in vivo deletion of TSC1 on OL differentiation and myelination (timeframe 12-24 months).

7a. Test loss of TSC1 using PLP-CreER^T-induced recombination in oligodendroglia in corpus callosum. Mate PLP-CreER^T and $Tsc1^{tm1Djk}/J$ mouse lines, treat with tamoxifen by IP injection (1 mg tamoxifen in 100 μ l sunflower oil, daily for 5 days to the nursing dams or pups for post-weaning timepoints). We will administer tamoxifen at postnatal days 6-10, 11-15 and 16-20 in order to delete mTOR at early, mid- or late stages of differentiation. We will assess OL lineage by immunolabeling for oligodendroglial markers (PDGFRA and NG2 for progenitors, CC1 for mature OLs) as well as cell proliferation (BrdU or Ki67) and cell death (TUNEL staining). Neurons will be labeled using NeuN. 8 animals per timepoint x 3 timepoints = 24 animals. Timeframe = months 12-18.

Milestone #17 Determine loss of TSC1 on OL differentiation in vivo.

7b. Test loss of TSC1 using PLP-CreER^T-induced recombination on myelination in corpus callosum. Mate PLP-CreER^T and *Tsc1*^{tm1Djk/J} mouse lines, treat with tamoxifen by IP injection (1 mg tamoxifen in 100 µl sunflower oil, daily for 5 days to the nursing dams or pups for post-weaning timepoints). We will administer tamoxifen at postnatal days 6-10, 11-15 and 16-20 in order to delete mTOR at early, mid- or late stages of differentiation. Brains will be fixed, dehydrated, embedded in epon and semi-thin sections will be obtained and stained with toluidine blue. The percentage of myelinated axons and the g-ratio will be determined. 8 animals per timepoint x 3 timepoints = 24 animals. Timeframe = months 12-18.

Milestone #18 Determine loss of TSC1 on myelination in vivo.

Progress: These analyses are proceeding on schedule for the next period.

KEY RESEARCH ACCOMPLISHMENTS:

- Established siRNA knockdown of TSC1 in primary rat OPCs in vitro.
- Determined that TSC is a critical upstream regulator of mTORC1 and mTORC2 in the oligodendrocyte lineage.
- Found that reduction of TSC1 results in increased activation of both mTORC1 and mTORC2 targets (P-S6 and P-Akt, respectively) in OPCs.
- Reduction of TSC1 in OPCs results in decreased expression of differentiation markers Sirt2 and MBP suggesting inhibition or delay of differentiation.
- Reduction of TSC1 in OPCs reduces total levels of Akt.

REPORTABLE OUTCOMES:

Abstracts and Presentations:

- Wood, T.L., Tyler, W.A., Jain, M.R., Cifelli, S.E., Mahajan, K., Li, Q., Ku, L., Feng, Y, and Li, H. Mechanisms for mTOR regulation of oligodendrocyte differentiation and myelination/remyelination. (2011) Symposium presentation - International Society for Neurochemistry, Athens, Greece.
- Cifelli, S.E., Tyler, W.A., Jain, M.R., Li, H. and Wood, T.L. mTOR-mediated regulation of oligodendrocyte differentiation (2011) Poster presentation – International Society for Neurochemistry, Athens, Greece.

CONCLUSION:

Our data obtained to date strongly support our hypothesis that TSC function in oligodendroglia is essential for their normal development and myelination functions. However, our data indicate that how TSC regulates mTOR signaling and the consequences of TSC disruption is more complicated than we originally proposed. Specifically, we anticipated that activation of the mTOR complexes by TSC deletion or reduction would result in accelerated oligodendrocyte differentiation and hypermyelination. Our findings indicate that the reduction in TSC is actually inhibiting oligodendrocyte differentiation. Our current interpretation of these findings is that mTOR complex signaling may be time-dependent and that sustained activation of the complexes inhibits the myelination program. We will continue to test our hypotheses through ongoing proposed studies with a particular focus on the in vivo transgenic mouse models. In vitro, we would like to extend our knockdown analyses to 4-5 days following siRNA transfection to determine if the differentiation is merely delayed and recovers. We also propose to focus on the in vivo deletion of TSC specifically in the oligodendrocyte lineage as proposed in Aim 2 as priority over the in vitro co-culture myelination studies.

“So what?”

Tuberous sclerosis complex (TSC) syndrome causes dysplastic and disorganized overgrowth within many organs including the brain. Most TSC patients exhibit various neurological disorders, however, the underlying mechanisms for these disorders in TSC remain largely unknown. To date, the focus of understanding brain dysfunction in TSC has focused on neurons. Based on our published data, we proposed to test the novel hypothesis that critical aspects of neurological dysfunction in TSC are due to disruption of differentiation and the production of myelin from the oligodendroglia. Our findings thus far support our hypothesis that TSC has essential functions in development of oligodendroglia, however, the exact function of TSC upstream of mTOR appears more complicated than we first proposed. These data strongly support continued analysis of TSC in regulation of this lineage.

REFERENCES:

Abstracts:

- 1) Wood, T.L., Tyler, W.A., Jain, M.R., Cifelli, S.E., Mahajan, K., Li, Q., Ku, L., Feng, Y, and Li, H. Mechanisms for mTOR regulation of oligodendrocyte differentiation and myelination/remyelination. *J. Neurochem.* 118 (Supp 1), p.87, 2011.
- 2) Cifelli, S.E., Tyler, W.A., Jain, M.R., Li, H. and Wood, T.L. mTOR-mediated regulation of oligodendrocyte differentiation. *J. Neurochem.* 118 (Supp. 1), p. 31, 2011.

APPENDICES:

Enclosed Appendices

- Wood et al., 2011, ISN Abstract
- Cifelli et al., 2011, ISN Abstract
- CV – T.L. Wood

SUPPORTING DATA: All figures and/or tables shall include legends and be clearly marked with figure/table numbers.

Figures included in text report.

S10-04

MECHANISMS FOR MTOR REGULATION OF OLIGODENDROCYTE DIFFERENTIATION & MYELINATION/REMYELINATIONWood, T. L.¹, Tyler, W. A.¹, Jain, M. R.², Cifelli, S. E.¹, Mahajan, K.¹, Li, Q.², Ku, L.³, Feng, Y.³ and Li, H.²¹New Jersey Medical School Cancer Center/UMDNJ, Dept. Neuroscience, Newark, NJ, USA²New Jersey Medical School Cancer Center/UMDNJ, Center for Advanced Proteomic Res, Dept. Biochem & Mol Biol, Newark, NJ, USA³Emory University School of Medicine, Dept. Pharmacology, Atlanta, GA, USA

Recent studies revealed that the mammalian target of rapamycin (mTOR) signaling pathway, a major target downstream of Akt, regulates oligodendrocyte differentiation/myelination (1, 2). The objectives of this study were i) to define the mTOR regulated proteome in differentiating oligodendrocyte progenitor cells (OPCs), and ii) to determine whether mTOR signaling is important for remyelination following a focal demyelinating injury. In order to define the mTOR regulated proteome, we applied an iTRAQ mass spectrometry-based proteomic approach. Among the 978 proteins

identified in this study, 328 (34%) exhibited a greater than 20% change ($p < 0.05$) in control versus rapamycin treated OPCs following 4 days of differentiation *in vitro*. Interestingly, 197 (20%) proteins were elevated in rapamycin treated cultures, while 131 (13%) proteins were down-regulated by rapamycin. Inhibiting mTOR decreased expression of myelin proteins, proteins involved in cholesterol and fatty acid synthesis, as well as many cytoskeletal proteins, cell signaling components, and nuclear/transcriptional regulators. Of particular interest was the identification of several critical mediators of oligodendrocyte differentiation including the pro-differentiation factors Fyn and Quaking. To address whether mTOR signaling is required for remyelination, we analyzed remyelination following a cortical focal demyelination in adult mice treated with either vehicle or the mTOR inhibitor rapamycin. Analysis of lesions revealed delayed remyelination at 21 days in the rapamycin-treated animals supporting the hypothesis that mTOR signaling is required for both developmental myelination as well as remyelination.

References:

1. Tyler et al. (2009). *J. Neurosci*, 29: 6367.
2. Narayanan et al. (2009). *J. Neurosci*, 29: 6860.

MO01-05

FUNCTIONAL MODULATION OF MICROGLIAL P2X4 RECEPTOR-CHANNELS BY UDP-ACTIVATED P2Y6 RECEPTORSBernier, L. P.¹, Ase, A. R.¹, Boue-Grabot, E.² and Seguela, P.¹¹*Montreal Neurological Institute, McGill University, Montreal, Canada*²*Universite Bordeaux Segalen, CNRS UMR 5293, Bordeaux, France*

P2X receptors are ATP-gated cation channels contributing to diverse physiological mechanisms including pain signalling and inflammatory response. The P2X4 subtype has been shown to be directly involved in microglial activation and central sensitization of nociceptive neurons, making its functional regulation a crucial process in chronic pain pathologies. The P2Y6 receptor is positively coupled to phospholipase C via Gq/11 proteins and is also expressed in microglia, where it plays a pivotal role in the initial response to nerve injury, triggering phagocytosis upon UDP-mediated activation. Interestingly, recent reports have shown that expression of both P2X4 and P2Y6 is upregulated in activated microglia following nerve injury. Here, we show that in primary mouse microglia, activation of P2Y6 modulates P2X4 function as P2Y6 activation by its agonist UDP induced a significant decrease in P2X4-mediated calcium entry. We recently observed that microglial P2X4 channels can dilate into a macropore upon prolonged ATP stimulation; this property was also inhibited by simultaneous activation of P2Y6 as measured via YO-PRO-1 uptake assay. We reproduced this modulation in the *Xenopus* oocyte expression system, where P2Y6 activation induced a decrease in P2X4 current amplitude, activation and desensitization rates, as well as an inhibition of P2X4 macropore formation. This interaction was blocked by U73122, a phospholipase C inhibitor, but was unaffected by blocking protein kinase C (PKC) with staurosporine. This suggests that the functional modulation of P2X4 relies on the hydrolysis of PI(4,5)P₂, a membrane-bound phosphoinositide recently shown to be a direct positive regulator of P2X4 channel function. These data indicate that metabotropic P2Y6 receptors can significantly affect both P2X4 current and macropore dilation, representing a novel cross-talk between purinoceptors in microglia. High extracellular levels of ATP and UDP are observed in conditions of nerve injury, therefore interactions between receptors sensitive to these agonists are critical in regulating pain-inducing microglial responses.

