BIOGRAPHICAL SKETCH

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NAME: WOOD, TERESA L

eRA COMMONS USER NAME (credential, e.g., agency login): TLWOOD409

POSITION TITLE: Distinguished Professor, Rena Warshow Chair in MS

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

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Carleton College, Northfield, MN	BA	01/1978	Biology
UCLA, Los Angeles, CA	PHD	01/1987	Mol Neurobiology
SUNY, Stony Brook, NY	Postdoctoral Fellow	1988	Neuroendocrinology
Columbia University, New York, NY	Postdoctoral Fellow	1992	Mol. Development

A. Personal Statement

The long-term goal of my research program is to elucidate the mechanisms that regulate growth and differentiation of normal mammary epithelial cells, and to determine how alterations in signaling pathways impact breast cancer susceptibility, progression and the metastatic phenotype. I have long-standing expertise in insulin-like growth factor (IGF) and insulin signaling in mammary gland development and breast cancer. The IGF ligands, IGF-I and IGF-II, the IGF type 1 receptor (IGF-1R) and insulin receptor (IR) are essential mediators of normal mammary epithelial development in vivo, and have been implicated in the initiation and progression of human breast tumors. I have published over 40 peer-reviewed articles on IGF signaling specifically; 16 of these on mammary epithelial development and/or breast cancer. These studies have included investigations of IGF ligand and receptor function in mammary epithelial proliferation and differentiation both in vitro and in vivo. We have developed assays to determine relative expression of IGF and insulin signaling receptors in rodents and humans and have used these assays to understand expression of these receptors in mammary and human breast epithelium. Recently, we developed mouse models of IGF-1R signaling disruption or *Igf1r* deletion in combination with *MMTV-Wnt1* transgene expression in mammary epithelium to investigate the role of IGF-1R and IR signaling in a model of triple negative breast cancer. We have also initiated studies to identify gene expression modules in subtypes of human triple negative breast cancers with low IGF-1R expression that have similar profiles to our mouse models to develop novel gene signatures of aggressive, metastatic breast tumors.

Ongoing and recently completed projects I would like to highlight include:

R01 CA204312-04
Wood (PI)
01/01/2017-12/31/2021
Pathways that regulate basal and metastatic phenotypes in triple negative breast cancers

R37 NS082203-08
Wood (PI)
09/30/2017- 07/31/2024
The role of mTOR Signaling in Oligodendrocyte Differentiation and CNS Myelination

New Jersey Commission on Cancer Research
Wood (PI)
06/01/2022--5/31/2024
Novel IGF1R Function in Breast Tumor Metastasis

1. Obr, A., Chang, Y-J, Ciliento, V, Maingrette, K, Bulatowicz, J, LeMenze, A, Shang, Q, Gallagher, E, LeRoith, D and Wood, TL (2022) Breast tumor IGF-1R regulates cell-cell adhesion and metastasis:

Alignment of mouse single cell and human breast cancer transcriptomics. Frontiers in Oncology, 12:990398. ResearchTopic “Women in Breast Cancer Vol. II: 2022” doi: 10.3389/fonc.2022.990398.

2. Obr AE, Kumar S, Chang YJ, Bulatowicz JJ, Barnes BJ, Birge RB, Lazzarino DA, Gallagher E, LeRoith D, Wood TL. Insulin-like growth factor receptor signaling in breast tumor epithelium protects cells from endoplasmic reticulum stress and regulates the tumor microenvironment. Breast Cancer Res. 2018 Nov 20;20(1):138. PubMed Central PMCID: PMC6245538.
3. Rota LM, Wood TL. Crosstalk of the Insulin-Like Growth Factor Receptor with the Wnt Signaling Pathway in Breast Cancer. Front Endocrinol (Lausanne). 2015;6:92. PubMed Central PMCID: PMC4460810.
4. Rota LM, Albanito L, Shin ME, Goyeneche CL, Shushanov S, Gallagher EJ, LeRoith D, Lazzarino DA, Wood TL. IGF1R inhibition in mammary epithelia promotes canonical Wnt signaling and Wnt1-driven tumors. Cancer Res. 2014 Oct 1;74(19):5668-79. PubMed Central PMCID: PMC4782979.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2020 -	Distinguished Professor, Rena Warshow Chair in MS, New Jersey Medical School, Rutgers University
2013 - 2020	Professor, Rena Warshow Chair in MS, RBHS-NEW JERSEY MEDICAL SCHOOL
2005 - 2013	Professor, Rena Warshow Chair in MS, UNIV OF MED/DENT OF NJ-NJ MEDICAL SCHOOL
1993 - 2005	Asst-Assoc Professor, PENNSYLVANIA STATE UNIV HERSHEY MED CTR, Hershey, PA
1992 - 2003	Instructor, UNIV OF MED/DENT NJ-R W JOHNSON MED SCH, Piscataway, NJ

