OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: BLOBE, GERARD CONRAD

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-4274-8901

Position Title: PROFESSOR

Organization and Location: Duke University, Durham, North Carolina, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Dana Farber Cancer Institute, Boston, Massachusetts, United States	Fellow	07/1997	06/2000	Medical Oncology
Brigham and Women's Hospital, Boston, Massachusetts, United States	Resident	06/1995	06/1997	Internal Medicine
Duke University, Durham, North Carolina, United States	Doctor of Medicine (MD)	08/1988	05/1995	Medicine
Duke University, Durham, North Carolina, United States	Doctor of Philosophy (PHD)	08/1988	05/1995	Cell Biology
University of Notre Dame, South Bend, Indiana, United States	Bachelor of Science (BS)	08/1984	05/1988	Biochemistry

Appointments and Positions

2000 - present	PROFESSOR, Duke University, Durham, North Carolina, United States
2017 - present	Associate Director of Training and Education, Duke University, Durham, North Carolina, United States
2012 - present	Professor of Medicine, Pharmacology and Cancer Biology, Duke University, Durham, North Carolina, United States
2006 - 2012	Associate Professor of Medicine, Pharmacology and Cancer Biology, Duke University, Durham, North Carolina, United States
2000 - present	Professor of Medicine, Pharmacology and Cancer Biology, Duke University, Durham, North Carolina, United States
2000 - 2006	Assistant Professor of Medicine, Pharmacology and Cancer Biology, Duke Universit, Durham, North Carolina, United States

Products

Products Closely Related to the Proposed Project

1. Huang JJ, Corona AL, Dunn BP, Cai EM, Prakken JN, Blobe GC. Increased type III TGF-β receptor shedding decreases tumorigenesis through induction of epithelial-to-mesenchymal transition. Oncogene. 2019 May;38(18):3402-3414. PubMed Central PMCID: PMC6586422.
2. Tian H, Liu J, Chen J, Gatza ML, Blobe GC. Fibulin-3 is a novel TGF-β pathway inhibitor in the breast cancer microenvironment. Oncogene. 2015 Nov 5;34(45):5635-47. PubMed Central PMCID: PMC4589427.
3. Tian H, Mythreye K, Golzio C, Katsanis N, Blobe GC. Endoglin mediates fibronectin/α5β1 integrin and TGF-β pathway crosstalk in endothelial cells. EMBO J. 2012 Oct 3;31(19):3885-900. PubMed Central PMCID: PMC3463850.
4. Mythreye K, Blobe GC. The type III TGF-beta receptor regulates epithelial and cancer cell migration through beta-arrestin2-mediated activation of Cdc42. Proc Natl Acad Sci U S A. 2009 May 19;106(20):8221-6. PubMed Central PMCID: PMC2688894.
5. Zhang M, Chen J, Leupold MC, Guo J, Shen X, Shirley CA, Khella CA, Mehta RN, O'Brien ET, Gatza ML, Blobe GC. Loss of ALK4 promotes cancer progression through regulating TGF-β receptor N-glycosylation. Nat Commun. 2025 Dec

17;17(1):854. PubMed Central PMCID: PMC12828005.

Other Significant Products Highlighting Contributions to Science

1. Mythreye K, Knelson EH, Gatza CE, Gatza ML, Blobe GC. TβRIII/β-arrestin2 regulates integrin α5β1 trafficking, function, and localization in epithelial cells. Oncogene. 2013 Mar 14;32(11):1416-27. PubMed Central PMCID: PMC3835656.
2. Dong M, How T, Kirkbride KC, Gordon KJ, Lee JD, Hempel N, Kelly P, Moeller BJ, Marks JR, Blobe GC. The type III TGF-beta receptor suppresses breast cancer progression. J Clin Invest. 2007 Jan;117(1):206-17. PubMed Central PMCID: PMC1679965.
3. Chen W, Kirkbride KC, How T, Nelson CD, Mo J, Frederick JP, Wang XF, Lefkowitz RJ, Blobe GC. Beta-arrestin 2 mediates endocytosis of type III TGF-beta receptor and down-regulation of its signaling. Science. 2003 Sep 5;301(5638):1394-7. PubMed PMID: 12958365.
4. Knelson EH, Gaviglio AL, Nee JC, Starr MD, Nixon AB, Marcus SG, Blobe GC. Stromal heparan sulfate differentiates neuroblasts to suppress neuroblastoma growth. J Clin Invest. 2014 Jul;124(7):3016-31. PubMed Central PMCID: PMC4071405.
5. Knelson EH, Gaviglio AL, Tewari AK, Armstrong MB, Mythreye K, Blobe GC. Type III TGF-β receptor promotes FGF2-mediated neuronal differentiation in neuroblastoma. J Clin Invest. 2013 Nov;123(11):4786-98. PubMed Central PMCID: PMC3809791.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

Certified by BLOBE, GERARD CONRAD in SciENcv on 2026-08-19 14:11:12

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: BLOBE, GERARD CONRAD

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-4274-8901

Position Title: PROFESSOR

Organization and Location: Duke University, Durham, North Carolina, United States