MO01-06

NITRIC OXIDE SYNTHASE III IS EXPRESSED IN HUMAN OLIGODENDROCYTESBoullerne, A. I.¹, Othman, A.¹, Frim, D. M.³, Polak, P.¹, Vujicic, S.¹, Dello Russo, C.⁴ and Arnason, B. G.²¹*Department of Anesthesiology, University of Illinois at Chicago, Chicago, USA*²*Department of Neurology, University of Chicago, Chicago, USA*³*Department of Surgery (Neurosurgery), University of Chicago, Chicago, USA*⁴*Institute of Pharmacology, Catholic Medical School, Rome, Italy*

Nitric Oxide Synthase III (NOS3, NOS-3, eNOS) has not been formerly characterized in oligodendrocyte, in contrast to the other NOS isoforms. We present converging data of NOS3 expression at the molecular and protein levels in primary culture of oligodendrocytes. NOS3 was detected at the protein level by immunocytochemistry, and

at the messenger level by quantitative PCR. We used antibodies from different companies that were strictly specific to NOS3 and did not recognize the other isoforms NOS1 (nNOS) and NOS2 (iNOS), as assessed by Western Blot. Immunostaining for NOS3 was found across species in human, rat and baboon primary oligodendrocyte cultures. NOS3 protein was found restricted to the cytoplasm, in the cell body and the thick processes branching out from the cell body. NOS3 was never present in the flat membrane extensions. NOS3 protein and mRNA were found at any time points during the 3 weeks culture necessary for human oligodendrocytes to regenerate large membranes expressing galactocerebroside, myelin basic protein (MBP) and myelin oligodendrocyte glycoprotein. NOS3 protein was found expressed early in the lineage in bipolar oligodendrocyte progenitors, and its expression was maintained at the mature stage of membrane-bearing human oligodendrocytes in long-term culture up to 2 months. NOS3 was also found in mouse oligospheres derived from E13 cells. NOS3 colocalized with caveolin-1, a protein bound to NOS3 and one of its main regulator in endothelial cells. Inhibition of NOS3 by the specific ligand N-[imino(methylamino)methyl]-L-ornithine (L-NMMA) led to a disruption of the organization pattern of MBP and the cytoskeleton component actin, that were accompanied by marked changes in oligodendrocyte arborization. NOS3 appears to be a signaling molecule for the cytoskeleton which is involved in intracellular trafficking, process extension and myelin production in oligodendrocytes.

MO01-07

MTOR-MEDIATED REGULATION OF OLIGODENDROCYTE DIFFERENTIATION

Cifelli, S. E., Tyler, W. A., Jain, M. R., Li, H. and Wood, T. L.

UMDNJ-NJMS, Newark, USA

Our previous study demonstrated that inhibition of mammalian target of rapamycin (mTOR), a downstream target of Akt, arrested oligodendrocyte differentiation at the O⁴⁺/GalC- late progenitor stage (Tyler et al., 2009). [[AUTHOR: Please provide full publication details for Tyler et al., 2009 in the reference list.]] Recent proteomic analysis revealed novel mTOR targets and a more complex picture of mTOR function in differentiating oligodendrocyte progenitor cells (OPCs). To further this analysis and search for direct targets of mTOR during oligodendrocyte differentiation we performed iTRAQ-MS analysis of protein samples isolated following 2d and 4d of differentiation in the presence or absence of rapamycin, an mTOR inhibitor. The changed proteins at 2d of differentiation, either increased or decreased in the presence of rapamycin, were further sorted based on molecular function. Cytoskeletal proteins represented the largest group downregulated by mTOR inhibition consistent with the hypothesis that mTOR regulates morphological complexity at the transition from the late progenitor to the immature oligodendrocyte. Proteins that were upregulated in the presence of rapamycin included those involved in regulating protein translation and translation initiation. As a major function of the mTOR/raptor complex is to positively regulate protein translation, the upregulation of translation factors in the presence of rapamycin suggests that the ability of mTOR signaling to finely tune the expression of specific transcripts via translational control plays a central role in regulating oligodendrocyte differentiation. Ongoing studies are directed towards validating identified targets in the mTOR-regulated proteome and elucidating direct nuclear targets of mTOR necessary for mediating oligodendrocyte differentiation.

CURRICULUM VITAE

Teresa L. Wood, Ph.D.

Present Address

Department of Neurology & Neurosciences
New Jersey Medical School/University of Medicine and Dentistry of New Jersey
University Hospital – Cancer Center H1200
205 S. Orange Avenue
Newark, NJ 07103
Phone: 973-972-6529

Education/Training

- 1974-1978 B.A. in Biology, Carleton College, Northfield, Minnesota
- 1980-1987 Ph.D. in Biology, Dept. Biology, University of California, Los Angeles, CA.
Thesis Title: "Gene Expression in the Mammalian Cerebellum"
Advisor: Allan J. Tobin, Ph.D.
- 1987-1988 Postdoctoral Fellowship, Dept. Neurobiology, State University of New York,
Stony Brook, NY.
Mentor: Jeffrey F. McKelvy, Ph.D.
- 1989-1992 Postdoctoral Fellowship, Dept. of Anatomy and Cell Biology, Columbia University
College of Physicians and Surgeons, New York, NY.
Mentor: John E. Pintar, Ph.D.

Professional Positions

- 5/1/92 – 9/30/93 Instructor, Department of Neurobiology and Cell Biology, Robert Wood Johnson
Medical School, UMDNJ, Piscataway, NJ.
- 10/1/93 – 6/30/99 Assistant Professor, Department of Neuroscience & Anatomy,
Penn State College of Medicine, Hershey, PA
- 7/1/99 – 9/30/05 Associate Professor, Department of Neural & Behavioral Sciences,
Penn State College of Medicine, Hershey, PA
- 10/1/05- 6/30/10 Adjunct Professor, Department of Neural & Behavioral Sciences,
Penn State College of Medicine, Hershey, PA
- 10/1/05- present Professor and Rena Warshow Chair in Multiple Sclerosis, Department of
Neurology and Neurosciences, New Jersey Medical School, UMDNJ, Newark, NJ

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Research Support

Current:

NIH/NIDDK 1RO1 DK60612-05 (Wood) IGF and IGF Receptor Function in Mammary Development, 09/30/07-07/31/12

National Multiple Sclerosis Society RG 4015A2/2 (Wood) The mTOR Pathway: A Master Regulator of Oligodendrocyte Differentiation, 11/01/09- 10/31/13

NIH/NCI RO1 CA128799-01A1 (LeRoith; Wood Investigator) Mechanisms for Increased Breast Cancer Risk in Type 2 Diabetes, 04/01/2008-01/31/2013

NIH F31NS065607 (A. Ziegler, PI; Wood/Levison, Sponsors) IGF2 and neural stem cell homeostasis, 02/12/09 – 02/11/12

UMDNJ Foundation Collaborative High Impact Award (Co-PIs: Wood, Herbig)
IGF Signaling Promotes Bypass of Cellular Senescence during Early Stage of Breast Cancer
07/01/2009-06/30/2010 No cost extension to 06/30/2011

New Jersey State Commission on Cancer Research Fellowship Award (L. Rota; Wood, Mentor) IGF Signaling in Normal and Malignant Breast Stem Cells, 12/01/2009-11/30/2011

NIH/NIDDK 3RO1 DK60612-07S1 (Wood) IGF and IGF Receptor Function in Mammary Development (ARRA-Supplement), 04/02/10-03/31/11

DOD Tuberous Sclerosis Complex Exploration/Hypothesis Award (Wood) TSC Regulates Oligodendroglial Differentiation and Myelination in the CNS, 9/30/10-9/29/12

Completed

Dean's Feasibility Grant, PSU/M.S. Hershey Medical Center. (Wood) *In vivo* Studies of the Insulin-like Growth Factor Binding Protein-2 in Mammary Tumorigenesis, 6/1/94-5/31/95

NSF/RPG IBN-9408860 (Wood) Functional Studies of the Insulin-like Growth Factor
—~~Binding~~ Protein-2 in CNS Neurogenesis, 9/1/94-8/31/96

MS PPO558 National Multiple Sclerosis Society Pilot Grant (Wood) CNTF Regulation of Peptide Growth Factors in Oligodendrocytes, 8/1/97-7/31/98

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NIH/R29 DK 48103-05 (Wood) Functional Studies of IGF Binding Protein-1, 12/01/94-11/30/99

NIH/R01 HD24565-09 (Hammond) Ovarian Growth Factors, 12/01/96-11/30/00, Co-Investigator

American Heart Association, Pennsylvania Affiliate Predoctoral Award (S. O'Donnell, Wood, Mentor) IGF Binding Protein Modulation of IGF Neurotrophic Actions in Hypoxic/Ischemic Stroke, 7/1/97 - 6/30/99

American Heart Association (J. Ness, Predoctoral Award; Wood, mentor) Mechanisms of Oligodendrocyte Cell Death and Trophic Factor Rescue in Periventricular White Matter Damage 07/01/00-06/30/02

NIH 1P01HD30704 (R.Vannucci) Perinatal Hypoxic-Ischemic Brain Damage: Neuroprotective Mechanisms (Project 3: S.Vannucci), 7/1/99-3/31/02, Co-Investigator