Honors

2017 - 2024	Javits Neuroscience Investigator Award (R37), NIH/NINDS
2019	Fellow, AAAS
2010	Excellence in Research Award, Foundation of UMDNJ
2005	University Professorship, UMDNJ
1999	Career Development Award, DOD Breast Cancer Res Program

C. Contribution to Science

1. IGF Signaling in Mammary Epithelial Growth: My laboratory has made important contributions to our understanding of IGF ligand and IGF receptor function in mammary epithelial growth and development. These data include our findings that: 1) IGF-I regulates cell cycle progression in mammary epithelial cells in coordination with EGF-related ligands, 2) IGF-I and IGF-II have distinct patterns of expression and are differentially regulated during mammary development, 3) IGF-II is expressed in a non-uniform pattern in mammary epithelium and is regulated by the transcription factor C/EBP-beta, 4) epithelial and stromally expressed IGF-I have distinct functions in postnatal mammary development, 5) the expression levels of the IGF-IR and ratio of IR-A:IR-B isoforms vary during specific stages of mammary development, and 6) the IGF-1R regulates mammary epithelial lineages in postnatal development and is important for alveolar proliferation during pregnancy-induced growth. The results of these studies demonstrated essential and complex roles for the IGF ligands and receptors in proliferation, ductal outgrowth, ductal branching, and alveolar development of mammary epithelium.

    a. Sun Z, Shushanov S, LeRoith D, Wood TL. Decreased IGF type 1 receptor signaling in mammary epithelium during pregnancy leads to reduced proliferation, alveolar differentiation, and expression of insulin receptor substrate (IRS)-1 and IRS-2. Endocrinology. 2011 Aug;152(8):3233-45. PubMed Central PMCID: PMC3138223.
    b. Rowzee AM, Ludwig DL, Wood TL. Insulin-like growth factor type 1 receptor and insulin receptor isoform expression and signaling in mammary epithelial cells. Endocrinology. 2009 Aug;150(8):3611-9. PubMed Central PMCID: PMC2717875.
    c. Loladze AV, Stull MA, Rowzee AM, Demarco J, Lantry JH 3rd, Rosen CJ, Leroith D, Wagner KU, Hennighausen L, Wood TL. Epithelial-specific and stage-specific functions of insulin-like growth factor-I

during postnatal mammary development. Endocrinology. 2006 Nov;147(11):5412-23. PubMed PMID: 16901968.

d. Stull MA, Richert MM, Loladze AV, Wood TL. Requirement for IGF-I in epidermal growth factor-mediated cell cycle progression of mammary epithelial cells. Endocrinology. 2002 May;143(5):1872-9. PubMed PMID: 11956170.

2. Assays for relative quantification of IGF receptor and IR isoforms in rodent and human tissues: A complication in the field of insulin and IGF signaling is the existence of multiple forms of signaling receptors through which insulin and the IGF ligands, IGF-I and IGF-II, exert biological actions. The levels of these receptors vary across cell types, tissues, developmental stages and pathological states. Thus, determining relative levels of the three receptors, IGF-1R, IR-A and IR-B is likely to have predictive value based on the specific "signature" of receptor expression. We developed a sensitive and specific QPCR assay to measure relative levels of the three IGF/insulin signaling receptors in mouse tissues and, recently, a variation on the assay to detect levels of these receptors in human tissues.