American Cancer Society, RPG CNE-97721 (Wood) Insulin-like Growth Factors in Breast Epithelial Proliferation, 7/1/99-6/30/02

NIH F31 CA83174 (M.Stull, Predoctoral Award) IGF Receptor in Mammary Growth and Tumorigenesis 08/01/99-03/31/03, Mentor

NIH/RO1 NS37560-04 (Wood) Oligodendrocyte Generation: A Multi-Factorial Approach, 12/01/98-03/31/03

USAMRMC BCRP-98, CDA (Wood) The Insulin-Like Growth Factors and Receptor in Hormone-Mediated Breast Growth and Tumorigenesis, 5/01/99-4/30/03

NIH 1F31 NS043080-02 (T. Frederick, Predoctoral Award) Cell Cycle Regulation in Oligodendrocyte Progenitors, 1/01/02-12/31/03, Mentor

PA Tobacco Settlement Fund (C.Smith) Manipulation of Signaling Pathways for the Treatment of Breast Cancer; Project 2 (Wood) Evaluation of Signaling and Translational Control Mechanisms in IGF Regulation of Breast Cancer Proliferation and Survival, 06/01/03-05/31/04

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PDF0100718 Susan G. Komen Breast Cancer Foundation (Wood, postdoctoral fellowship for D. Kardash-Richardson) Insulin-like Growth Factor Receptor Signaling in Breast Epithelial Cell Proliferation: In Vivo and In Vitro Approach, 10/01/01-09/30/04

Life Sciences Greenhouse of PA (Wood) Merging Modeling and Empirical Approaches: Identification of IGF-I Coordinated Signaling Pathways, 08/01/03-07/31/04

NIH/1R13 CA100040-01 (Wood) IGFs in Physiology and Disease, 03/09/03-01/31/04

NIH/RO1 (Levison), Cerebral Dysgenesis after Perinatal Hypoxia-Ischemia, Co-Investigator, 07/01/04-06/30/04

PA Tobacco Settlement Fund (J. Bond) Manipulation of Signaling Pathways for the Treatment of Breast Cancer; Project 2 (Wood) Receptor-Mediated Oncogenic Signaling in Mammary Epithelium: Downstream Interactions and the Role of the mTOR-Mediated Signaling Pathway, 07/01/04-06/30/05

NIH 1RO1 DK60612-04 (Wood) IGF and IGF Receptor Function in Mammary Development 2/1/02-1/31/06

NIH/RO1 NS37560-08 (Wood) Oligodendrocyte Generation: A Multi-Factorial Approach, 04/01/03-03/31/08 (no cost extension through 3/31/09)

NIH/R21CA120850-02 (Wood) Nestin: A Putative Marker of a Mammary Stem and Progenitor Cell Lineage, 04/01/06-03/31/08

NJMS/UMDNJ Foundation Bridge Fund (Wood) IGF and IGF Receptor Function in Mammary Development, 03/01/07-02/28/08

NIH/RO1 NS050742-04 (Wood) Mechanisms of Death and Survival in Oligodendroglia, 09/23/05-6/30/10

New Jersey State Commission on Spinal Cord Research Fellowship Award (K. Mahajan; Wood, Mentor) IGF-1 Mediated Oligodendrocyte Progenitor Survival in SCI 06/15/2008-06/30/2010

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UMDNJ Translational Research Mini-Grant (Wood) Assay for Measurement of IGF Type I Receptor and Insulin Receptor Expression in Human Cells and Tissues, 12/01/2009-11/30/2010

Pending

Awards

NRSA Predoctoral Fellowship Award, UCLA, 1982-1986
NRSA Postdoctoral Fellowship, SUNY, Stony Brook, 1987-1988
NRSA Postdoctoral Fellow, Columbia University, 1989-1990
Travel award recipient for International IGFBP Meeting, Tuebingin, Germany, 1995
Travel award and Winter Conference on Brain Research Fellow, Snowmass, Colorado, 1996
Excellence in Teaching Award 1999, Pennsylvania State University College of Medicine, Presented by Medical Class of 2002
Career Development Award, Dept. of Defense Breast Cancer Research Program, 1999-2003
Service Award, National MS Society, Central PA Chapter, 2004
UMDNJ University Professorship, 2005-2010
Medal of Excellence Award, Musical Moments for Multiple Sclerosis Research, 2008
Excellence in Research Award, Foundation of UMDNJ, 2010

Patents Filed

U.S. Utility Application Entitled "Assay for the Measurement of IGF Type I Receptor and Insulin Receptor Expression"
Serial No.: 12/721,327; filed on March 10, 2010 with the U.S. Patent and Trademark Office

U.S. Utility Application Entitled "Growth and Self-Renewal of Stem Cells"
Serial No.: 13/041,760; filed on March 7, 2011 with the U.S. Patent and Trademark Office

Editorial/Reviewing Responsibilities

Peer-Reviewed Journals:

Endocrinology, Molecular Endocrinology, American Journal of Physiology, Molecular and Cellular Endocrinology, Regulatory Peptides, Neuroscience Letters, Journal of Neurobiology, Journal of Cellular Physiology, Journal of Biological Chemistry, Lung, Cancer Research, Journal of Endocrinology, Developmental Neuroscience, Journal of Neuroscience, Journal of Neuroscience Research, Journal of Neurochemistry, Journal of Clinical Investigation, Molecular & Cellular Biology, Breast Cancer Research, GLIA, Brain Research, Carcinogenesis, PNAS

Editorial Boards:

Journal of Mammary Gland Biology and Neoplasia, November, 2000 - present
Endocrinology, 2001 – 2004
Journal of Biological Chemistry, 2006-present
Developmental Neuroscience, 2007-present
ASN-Neuro, Reviewing Editor, 2008-present

Guest Editor:

Co-Editor - The Insulin-Like Growth Factors and Insulin-Like Growth Factor Binding Proteins in the Mammary Gland and in Breast Cancer, *Journal of Mammary Gland Biology and Neoplasia*, January, 2000
Co-Editor - The Cell Cycle in Mammary Development and Breast Cancer, *Journal of Mammary Gland Biology and Neoplasia*, January, 2004

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Co-Editor – The IGF System in Mammary Development and Breast Cancer, *Journal of Mammary Gland Biology and Neoplasia*, December, 2008

Promotion Review:

1998 Scientist Reviewer for National Center for Toxicological Research, Dept. of Health and Human Services

Granting/Funding Agencies:

1994 Outside reviewer, General Medicine Study Section, NIH
 1996-1997 Grant Reviewer, Spinal Cord Research Foundation
 1998 Reviewer, Cancer Center Research Grant Review Committee, PSU/College of Medicine
 1999 Independent Grant Reviewer, Department of Veterans Affairs
 1999 Outside reviewer, National Science Foundation
 2000 Reviewer, Special Emphasis Panel ZRG1 SSS-P (01), NINDS, NIH
 2001 Reviewer, Life Sciences Consortium Seed Grants, Penn State University
 2001 Reviewer, Alberta Heritage Foundation for Medical Research
 2002 Reviewer, Natural Sciences and Engineering Research Council of Canada
 2003 Ad Hoc Reviewer, MDCN-6 Study Section, NINDS, NIH
 2004 Member of review panel for NIH/NCI RFA on “Mouse Models of Human Cancer Consortium”
 2004 Ad Hoc Reviewer, NDBG Study Section, NINDS, NIH, February/October
 2004 Reviewer, MDCN-A Study Section, NIH
 2005 Ad Hoc Reviewer, NDBG Study Section, NINDS, NIH, February
 2005 Ad Hoc Reviewer, Molecular Oncology Study Section, NCI, NIH, October
 2004 Ad Hoc Reviewer, NDBG Study Section, NINDS, NIH, February, June
 2005 Ad Hoc Reviewer, NDBG Study Section, NINDS, NIH, February
 2006 Ad Hoc Reviewer, NDGB Study Section, NINDS, NIH, February, June, October
 2006, 2010 Reviewer, European Leukodystrophy Foundation
 2006-2007 Reviewer, regular member, NDGB/NIH Study Section
 2007-2008 Reviewer, regular member, CMBG/NIH Study Section
 2008 University of Michigan Diabetes Research and Training Center Grants
 2009 Ad Hoc Reviewer, NIH Molecular Oncology Study Section
 2009 Mail Reviewer, NIH Challenge Grants
 2010-2014 Member, Review Panel A, National MS Society
 2011` Chair, NIH SEP Molecular Neuroscience, ZRG1 MDCN-N (02) – Spring & Fall

Professional Societies

Society for Neuroscience
 Endocrine Society
 AAAS
 International IGF Society
 American Society for Neurochemistry
 American Society for Cell Biology
 International Society for Neurochemistry

Service to Professional Societies:

Society Officer and Council Member, International IGF Society 1997-2010
 President, International IGF Society, 2010-2012
 Abstract Reviewer, Endocrine Society, 2000-current
 Member of Scientific Program Steering Committee, Endocrine Society 2000-2003

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Presidential Advisory Committee, American Society for Neurochemistry 2004-2007
 Council, American Society for Neurochemistry 2005-2009
 International ISN/ASN 2013 Meeting Proposal Chair, American Society for Neurochemistry,
 2009-2010

Scientific Conferences:

Invited Member of the Scientific Organizing Committee for the International IGF Meeting held in Brighton, England in October, 1999
 Initiator and co-chair of the first Gordon Research Conference on IGFs in Physiology and Disease, March, 2003
 Member of Scientific Planning Committee for American Society for Neurochemistry Meeting, 2003, 2009
 Member of Scientific Program Committee for the Joint GH-IGF Symposium, 2004, 2006
 Program Chair, American Society for Neurochemistry Annual Meeting, 2008
 Chair of Program Committee for Basic IGFs for 2010 International Conference of the Growth Hormone Society and International IGF Society
 Gordon Research Conference on Mammary Gland Biology, 2012 Vice-Chair, 2013 Co-chair

Invited Seminars

1993

The Wistar Research Institute, PA, "The IGF Binding Protein-2 Gene: Developmental Expression and Genetic Deletion by Gene Targeting"
 Department of Biochemistry, UMDNJ, Newark, NJ, "The IGF Binding Protein-2 Gene: Developmental Expression and Genetic Deletion by Gene Targeting"
 Center for Biotechnology and Medicine, UMDNJ, Piscataway, NJ, "The IGF Binding Protein-2 Gene: Developmental Expression and Genetic Deletion by Gene Targeting"1994
 Department of Endocrinology, PSU/Hershey Medical Center, PA, "Functional Studies of the IGF Binding Proteins: Lessons from Mouse Models"
 Department of Pharmacology, PSU/Hershey Medical Center, PA, "Using Gene-Targeted Mouse Lines to Study IGF Binding Protein Expression and Function in Reproductive Tissues"

1995

Department of Endocrinology, PSU/Hershey Medical Center, PA, "Expression of IGFs and IGFBPs in Developing Mammary Gland"
 Fifth International Insulin and IGF Symposium, Gainesville, FL, "Regulation of Brain IGFBP-2 and the Type I IGF Receptor by Ciliary Neurotrophic Factor"
 Third International Symposium on IGFBPs, Tuebingen, Germany, "Cytokines Regulate IGF Binding Proteins in the CNS"
 Department of Biology, PSU, PA, "Cytokine Regulation of Injury-Associated Growth Factors in the CNS"

1996

Winter Conference on Brain Research, Snowmass, Colorado, "Regulation of Brain IGFBP-2 and the Type I IGF Receptor by Ciliary Neurotrophic Factor"
 Department of Biochemistry, PSU/College of Medicine, PA, "IGFs and their Binding Proteins: Induction by Trauma and Cytokines in the Brain"
 Genetics Colloquium, PSU, State College, PA, "Using Gene-Targeted Mouse Lines to Study IGF Binding Protein Expression and Function in Reproductive Tissues"
 Department of Anatomy, West Virginia University, Morgantown, West Virginia, "Gene Targeting Approaches to Reveal IGF and IGF Binding Protein Functions"

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1997

- Department of Endocrinology, PSU/College of Medicine, Hershey, PA, "Update on the IGFBP-2 Knock-out Mouse"
- Cephalon Pharmaceuticals, West Chester, PA, " Developmental Expression and Targeting of the IGFBP-2 Gene"
- Cell and Molecular Biology Seminar Series, PSU/College of Medicine, Hershey, PA, "IGF Binding Proteins in Development and CNS Injury: Regulators of IGF Availability"
- Department of Neurology, University of Michigan, Ann Arbor, MI, "Trophic Factors in the CNS: In Vivo Approaches to Investigate Regulation and Function"
- The Wistar Institute and The University of Pennsylvania, Philadelphia, PA, "Manipulating adult oligodendrocytes in vivo: Growth and trophic factor synergisms"

1998

- Winter Conference on Brain Research, Snowbird, Utah, Workshop Organizer and Speaker, "Strategies for Remyelination: From Stem Cells to Sheaths"
- Genetics Colloquium, PSU, State College, PA, "Regulation and Function of the IGFs and IGFBPs during Normal Development of the Mouse Mammary Gland"
- Department of Cell Biology, University of North Carolina, Chapel Hill, NC, "Insulin-Like Growth Factors in the Developing Mammary Gland"
- Department of Anatomy, Uniformed Services University of the Health Sciences, Bethesda, MD, "Mechanisms of Ciliary Neurotrophic Factor Action in the CNS"

1999

- Gordon Conference on Mammary Gland Biology, Henniker, NH, "Roles for the IGFs and IGF Binding Proteins in Mammary Ductal Growth"
- 5th International Symposium on Insulin-Like Growth Factors, Brighton, England, "IGF-Mediated Growth of Mammary Epithelium during Ductal Development in the Mouse"
- Department of Molecular and Cellular Physiology, PSU/College of Medicine, "The IGFs and IGFBPs in Mammary Epithelial Growth in the Mouse"

2000

- Department of Physiology, University of Colorado School of Med, Denver, CO, "Deciphering Functions of the IGFs and IGFBPs in the Postnatal Mammary Gland"
- Department of Biochemistry, UMDNJ, Newark, NJ, "IGF-Mediated Growth of Mammary Epithelium in the Mouse"
- Gordon Conference on Myelin, Invited Speaker, Luca, Italy, "Growth Factor Interactions in Oligodendrocyte Generation"
- Baylor College of Med Postdoctoral Association Seminar Series, Houston, TX, "Deciphering Functions of the IGFs and IGFBPs in the Developing Mammary Gland"
- Rutgers University, Department of Animal Sciences, "Deciphering Functions of the IGFs and IGFBPs in the Developing Mammary Gland"

2001

- Kutztown University, "Transgenic and Gene-Targeting Approaches to Investigate Gene Function" Penn State Cancer Center, "IGF-Mediated Growth of Breast Epithelium"

2002

- Clinical Endocrinology Branch, NIH, "Role of IGFs and IGF-IR in Mammary Epithelial Growth"
- Department of Endocrinology, New York University, "Deciphering Functions of the IGFs and IGFBPs in the Developing Mammary Gland"
- Department of Pathology, University of Virginia, "The IGFs and IGF-IR in Mammary Epithelial Growth and Function"

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- Rutgers University, Department of Animal Sciences, “The IGFs and IGF-IR in Mammary Epithelial Growth and Function”
- Department of Pharmacology, Penn State College of Medicine, “The IGFs and IGF-IR in Mammary Epithelial Growth and Function”
- Department of Cell Biology, Georgetown University School of Medicine, “The IGFs and IGF-IR in Mammary Epithelial Growth and Function”
- Department of Biomedical Sciences, Ohio University, “The IGFs and IGF-IR in Mammary Epithelial Growth and Function”
- Neuroscience Program sponsored Research Day, Penn State University, “Proliferation and Cell Cycle Regulation in Oligodendrocyte Progenitors”
- Department of Physiology, University of Chicago Medical Center, “The IGFs and IGF-IR in Mammary Epithelial Growth and Function”
- Third Hershey Conference on Developmental Cerebral Blood Flow and Metabolism, Invited Speaker, “Glutamate-Mediated Apoptosis and Trophic Factor Protection of Immature Oligodendrocytes”
- Weiss Center for Research, “Death and Survival in the Oligodendrocyte Lineage: Differential Effects of Trophic Factors on Akt Activation”
- Department of Neuroscience, University of Connecticut Health Center, “Survival of Oligodendrocyte Progenitors: Differential Effects of Trophic Factors on Akt Activation”

2003

- Department of Neuroscience, Syracuse University Medical Center, “Proliferation and Survival in the Oligodendrocyte Lineage”
- Endocrinologie Moleculaire, Inserm, Faculte De Medecine Necker, Paris, France, “IGF-I in Cell Cycle Checkpoint Progression: General and Tissue-Specific Effects”
- Department of Neurology & Neurosciences, UMDNJ, Newark, “Proliferation and Survival in the Oligodendrocyte Lineage”
- Juvenile Diabetes Foundation/Penn State University Workshop on Diabetic Retinopathy, “Trophic Factors and Survival Pathways in Neural Cells”
- 8th International Pituitary Congress, NYC, “Overview of GH and IGF Actions in the Central Nervous System”
- Athens Conference on GH, IGF and Prolactin, Athens, Ohio, “Context Dependency of IGF Actions in Proliferation, Survival and Differentiation”

2004

- Winter Conference on Brain Research, Copper, Colorado, Invited Symposium speaker, “Glutamate-Mediated Death and Trophic Factor Protection of Oligodendrocyte Progenitors”
- Department of Pharmacology, University of Florida, Gainesville, Florida, “Mechanisms of Excitotoxic Death and Trophic Factor Protection in Oligodendrocyte Progenitors”
- NIH, Division of Diabetes & Metabolism, Bethesda, MD, “IGF Regulation of Cell Cycle and Differentiation in Mammary Epithelial Cells”
- Gordon Research Conference on Myelin Biology, Il Ciocco, Italy, Invited speaker, “Convergence of Signaling Pathways on Cell Cycle Targets in Oligodendrocyte Progenitors”
- Penn State Children’s Hospital, Pediatric Research Day, June 3, Hershey, PA, “Mechanisms of Death and Survival in the Perinatal Brain”
- Annual Meeting of the Endocrine Society, New Orleans, Invited Symposium speaker, “Insulin-Like Growth Factors and Cell Cycle Progression in the Mammary Gland”
- Endocrine Retreat 2004, Bel Air Castle, Beaugency, France, Invited Speaker, “IGF Receptor Signaling Pathways in Oligodendrocyte Progenitors”
- Ipsen Foundation Symposium – Deciphering Growth, Paris, France, “IGF-Mediated Pathways that

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Regulate Brain Growth”

2005

Universidad Central del Caribe, April 14, Bayamon, Puerto Rico, “Mechanisms of Excitotoxic Death and Trophic Factor Protection in Oligodendrocyte Progenitors”

New Jersey Medical School, UMDNJ Tumor Board, October 17, “Insulin-like Growth Factor Signaling and Function in Mammary Epithelial Cells and Breast Cancer Cells”

International Conference: The Role of the IGF System in Cancer, November 10-12, Taormina, Italy, “The IGF-IR in Breast Development and Cancer”

Albert Einstein College of Medicine of Yeshiva University, Department of Pathology, November 29, “IGF Receptor Signaling Pathways and Targets in Oligodendrocyte Progenitors”

2006

Department of Reproductive Sciences, University of Colorado Health Sciences Center, January 20, “Functions of Epithelial and Stromal IGF-I in Mammary Development”

Department Neurology & Neurosciences, Grand Rounds, NJMS/UMDNJ, March 1, “Pathways of Death and Survival in Oligodendrocytes”

American Society for Neurochemistry, Portland, OR, March 12, “IGF-I-Mediated Signaling Pathways and Downstream Targets in Oligodendrocyte Progenitors”