   a. Flannery CA, Saleh FL, Choe GH, Selen DJ, Kodaman PH, Kliman HJ, Wood TL, Taylor HS. Differential Expression of IR-A, IR-B and IGF-1R in Endometrial Physiology and Distinct Signature in Adenocarcinoma. J Clin Endocrinol Metab. 2016 Jul;101(7):2883-91. PubMed Central PMCID: PMC4929835.

   b. Flannery CA, Rowzee AM, Choe GH, Saleh FL, Radford CC, Taylor HS, Wood TL. Development of a Quantitative PCR Assay for Detection of Human Insulin-Like Growth Factor Receptor and Insulin Receptor Isoforms. Endocrinology. 2016 Apr;157(4):1702-8. PubMed Central PMCID: PMC4816738.

   c. Ziegler AN, Schneider JS, Qin M, Tyler WA, Pintar JE, Fraidenraich D, Wood TL, Levison SW. IGF-II promotes stemness of neural restricted precursors. Stem Cells. 2012 Jun;30(6):1265-76. PubMed Central PMCID: PMC5581406.

   d. Rowzee AM, Ludwig DL, Wood TL. Insulin-like growth factor type 1 receptor and insulin receptor isoform expression and signaling in mammary epithelial cells. Endocrinology. 2009 Aug;150(8):3611-9. PubMed Central PMCID: PMC2717875.

3. The IGF-1R in TNBC and Cross-talk with Wnt Signaling: It is critical to develop a clear understanding of the pathways and molecules that control tumor phenotypes to more effectively treat patients with breast cancer and to identify biomarkers of aggressive, metastatic tumor profiles. Our studies revealed the novel finding that reduced signaling through the IGF-1R in mammary epithelial cells in the MMTV-Wnt1 mouse model of TNBC 1) enhances the basal phenotype of the resulting tumors, and 2) alters the phenotype to a metastatic tumor. Recently, we demonstrated that signaling between epithelial cells with reduced IGF-1R signaling and the stroma alters the tumor microenvironment to enhance the metastatic phenotype in mouse models. Our ongoing investigations support the relevance of this model in a subtype of human TNBCs.

   a. Obr, A., Chang, Y-J, Ciliento, V, Maingrette, K, Bulatowicz, J, LeMenze, A, Shang, Q, Gallagher, E, LeRoith, D and Wood, TL (2022) Breast tumor IGF-1R regulates cell-cell adhesion and metastasis: Alignment of mouse single cell and human breast cancer transcriptomics. Frontiers in Oncology, 12:990398. ResearchTopic “Women in Breast Cancer Vol. II: 2022” doi: 10.3389/fonc.2022.990398.

   b. Obr AE, Kumar S, Chang YJ, Bulatowicz JJ, Barnes BJ, Birge RB, Lazzarino DA, Gallagher E, LeRoith D, Wood TL. Insulin-like growth factor receptor signaling in breast tumor epithelium protects cells from endoplasmic reticulum stress and regulates the tumor microenvironment. Breast Cancer Res. 2018 Nov 20;20(1):138. PubMed Central PMCID: PMC6245538.

   c. Rota LM, Wood TL. Crosstalk of the Insulin-Like Growth Factor Receptor with the Wnt Signaling Pathway in Breast Cancer. Front Endocrinol (Lausanne). 2015;6:92. PubMed Central PMCID: PMC4460810.

   d. Rota LM, Albanito L, Shin ME, Goyeneche CL, Shushanov S, Gallagher EJ, LeRoith D, Lazzarino DA, Wood TL. IGF1R inhibition in mammary epithelia promotes canonical Wnt signaling and Wnt1-driven tumors. Cancer Res. 2014 Oct 1;74(19):5668-79. PubMed Central PMCID: PMC4782979.