Dept. Medicine, Brown University Medical School, March 28, “IGF Receptor Trafficking and Sustained Akt Phosphorylation in Neural Progenitors”

Department of Biochemistry & Molecular Biology, New Jersey Medical School/UMDNJ, April 6, “IGF Receptor Signaling Pathways and Targets in Oligodendrocyte Progenitors”

Fifth Hershey Conference on Developmental Cerebral Blood Flow and Metabolism, Invited Speaker, June 2, “Death and Survival Pathways in Perinatal Oligodendrocytes”

Department of Biology, Rutgers University, September 26, “IGF Receptor Signaling Pathways and Trafficking in Oligodendrocyte Progenitors”

2007

Gordon Research Conference on IGFs in Physiology and Disease, March, 19, “IGF-I is a Master Regulator of CNS Progenitor Development”

NJMS Tumor Board, May, 7, “Insulin-like Growth Factors and Receptors in Mammary Epithelial Growth”

ImClone Systems, New York, May 10, “New considerations for understanding IGF-IR signaling in mammary and neural epithelial cells”

New Jersey Medical School, Symposium on Neuroprotection and Neurorepair: Pharmacology to Stem Cells, May 14, “Pathways and Targets of IGF-I Mediated Neuroprotection”

NovoNordisk/Hagedorn Research Institute, Copenhagen, September 13, “IGF Signaling Pathways in CNS Progenitors”

National Multiple Sclerosis Society Regional Conference, Parsippany, NJ, October 14, “Stem Cells & Beyond: Emerging Therapies for CNS Repair in MS”

Dept. Physiology, University of Cincinnati, Nov 13, “Insulin, IGF and Hybrid Receptors in Mammary Epithelial Cells – the Plot Thickens for IGF Signaling”

2008

Program Project Grant Retreat, Denver Health Sciences Center, January 17, “New Perspectives on IGF Signaling in Mammary Gland Development and Breast Cancer”

Winter Conference on Brain Research, January 30, “IGF Signaling and Oligodendrocyte Development”

Endocrine Grand Rounds, NYU School of Medicine, February 15, “New Perspectives on IGF Signaling in Mammary Gland Development and Breast Cancer”

Department of Pharmacology, Emory University School of Medicine, April 1, “IGF Signaling

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Pathways and Function in Oligodendrocyte Progenitors”

University of Sydney, Australia, May 6, “IGF Signaling in Mammary Epithelial Cells”

School of Molecular and Biomedical Science, University of Adelaide, Australia, May 14,

“Diverse Roles for IGF-I and PI3K/Akt Signaling in CNS Progenitors”

IGF-OZ 2008 Meeting on The IGF System and Related Proteins in Development and Disease,

Adelaide, Australia, May 15-16, Keynote International Speaker, “New Perspectives on IGF Signaling in Mammary Development and Breast Cancer”

Chicago Myelin Afficionado Group, Aug. 25, “Diverse Roles for IGF-I and PI3K/Akt Signaling in Oligodendrocyte Progenitors”

UCLA, October 31, “Diverse Roles for IGF-I and PI3K/Akt Signaling in Oligodendrocyte Progenitors”

2009

Pathology Department, NJMS/UMDNJ, January 8, “New Perspectives on IGF Signaling in Mammary Development and Breast Cancer”

Program Project Grant Retreat, Denver Health Sciences Center, January 23, “Mysteries of IGF-IR and Insulin Receptor Signaling in Mammary Epithelial Cells”

Center for Neuroscience Research, Children’s Research Institute, Children’s National Medical Center, Washington D.C., April 3, “Diverse Roles for IGF-I and PI3K/Akt Signaling in Oligodendrocyte Progenitors”

Institutes of Brain Science, Fudan University, Shanghai, China, April 9, “The Mammalian Target of Rapamycin (mTOR) Pathway in Differentiation of Oligodendroglia”

Second Shanghai Forum in Neonatology, Shanghai, China, April 10-11, “Cell Death and Survival Pathways in Oligodendrocyte Progenitors: Why Glioprotective Strategies may differ from Neuroprotective Strategies”

Developmental Biology Program for Pediatric Disorders, CHOP/UPENN, June 2, “The Mammalian Target of Rapamycin (mTOR) Pathway in Differentiation of Oligodendroglia”

Endocrine Society Annual Meeting, Invited Symposium Speaker, Washington D.C., June 12, “IGF Regulation of Neural Stem/Progenitor Cells”

Myelin Satellite Meeting, Gyeongju, South Korea, August 20, “PI3K/Akt/mTOR Signaling in Oligodendrocyte Differentiation”

International Society for Neurochemistry Conference, Invited Symposium Speaker, Busan, South Korea, August 26, “PI3K/Akt/mTOR Signaling in Oligodendrocyte Differentiation”

Euroglia 2009 Conference, Paris, France, September 11, “The PI3K/Akt/mTOR Pathway in Oligodendrocyte Differentiation”

2010

Program Project Grant Retreat, Denver Health Sciences Center, January 21, “Disruption of IGF Signaling during Alveolar Differentiation”

Myelin Gordon Research Conference, February 16, “Targets of mTOR Signaling and Oligodendrocyte Differentiation”

Department of Molecular, Cellular & Developmental Biology, University of Michigan, Ann Arbor, April 9, “PI3K/Akt/mTOR Signaling in Oligodendrocyte Differentiation”

Department of Animal Sciences, Rutgers University, New Brunswick, April 23, “New Perspectives on IGF-IR and Insulin Receptor in Mammary Epithelial Cells”

SUNY Glial Biology Seminar Series, Stony Brook, NY, April 30, “Unraveling mTOR Signaling and the Differentiation Program in Oligodendroglia”

Department of Cell Biology, New York University, New York, May 18, “Unraveling mTOR Signaling and the Differentiation Program in Oligodendroglia”

Hershey Conference on Developmental Brain Injury, Snowbird, Utah, June 3, “Mechanism of

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Glutamate Excitotoxicity in Oligodendrocyte Progenitors”

Endocrine Society Annual Meeting, San Diego, CA, June 19, “Insulin-like Growth Factor Signaling Regulates Stem/Progenitor Cells in the Epithelium of Virgin Mouse Mammary Glands”

Foundation des Treilles Conference on Myelinating Glia: Development, Function and Pathobiology, October 19, “Signaling in the Oligodendrocyte Lineage”

2011

Program Project Grant Retreat, Denver Health Sciences Center, January 21, “IGF Regulation of Mammary Epithelial Lineage and Differentiation”

Winter Conference on Brain Research, Keystone, CO, January 26, “mTOR Signaling in Oligodendrocyte Differentiation and Myelination”

Genetics Department, Einstein College of Medicine, February 16, “IGF Regulation of Mammary Epithelial Lineage and Differentiation”

Neurology Grand Rounds, Robert Wood Johnson Medical School/UMDNJ, March 16, “Mechanisms of Remyelination and Repair in Multiple Sclerosis: From Mice to (Wo)Men”

Honorary Symposium for Dr. Margaret Neville, Department of Obstetrics & Gynecology, Denver Health Sciences Center, Denver, CO, May 11, Keynote speaker, “What Breasts and Brains can tell us about IGF Receptors in Stem/Progenitor Cell Regulation”

International Society for Neurochemistry, Athens, Greece, August 30, “mTOR Signaling in Oligodendrocyte Differentiation”

Dept. Anatomy & Cell Biology, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada, September 22, “IGF Regulation of Mammary Epithelial Lineage and Differentiation”

Biomedical Engineering Program, NJIT, Newark, NJ, November 4

2012

Dept. Yale University School of Medicine, February 24,

Teaching Responsibilities

1980 - 1984	Teaching Assistant, Introduction to Cell and Molecular Biology and Biology Laboratory Techniques, UCLA
1982 - 1984	Co-Instructor, Underwater Research, Shoals Marine Laboratory, Cornell University and University of New Hampshire
1989 - 1990	Instructor, Molecular Probes of the Nervous System, Cold Spring Harbor Laboratories
1994 - 1995	Medical Embryology, PSU/College of Medicine (4 lectures)
1994 - 2000	Molecular Genetics, graduate core curriculum (6 lectures)
1995	Advanced Topics in Cellular and Molecular Physiology
1995 - 1998	Cellular and Molecular Neuroscience (2 lectures)
1995 - 2002	Advanced Topics in Neuroscience (10 week block in Topics in Developmental Neurobiology; (10 week block in Topics in Stem Cell Biology)
1996 - 1999	Medical Histology, PSU College of Medicine (1 lecture and laboratory)
1996 - 1998	Course Director and Instructor, Medical Embryology, PSU/College of Medicine (8 lectures)
1997	Biology of Neoplasia (1 lecture)
1999 - 2004	Medical Histology, PSU/College of Medicine (1 lecture and 4 laboratories)
1999 - 2004	Neurochemistry, PSU/COM neuroscience graduate curriculum (1 lecture)
1999 - 2004	Cellular and Molecular Neuroscience, PSU/COM (3 lectures)
2000 - 2002	Neurobiology, PSU/University Park (2 lectures)
2002 - 2003	Research Problems in Molecular Medicine, Penn State COM (5

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2002 – 2005	sections), graduate curriculum for LSC Program in Molecular Medicine Molecular Biology, PSU/COM (5 lectures)
2004	Genetic Approaches to Biomedical Problems, PSU/COM (1 lecture, 3 discussion sections)
2004	Advanced Topics in Neuroscience, PSU/COM (8 week block: Problems in Multiple Sclerosis; (1 lecture; 7 facilitated learning sessions)
2006	Developmental Neurobiology – Rutgers/UMDNJ (3 lectures)
2007-2009	Molecular & Cellular Biology Module 5/Neurophysiology Part II GSBS/UMDNJ(course director; 6 alternative learning sessions)
2007-2009	GSBS/UMDNJ, Evening Grad Core Course – 2 lectures
2007-	Professional Skills Course – GSBS/UMDNJ Graduate curriculum (18 sessions/6 lectures)
2008-	Mind, Brain & Behavior – NJMS/UMDNJ Medical curriculum (4 laboratories)
2009-	Molecular & Cellular Biology Graduate Core Course, GSBS/UMDNJ (Co- director, Modules 1 & 5, 8 alternative learning sessions; 2 lectures)
2009-2010	Foundations in Neuroscience, Integrated Neuroscience Core Course, GSBS/UMDNJ (1 lecture)
2011-	Demyelinating Diseases, GSBS/UMDNJ (12 sessions/critical readings/presentations)
2011-	Cell & Developmental Neuroscience, GSBS/UMDNJ, Director, 4 lectures

AdvisingPh.D. Students:

Completed:

Monica Richert, 1994-1998, Penn State Hershey Med Center, Cell and Molecular Biology
 Steven O'Donnell, 1995-1999, Penn State Hershey Med Center, Neuroscience
 Fengjun Jiang, 1995-2000, Penn State Hershey Med Center, Neuroscience
 Mike Allar, 1998-2002, Penn State Hershey Med Center, Anatomy
 Jennifer Ness, 1999-2002, Penn State Integrated Biosciences, Molecular Medicine Option
 Malinda Stull, 1998-2003, Penn State Hershey Med Center, Cell and Molecular Biology
 Terra Frederick, 1999-2003, Penn State Integrated Biosciences, Molecular Medicine Option
 Robert Romanelli 2002-2006, Penn State Hershey Med Center, Cell and Molecular Biology
 William Tyler 2002-2007, Penn State Hershey Med Center, Cell and Molecular Biology
 Anne Rowzee 2002-2007, Penn State Hershey Med Center, Cell and Molecular Biology
 Jungsoo Min 2004-2009, Penn State Integrated Biosciences, Molecular Medicine Option
 Zhaoyu Sun 2005-2010, NJMS/UMDNJ Biosciences
 Kedar Mahajan 2007-2010, NJMS/UMDNJ MD/PhD Program

In Progress:

Lauren Rota, 2008-present, NJMS/UMDNJ Biosciences
 Stacey Cifelli, 2009-present, NJMS/UMDNJ Integrated Neurosciences
 Lauren Mursch, 2011-present, NJMS/UMDNJ Neuroscience

Masters Students:

Danielle Scarola, 2011-present, NJMS/UMDNJ Biosciences

Completed:

Aimee Loladze 2006, Penn State, Integrated Biosciences, Molecular Medicine
 Lauren Rota, 2008, NJMS/UMDNJ Biosciences
 Soumyashree Das, 2010, NJIT

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Postdoctoral Fellows:

Jennifer Ness, Ph.D., 2002-2003
 Dawn Kardash-Richardson, Ph.D., 2000-2004
 Malinda Stull, Ph.D., 2003
 Vaho Loladze, Ph.D., 2003-2004
 Sain Shushanov, Ph.D., 2004-2007
 Robert Romanelli, Ph.D., 2006
 William Tyler, Ph.D., 2007-2008
 Anne Rowzee, Ph.D., 2007-2008
 Soppio Simonishvili, Ph.D., 2004-2009
 Jungsoo Min, Ph.D., 2009-2010
 Marcus Shin, Ph.D., 2011-

Other Laboratory Trainees:

Nathan Swilling, 1994, Summer Whitaker Foundation Scholar
 Andrew Wang, 1995, Summer Whitaker Foundation Scholar
 Megan Williams, 1997, Summer Whitaker Foundation Scholar
 Debra Thiel, 1998, Summer Whitaker Foundation Scholar
 Justin Stahl, 1998, Medical Student Research Project
 Beverly Baptiste, 1999, Rotation student, Cell and Molecular Biology
 Terra Frederick, 1999, Rotation student, Molecular Medicine
 Matt Silvis, 1999, Summer Medical Student Research
 Aimee vanOlden, 2000, Rotation student, Molecular Medicine
 Stephanie Stoehr, 2001, Rotation student, Molecular Medicine
 Ryan Felling, 2001, Rotation student, M.D./Ph.D.
 Bill Tyler, 2001, Rotation student, Cell and Molecular Biology
 Pei-Chun Yeh, 2001, Rotation student, Genetics
 Melissa Nowotarski, 2002, Rotation student, Cell and Molecular Biology
 Anne Rowzee, 2002, Rotation student, Cell and Molecular Biology
 Wei Jin, 2003, Rotation student, Genetics
 Nu-Chu Liang, 2003, Rotation student, Neuroscience
 Jessica Rudy-Heimlick, 2003, Rotation student, Molecular Medicine
 Yan Yan, 2004, Rotation student, Genetics
 Jungsoo Min, 2004, Rotation student, Molecular Medicine
 Krista Buono, 2006, Rotation Student, NJMS/UMDNJ Biomedical Sciences
 Kedar Mahajan, 2006, 2007, Rotation Student, NJMS/UMDNJ MD/PhD
 Stacey Cifelli, 2008, Rotation Student, NJMS/UMDNJ Integrated Neurosciences
 Mark Nicolau, 2008-2009, Masters Student/MD Student, NJMS/UMDNJ
 Douglas Clements, 2009, Masters Student, NJMS/UMDNJ
 Tiffany Porras, 2010- , High School Student, Hendrick Hudson High School/SUNY Albany
 Science Research Program
 Lauren Mursch, 2010, Rotation Student, NJMS/UMDNJ, Neuroscience Program
 Danielle Scarola, 2011, Masters Student, NJMS/UMDNJ
 Jason Domegauer, 2011, MD/PhD Student, NJMS/UMDNJ

Thesis Committees:

Completed:

PSU/College of Medicine:

Stacy Hudgins, Anatomy (Masters), 1997
 Nadine Dejneka, Pharmacology, 1998

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Dan Campbell, Neuroscience, 1998
 Lisa Falls, Biochemistry and Molecular Biology, 1998
 Khristy Manges, Neuroscience, 1999
 Scott Millhouse, Microbiology and Immunology, 1999
 Patricia Opresko, Biochemistry and Molecular Biology, 2000
 Tina Cairns, Cell and Molecular Biology, 2000
 Christopher J. Kuhlow, Anatomy (Masters), 2001
 Shelley Gestle, Biochemistry and Molecular Biology, 2001
 Matthew Snyder, Anatomy (Masters), 2001
 Christopher Freet, Anatomy (Masters), 2001
 Brandy Furman, Neuroscience, 2001
 Ridwan Lin, M.D./Ph.D., Neuroscience, 2001
 Carolyn Pizzoli, M.D./Ph.D. Cell and Molecular Biology, 2001
 Phil Albrecht, Neuroscience, 2001
 Akiva Mintz, M.D./Ph.D. Cell and Molecular Biology, 2002
 Christine Silvis, Cell and Molecular Physiology, 2002
 Vinayshree Kumar, Physiology, 2002
 Laura Palmer, Biochemistry and Molecular Biology, 2002
 Liqun Zhang, Neuroscience, 2003
 Jia-Hai Lee, Biochemistry and Molecular Biology, 2003
 Tricia Hogan, Cell and Molecular Biology, 2003
 Geoffry Knudsen, Biochemistry, Microbiology and Molecular Biology, 2003
 Christine Brazel, Cell and Molecular Biology, 2003
 David Drubin, Integrative Biosciences, Molecular Medicine Option, 2004
 Katie Streicher, Integrative Biosciences, Immunobiology Option, 2004
 Melissa Cunningham, M.D./Ph.D. Cell and Molecular Biology, 2004
 Beverly Baptiste, M.S., Cell and Molecular Biology, 2004
 Jason Heaney, Physiology, 2004
 Michael Romanko, Integrative Biosciences, Molecular Medicine Option, 2004
 Robin Kilker, M.D./Ph.D., Cell and Molecular Biology, 2004
 Jelena Lazovic-Stojkovic, Integrative Biosciences, Molecular Medicine Option, 2004
 Michael Debies, Cell and Molecular Biology, 2005
 Ryan Felling, M.D./Ph.D., Neuroscience, 2005
 Christine Liberto, Masters of Science, Cell and Molecular Biology, 2006
 Wei Jin, PSU, Genetics, 2008
 Sarah Gramling, PSU, Integrative Biosciences, Molecular Toxicology Option, 2008
 Nan Li, PSU, Genetics, 2009

Other:

H. Wayne Lambert, Cell Biology, University of North Carolina, Chapel Hill, NC, 2000

UMDNJ/NJMS

Dhivyaa Alagappan, UMDNJ Biomedical Sciences, 2008
 Christopher Hansen, NJMS/UMDNJ Masters of Science, 2008
 Pedro Rodriguez, UMDNJ Biomedical Sciences, 2009
 Jennifer Woodbury, UMDNJ MD/PhD Program, 2009
 Homer Adams, UMDNJ Biomedical Sciences
 Emyln Capili, UMDNJ Masters Program
 Ru Chen, UMDNJ Interdisciplinary Program

In Progress:

(Cont.)