4. IGF/Insulin Signaling in Stem Cells: The insulin-like growth factors have long been associated with fetal growth and with fetal and neonatal brain growth. Unlike IGF-I that is a downstream mediator of growth

hormone on postnatal body growth, IGF-II has predominantly been considered a fetal growth factor. However, its high expression throughout the adult brain in the choroid plexus makes it a candidate for functioning in adult neural stem cell homeostasis. Our recent studies strongly support a distinct function for IGF-II in maintenance of neural stem cells in vitro and in vivo in both the sub ventricular zone and sub granular zone of the adult brain.

a. Chidambaram S, Velloso FJ, Rothbard DE, Deshpande K, Cajuste Y, Snyder KM, Fajardo E, Fiser A, Tapinos N, Levison SW, Wood TL. Subventricular zone adult mouse neural stem cells require insulin receptor for self-renewal. Stem Cell Reports. 2022 Jun 14;17(6):1411-1427. PubMed Central PMCID: PMC9213826.
b. Ziegler AN, Feng Q, Chidambaram S, Testai JM, Kumari E, Rothbard DE, Constancia M, Sandovici I, Cominski T, Pang K, Gao N, Wood TL, Levison SW. Insulin-like Growth Factor II: An Essential Adult Stem Cell Niche Constituent in Brain and Intestine. Stem Cell Reports. 2019 Apr 9;12(4):816-830. PubMed Central PMCID: PMC6450461.
c. Ziegler AN, Levison SW, Wood TL. Insulin and IGF receptor signalling in neural-stem-cell homeostasis. Nat Rev Endocrinol. 2015 Mar;11(3):161-70. PubMed Central PMCID: PMC5513669.
d. Ziegler AN, Schneider JS, Qin M, Tyler WA, Pintar JE, Fraidenraich D, Wood TL, Levison SW. IGF-II promotes stemness of neural restricted precursors. Stem Cells. 2012 Jun;30(6):1265-76. PubMed Central PMCID: PMC5581406.

5. My lab has been at the forefront of the field for understanding the function of the mammalian target of rapamycin (mTOR) signaling in oligodendrocyte differentiation and myelination. Our initial studies in this field were designed to understand the function of IGF signaling and downstream PI3K/Akt pathways in oliogodendrocyte progenitor proliferation and survival. We then expanded our investigations into downstream pathways that regulate oligodendrocyte differentiation. We demonstrated that mTOR promotes differentiation of oligodendrocytes from their progenitor cells in vitro and in a genetic mouse model. We have recently identified specific targets of mTOR including the bone morphogenetic signaling pathway and cytoskeleton the mediate oligodendrocyte differentiation and maturation. Finally, we revealed a difference in how mTOR regulates developmental myelination in brain and spinal cord.

a. Khandker L, Jeffries MA, Chang YJ, Mather ML, Evangelou AV, Bourne JN, Tafreshi AK, Ornelas IM, Bozdagi-Gunal O, Macklin WB, Wood TL. Cholesterol biosynthesis defines oligodendrocyte precursor heterogeneity between brain and spinal cord. Cell Rep. 2022 Mar 1;38(9):110423. PubMed Central PMCID: PMC8988216.
b. Jeffries MA, McLane LE, Khandker L, Mather ML, Evangelou AV, Kantak D, Bourne JN, Macklin WB, Wood TL. mTOR Signaling Regulates Metabolic Function in Oligodendrocyte Precursor Cells and Promotes Efficient Brain Remyelination in the Cuprizone Model. J Neurosci. 2021 Oct 6;41(40):8321-8337. PubMed Central PMCID: PMC8496195.
c. Ornelas IM, Khandker L, Wahl SE, Hashimoto H, Macklin WB, Wood TL. The mechanistic target of rapamycin pathway downregulates bone morphogenetic protein signaling to promote oligodendrocyte differentiation. Glia. 2020 Jun;68(6):1274-1290. PubMed Central PMCID: PMC7368967.
d. Musah AS, Brown TL, Jeffries MA, Shang Q, Hashimoto H, Evangelou AV, Kowalski A, Batish M, Macklin WB, Wood TL. Mechanistic Target of Rapamycin Regulates the Oligodendrocyte Cytoskeleton during Myelination. J Neurosci. 2020 Apr 8;40(15):2993-3007. PubMed Central PMCID: PMC7141876.