Cassandre Noel, UMDNJ Masters Program

Service to the University

- 1994-1995 Consultant for Transgenic Facility
- 1994-1995 Member of Faculty Recruitment Committee, Department of Neuroscience & Anatomy
- 1994-1995 Member of Graduate Recruitment Committee for Neuroscience and Anatomy Graduate Program
- 1995-1997 Member of Steering Committee for Graduate Recruitment
- 1994-2004 Faculty Evaluator, PSU/College of Medicine Graduate Research Forum
- 1995 Judge for Penn State Graduate Research Exhibition
- 1994-2009 Member of Graduate Faculty, PSU Graduate School
- 1994-2005 Member of Neuroscience, Cell & Molecular Biology, and Genetics Graduate Programs
- 1994-2004 Member of Interview Committee for Cell and Molecular Biology Graduate Program
- 1995-2005 Co-Director of Transgenic Facility, PSU/College of Medicine
- 1995-2004 Member of Advisory Committee for the Intercollege Graduate Program in Cell and Molecular Biology
- 1995-2005 Member of Executive Committee for the Intercollege Graduate Program in Genetics
- 1996-2005 Member of LSC Graduate Program in Neuroscience
- 1998-2005 Member of LSC Graduate Programs in Molecular Medicine
- 2000-2003 Member of LSC Steering Committee
- 2000-2004 Director of PSU Life Sciences Consortium Graduate Program in Molecular Medicine
- 2000-2004 Associate Director of the Graduate Program in Cell and Molecular Biology
- 2000-2004 Program Leader, Cancer Cell Biology Program, Penn State Cancer Institute
- 2000 Member of Committee for Biomedical Department Websites Project
- 2001-2002 Member of the LSC Nominating Committee
- 2001-2002 Member of Tobacco Review Settlement Board, Penn State University
- 2002-2003 Chair, Neuroscience Advisory Committee for Neuroscience at Penn State COM
- 2002-2003 Member of Search Committee for Department of Psychiatry Chair, Penn State COM
- 2003 Member of RA-10 Investigative Committee for PSU
- 2003-2005 Member of Scientific Leadership Committee for the Penn State Cancer Institute
- 2004-2005 Member of the IBIOS Graduate Program Committee for PSU
- 2005 Faculty participant, Junior Faculty Research Program, Penn State College of Medicine
- 2005 Member, President's Strategic Advisory Council, UMDNJ
- 2005 Member, Faculty Search Committee for the NJMS Cancer Center
- 2005-2007 Chair, Committee to Develop Neuroscience Research Institute, New Jersey Medical School
- 2006 Member, Qualifying exam committee, Integrative Neurosciences Graduate Program
- 2007 Chair, Faculty oversight committee for NJMS Transgenic Facility
- 2007-2008 Member, Faculty Search Committee, Cancer Center
- 2008 Member, Qualifying Exam Committees, Rivka Stone, MD/PhD; Alexandra Terskiy, MD/PhD; Jessica Fishlock, MD/PhD
- 2008 Reader for PhD Thesis, PhD examination committee: Brian Benn
- 2008-2009 Member, Search Committee for Associate Dean of the Graduate School of Biomedical Sciences at UMDNJ
- 2008 Chair, Committee on Goals for Graduate Education at NJMS/UMDNJ
- 2009-2010 Member, Committee to Revise Graduate Core Curriculum

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- 2009-2010 Member, UMDNJ Investigative Panel for Allegations of Research Misconduct
 2009-2010 Member, Task Force to Evaluate NeuroPsychiatric Clinical and Research Services at UMDNJ-New Jersey Medical School
 2010- Director, Graduate Program Track in Cell Biology, Neuroscience and Physiology, Graduate School of Biomedical Sciences, UMDNJ, Newark Division

Service to the Community

- Invited speaker, American Cancer Society, Relay for Life, Millersville, PA July 21, 2001
 Invited speaker, American Cancer Society, Relay for Life, Kutztown, PA June 1, 2002
 Invited speaker, American Cancer Society's Making Strides Against Breast Cancer Kick-Off Breakfast, Harrisburg, PA, August 21, 2002
 Invited speaker, PA Chapter of the National Multiple Sclerosis Society, Women with MS Breakfast, September 19, 2002
 Invited speaker, Parson's E&C "Tournament for Life" Benefit for the American Cancer Society, August 18, 2003
 Invited speaker, Benefit Fundraiser for the PA Chapter of the Multiple Sclerosis Society, October 23, 2003
 Invited speaker, MS Support Group of Palmyra, September, 14, 2004
 Invited speaker, National MS Society Tour of Champions, San Diego, CA, October 16, 2004
 Invited speaker, Central PA Chapter MS Society, Team MS Rally, Hershey, PA, February 5, 2005
 Invited speaker, National Multiple Sclerosis Society Regional Conference, NJ, October 14, 2007
 Invited speaker, National Multiple Sclerosis Society New Jersey Conference, September 14, 2010

Publications

1. **Wood, T.L.**, Frantz, G.D., Menkes, J.H. and Tobin, A.J. (1986) Regional distribution of messenger RNAs in postmortem human brain. *J. Neuroscience Res.* 16:311-324.
2. Christakos, S., **Wood, T.L.**, Varghese, S. and Tobin A.J. (1987) Molecular cloning and regulation of the mammalian 28,000 M_r vitamin D-dependent calcium binding protein (Calbindin D_{28K}). In: Calcium Binding Proteins in Health and Disease, eds. Norman, A.W., Vanaman, T.C. and Means, A.R. (Academic Press, N.Y., N.Y.), pp.276-284.
3. **Wood, T.L.**, Kobayashi, Y., Frantz, G., Varghese, S., Christakos, S. and Tobin, A.J. (1988) Molecular cloning of mammalian 28,000 M_r vitamin D-dependent calcium binding protein (Calbindin D_{28K}): Expression of Calbindin D_{28K} RNAs in rodent brain and kidney. *DNA* 7:585-593.
4. **Wood, T.L.**, Berelowitz, M. and McKelvy, J.F. (1989) Hormonal feedback regulation of brain IGF-I and IGF-II gene expression. In: Molecular and Cellular Biology of Insulin-like Growth Factors and their Receptors, eds. LeRoith, D. and Raizada, M.K. (Plenum Press, N.Y., N.Y.), pp.209-217.
5. Olchovsky, D., Bruno, J., **Wood, T.L.**, Gelato, M., Leidy, J.W., Gilbert, J.M.Jr. and Berelowitz, M. (1990) Altered pituitary growth hormone regulation in streptozotocin-diabetic rats: a combined hormone-defect of hypothalamic somatostatin and growth hormone-releasing factor. *Endocrinology* 126:53-61.

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6. **Wood, T.L.**, Brown, A.L., Rechler, M.M. and Pintar, J.E. (1990) The expression pattern of an insulin-like growth factor (IGF)-binding protein gene is distinct from IGF-II in the midgestational rat embryo. *Mol. Endocrinology* 4:1257-1263.
7. **Wood, T.L.**, Berelowitz, M., Gelato, M., Roberts, C., Jr., LeRoith, D., Millard, W. and McKelvy, J.F. (1991) Hormonal regulation of rat hypothalamic neuropeptide mRNAs: Effect of hypophysectomy and hormone replacement on GRF, SRIF and the insulin-like growth factors. *Neuroendocrinology* 53: 298-305.
8. Pintar, J.E., **Wood, T.L.**, Streck, R.D., Havton, L., Rogler, L. and Hsu, M.-S. (1991) Expression of IGF-II, the IGF-II/mannose-6-phosphate receptor and IGFBP-2 during rat embryogenesis. In: Molecular Biology and Physiology of Insulin and Insulin-Like Growth Factors, eds. Raizada, M.K. and LeRoith, D. (Plenum Press, N.Y., N.Y.), pp. 325-333.
9. **Wood, T.L.**, Streck, R.D. and Pintar, J.E. (1992) Expression of the IGFBP-2 gene in post-implantation rat embryos. *Development* 114, 59-66.
10. Streck, R.D., **Wood, T.L.**, Hsu, M.-S. and Pintar, J.E. (1992) The transcript for insulin-like growth factor binding protein-2 is extremely abundant in the apical ectodermal ridge of rat embryonic limbs. *Dev. Biol.* 151, 586-596.
11. Cerro, J., Grewal, A., **Wood, T.L.** and Pintar, J.E. (1993) Tissue-specific expression of the insulin-like growth factor binding protein (IGFBP) mRNAs in mouse and rat development. *Regulatory Peptides* 48:189-198.
12. **Wood, T.L.**, Rogler, L., Streck, R.D., Cerro, J., Green, B., Grewal, A. and Pintar, J.E. (1993) Targeted disruption of the IGFBP-2 gene. *Growth Regulation* 3:3-6.
13. Green, B.N., Jones, S.B., Streck, R.D., **Wood, T.L.**, Rotwein, P. and Pintar, J.E. (1994) Distinct expression patterns of insulin-like growth factor binding proteins 2 and 5 during fetal and post-natal development. *Endocrinology* 134:954-962.
14. Fliegner, K.H., Kaplan, M.P., **Wood, T.L.**, Pintar, J.E. and Liem, R.K.H. (1994) Expression of the gene for the neuronal intermediate filament protein α -internexin coincides with the onset of neuronal differentiation in the developing rat nervous system. *J. Comp. Neurology* 342:161-173.
15. **Wood, T.L.** (1995) Gene targeting and transgenic approaches to IGF and IGF binding protein function. Invited Review. *Am. J. Physiol.* 269 (Endocrinol. Metab. 32): E613-E622.
16. **Wood, T.L.**, O'Donnell, S.L. and Levison, S.W. (1995) Cytokines regulate IGF binding proteins in the CNS. *Prog. in Growth Factor Res.* 6(2-4):181-187.
17. LeRoith, D., Neuenschwander, S., **Wood, T.L.** and Henninghausen, L. (1995) Insulin-like growth factor-1 and insulin-like growth factor binding protein-3 inhibit involution of the mammary gland following lactation: studies in transgenic mice. *Prog. in Growth Factor Res.* 6(2-4):433-436.

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18. Neuenschwander, S., Schwartz, A., **Wood, T.L.**, Roberts, Jr., C.T., Henninghausen, L., and LeRoith, D. (1996) Involution of the lactating mammary gland is inhibited by the IGF system in a transgenic mouse model. *J. Clin. Invest.* 97(10):2225-2232.
19. Levison, S.W., Ducceschi, M.H., Young, G.M., and **Wood, T.L.** (1996) Acute exposure to CNTF *in vivo* induces multiple components of reactive gliosis. *Exp. Neurology* 141(2):256-268.
20. Pintar, J.E., Cerro, J.A. and **Wood, T.L.** (1996) Genetic approaches to the function of insulin-like growth factor-binding proteins during rodent development. *Hormone Research* 45(3-5):172-177.
21. Hernández-Sánchez, C., **Wood, T.L.** and LeRoith, D. (1997) Developmental and tissue specific sulfonylurea receptor gene expression. *Endocrinology* 138:705-711.
22. Butler, A.A., Blakesley, V.A., Poulaki, V., Tsokos, M., **Wood, T.L.** and LeRoith, D. (1998) Stimulation of murine fibrosarcoma growth by recombinant human insulin-like growth factor-I (IGF-I) treatment in nude mice. Dependency on IGF-I dose and IGF-I receptor number. *Cancer Research* 58:3021-3027.
23. Wandji, S.-A., **Wood, T.L.**, Crawford, J.L., Levison, S.W., and Hammond, J.M. (1998) Expression of mouse ovarian IGF system components during follicular development and atresia. *Endocrinology* 139:5205-5214.
24. Richert, M.M. and **Wood, T.L.** (1999) Expression and regulation of insulin-like growth factors and their binding proteins in the normal breast. In: Contemporary Endocrinology: Endocrinology of Breast Cancer, ed. Manni, A. (Humana Press, Totowa, N.J.), pp. 39-52.
25. Richert, M.M. and **Wood, T.L.** (1999) The insulin-like growth factors and IGF type I receptor during postnatal growth of the murine mammary gland: Sites of mRNA expression and potential functions. *Endocrinology* 140:454-461.
26. Jiang, F., Levison, S.W. and **Wood, T.L.** (1999) Ciliary neurotrophic factor induces expression of the IGF type I receptor and FGF receptor 1 mRNAs in adult rat brain oligodendrocytes. *J. Neurosci. Res.* 57:447-457.
27. **Wood, T.L.** and Yee, D. (2000) Introduction: The IGFs and IGFbps in the normal mammary gland and in breast cancer. (Special Issue on the IGFs and IGFbps in mammary gland development and breast cancer, **T.L.Wood** and D.Yee guest editors). *J. Mam. Gland Biol. & Neopl.* 5:1-5.
28. **Wood, T.L.**, Richert, M.M., Stull, M.A. and Allar, M.A. (2000) Insulin-like growth factors and insulin-like growth factor binding proteins during postnatal development of murine mammary glands. *J. Mam. Gland Biol. & Neopl.* 5:39-42.
29. **Wood, T.L.**, Rogler, L.E., Schuller, A., Czick, M. and Pintar, J.E. (2000) Selective alterations in organ sizes in mice with a targeted disruption of the IGF binding protein-2 gene. *Molecular Endocrinology* 14:1472-1482.

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30. Vannucci, S.J., Willing, L.B., Goto, S., Alkayed, N.J., Brucklacher, R.M., **Wood, T.L.**, Towfighi, J., Hurn, P.D. and Simpson, I.A. (2001) Experimental stroke in the female diabetic, *db/db*, mouse. *J. Cereb. Blood Flow Metab.* 21:52-60.
31. Jiang, F., Frederick, T.J. and **Wood, T.L.** (2001) IGF-I and FGF-2 synergize to stimulate oligodendrocyte progenitors to enter the cell cycle. *Dev. Biology* 232:414-423.
32. Ness, J.K., Romanko, M.J., Rothstein, R.P., **Wood, T.L.** and Levison, S.W. (2001) Perinatal hypoxia/ischemia induces apoptotic and excitotoxic death of periventricular white matter oligodendrocyte progenitors. *Dev. Neurosci.* 23:203-208.
33. Stull, M.A., Richert, M.M., Loladze, A.V. and **Wood, T.L.** (2002) Requirement for insulin-like growth factor-I in epidermal growth factor-mediated cell cycle progression of mammary epithelial cells. *Endocrinology* 143:1872-1879.
34. O'Donnell, S.L., Vannucci, S.J., Frederick, T.J., Krady, K. and **Wood, T.L.** (2002) IGF-I and microglial/macrophage proliferation in the ischemic mouse brain. *GLIA* 39:85-97.
35. Ness, J.K. and **Wood, T.L.** (2002) IGF-I but not NT-3 sustains Akt activation and provides long-term protection of immature oligodendrocytes from L-glutamate mediated apoptosis. *Mol. Cellular Neurosci.* 20:476-488.
36. Ness, J.K., Mitchell, N.E. and **Wood, T.L.** (2002) IGF-I and NT-3 signaling pathways in developing oligodendrocytes: Differential regulation and activation of receptors and the downstream effector Akt. *Dev. Neurosci.* 24:437-445.
37. Grimm, S.L., Teagroves, T.N., Kabotyanski, E.B., Hovey, R.C., Vonderhaar, B.K., Lydon, J.P., Miyoshi, K., Hennighausen, L., Ormandy, C.J., Lee, A.V., Stull, M.A., **Wood, T.L.** and Rosen, J.M. (2002) Disruption of steroid and prolactin receptor patterning in the mammary gland correlates with a block in lobuloalveolar development. *Mol. Endo.* 16:2675-2691.
38. **Wood, T.L.**, Stull, M.A., Kardash-Richardson, D. and Allar, M. (2003) The insulin-like growth factors in Mammary Development and Breast Cancer. In: Insulin-Like Growth Factors, ed. LeRoith, D., Zumkeller, W. and Baxter, R. (Kluwer Academic/Plenum Publishers, NY, NY), pp. 188-205.
39. Thompson, K., Menzies, S., Muckenthaler, M., Torti, F.M., **Wood, T.**, Torti, S.V., Hentze, M.W. Beard, J. and Connor, J. (2003) Mouse brains deficient in H-ferritin have normal iron concentration but a protein profile of iron deficiency and increased evidence of oxidative stress. *J. Neurosci. Res.* 71:46-63.
40. Stull, M.A. and **Wood, T.L.** (2003) Expression of IGF system components in the normal mammary gland. Invited Review, special edition on the Insulin-Like Growth Factors, D.Yee (Ed), *Breast Disease* 17:15-26.
41. Ness, J.K., Scaduto, R. and **Wood, T.L.** (2004) IGF-I prevents glutamate-mediated bax translocation and cytochrome c release in pro-oligodendroblasts. *GLIA* 46:183-194.

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42. Frederick, T.J. and **Wood, T.L.** (2004) IGF-I and FGF-2 coordinately enhance cyclin D1 and cyclin E-cdk2 association and activity to promote G₁ progression in oligodendrocyte progenitor cells. *Mol. Cellular Neurosci.* 25:480-492.
43. Heron-Milhavet, L., Xue-Jun, Y., Vannucci, S.J., **Wood, T.L.**, Willing, L.B., Stannard, B., Hernandez-Sanchez, C., Mobbs, C., Virsolvy, A. and LeRoith, D. (2004) Protection against hypoxic-ischemic injury in transgenic mice overexpressing KIR6.2 channel pore in forebrain. *Mol. Cellular Neurosci.* 25:585-593.
44. Stull, M.A., Rowzee, A.M., Loladze, A.V. and **Wood, T.L.** (2004) Growth factor regulation of cell cycle progression in mammary epithelial cells. *J. Mammary Gland Biol & Neoplasia* 9:15-22.
45. Allar, M.A. and **Wood, T.L.** (2004) Expression of the insulin-like growth factor binding proteins during postnatal development of murine mammary glands. *Endocrinology* 145:2467-2477.
46. **Wood, T.L.**, Frederick, T.J. and Ness, J.K. (2005) IGF-I and brain growth: Multifarious effects on developing neural cells and mechanisms of action. In: Research and Perspectives in Endocrine Interactions, Deciphering Growth, eds. Carel, J.-C., Kelly, P.A. and Christen, Y. (Springer-Verlag, Berlin Heidelberg), pp. 77-93.
46. Loladze, A.V., Stull, M.A., Rowzee, A.M., DeMarco, J., Lantry, J.H., III, Rosen, C., LeRoith, D., Wagner, K.-U., Hennighausen, Rosen, C.J. and **Wood, T.L.** (2006) Epithelial-specific and stage-specific functions of IGF-I during postnatal mammary development. *Endocrinology* 147:5412-5423. <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?>
47. Ning, Y., Hoang, B., Schuller, A.G.P., Hsu, P., **Wood, T.L.** and Pintar, J.E. (2007) Delayed mammary gland involution in mice with mutation of insulin-like growth factor binding protein 5. *Endocrinology* 148:2138-2147.
48. **Wood, T.L.**, Loladze, V., Altieri, S., Gangoli, N., Levison, S.W., Brywe, K.G., Mallard, C., and Hagberg, H. (2007) Delayed IGF-I administration rescues oligodendrocyte progenitors from glutamate induced cell death and hypoxic-ischemic brain damage. *Dev. Neurosci.* 29:302-310.
49. Frederick, T.J., Min, J., Altieri, S., Mitchell, N.E. and **Wood, T.L.** (2007) Synergistic induction of cyclin D1 in oligodendrocyte progenitor cells by IGF-I and FGF-2 requires differential stimulation of multiple signaling pathways. *GLIA* 55:1011-1022.
50. Romanelli, R.J., LeBeau, A.P., Fulmer, C., Lazzarino, D., Hochberg, A. and **Wood, T.L.** (2007) IGF type I receptor internalization and recycling mediate the sustained phosphorylation of Akt. *J. Biol. Chem.* 282:22513-22524.
51. Romanelli, R.J. and **Wood, T.L.** (2008) Directing traffic in neural cells: Determinants of receptor tyrosine kinase localization and cellular responses. *J. Neurochem.* 105:2055-2068.
53. DeMambro, V.E., Clemmons, D.R., Horton, L.G., Bouxsein, M.L., **Wood, T.L.**, Beamer, W.G., Canalis, E. and Rosen, C.J. (2008) Gender-specific changes in bone turnover and skeletal architecture in IGFBP-2 null mice. *Endocrinology* 149:2051-2061.

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