Personal Statement

One of the aspects of a career in academic medicine that I truly cherish and embrace is the opportunity to interact with, teach, train and mentor the next generation of scientists and physician-scientists. Over the past 15 years, I have had a total of 102 trainees come through the lab, including 32 undergraduates, 16 graduate students, and 20 post-doctoral associates many of whom have moved onto other positions in academia, including prior K99 awardees Nam Lee (U. of Arizona, R01 funded) and Nadine Hempel (Pitt, R01 funded), prior K08 awardee Brent Hanks (UNC-CH, R01 funded) and Mythreye Karthikeyan (UAB, R01 funded). I have been actively involved in the training of graduate students through the Department of Pharmacology and Cancer Biology and the Programs of Cellular and Molecular Biology, Molecular Cancer Biology, and Developmental Biology, with 36 graduate students rotating through the lab, 16 graduate students joining the lab, and 16 students completing their dissertation research. In addition to mentoring those within the lab, I have been involved in mentoring and training within the broader Duke University community. I currently serve as the Associate Director for Training and Education for the Duke Cancer Institute, directing and coordinating all cancer related training and education across the training continuum. I have also been active in the Medical Scientist Training Program, serving on the Admissions and Steering Committee of the program. I have been involved in teaching, with lectures to the graduate students, medical students and medical residents and fellows each year. In terms of my research, I have a long-standing interest and expertise in TGF-beta superfamily signaling, with a specific focus on cancer biology and effects of the TGF-beta superfamily co-receptors, endoglin and TbetaRIII, on signaling and the tumor microenvironment, including their immunomodulatory roles. As a physician scientist, I am particularly interested in moving forward the state of knowledge in the TGF-beta superfamily signaling field so that these pathways can be better utilized as prognostic biomarkers or as therapeutic targets, including in conjunction with immunotherapy. As a principal investigator, I have had a track record of productivity in the area of the TGF-beta superfamily signaling field in general, including publications in The EMBO J, The JCI, Mol Biol Cell, JNCI, Oncogene, and Cancer Research. Finally, I have had consistent funding from the NCI (7 R01s, 1 R21) and well as from foundations (Komen, AHA, ACS) for the past 26 years, with current funding from the NCI and NIGMS. Overall, my experience in cancer research, research training, and mentorship make me ideally suited to serve as a mentor for the teacher/undergraduate mentored research experiences included in this R25 project.

Honors

2023 - 2023	Fellow, American Association for the Advancement of Science
2012 - 2017	Associate Editor, The Journal of Clinical Investigation
2010 - 2016	Susan G. Komen Scholar, Susan G. Komen for the Cure
2009 - 2014	Editorial Board, The Journal of Biological Chemistry
2008 - 2008	American Society of Clinical Investigation, American Society of Clinical Investigation
2005 - 2005	Gertrude B. Elion Cancer Research Award, AACR
2002 - 2002	V Foundation Scholar Award, V Foundation
1998 - 2000	Postdoctoral Research Fellowship from the Howard Hughes Medical Institute, Howard Hughes Medical Institute

Contributions to Science

1. **Defined the role of the type III transforming growth factor-beta (TGF-beta) receptor (Tbeta RIII) in human cancers.**TbetaRIII is a TGF-beta superfamily co-receptor. Despite being the most abundant and ubiquitously expressed TGF-beta superfamily receptor, its role in signaling and cancer biology had represented long-standing challenges in the field. My laboratory established that while TbetaRIII is not mutated in human cancers, loss of TbetaRIII expression is a frequent event in broad spectrum of human cancers, including cancers of the breast, lung, ovary, pancreas and prostate. We established that TbetaRIII loss is mediated by loss of the TGFBR3 genomic locus, epigenetic silencing and transcriptional silencing by elevated levels of TGF-beta in advanced tumors. Functionally, my laboratory has demonstrated that loss of TbetaRIII expression contributes to

cancer progression, by (1) disrupting the polarity of epithelial cells, (2) enhancing the motility and invasiveness of cancer cells and (3) promoting an immunotolerant tumor microenvironment, through loss of soluble TbetaRIII production in the tumor microenvironment. These studies are currently being translated into a clinical trial of a TGF-beta inhibitor delivered in conjunction with immunotherapy. (Dong, JCI, 2007)

2. **Defined significant roles for TbetaRIII in regulating the cell surface expression, endocytosis and signaling of TGF-beta superfamily signaling receptors in addition to mediating TGF-beta superfamily receptor independent signaling.** The abundantly expressed TGF-beta superfamily coreceptor, TbetaRIII, had been characterized as a ligand binding receptor, which functioned to present ligand to the "signaling" type II TGF-beta receptor (TbetaRII). My laboratory established that the short, conserved cytoplasmic domain of TbetaRIII mediates interactions with the scaffolding proteins, GIPC and beta-arrestin2, with the interaction with GIPC stabilizing the receptors on the cell surface and enhancing their signaling, and the interaction with beta-arrestin2 resulting in receptor internalization and downregulation of signaling. We have further established that TbetaRIII interacts with both TGF-beta and bone morphogenetic protein (BMP) receptors, to regulate their trafficking and signaling. We also defined TbetaRIII as a BMP co-receptor. Finally, we have established that TbetaRIII regulates signaling beyond TGF-beta superfamily signaling, including activating Cdc42 to regulated directed cell migration, interacting with alpha5beta1 integrin to regulate its trafficking and signaling, and interacting with fibroblast growth factor (FGF2) and its receptors to enhance FGF signaling. (Chen et al, Science, 2003; Mythreye et al, Oncogene, 2013)

3. **Defined roles and mechanisms regulating endoglin and ALK1 signaling and vascular biology.** The TGF-beta superfamily co-receptor, endoglin, and the type I TGF-beta superfamily receptor, ALK1, are mutated in the human disease, hereditary hemorrhagic telangiectasia, and have essential roles in angiogenesis. Endoglin was known to bind TGF-beta superfamily ligands when in complex with TGF-beta superfamily receptors, while ALK1 was known to complex with endoglin and signal to BMP Smads. However, how endoglin and ALK1 contributed to angiogenesis and vascular disease was unknown. My laboratory established that the short, conserved cytoplasmic domain of endoglin mediates interactions with the scaffolding proteins, GIPC and beta-arrestin2, with the interaction with GIPC promoting signaling to Smad1/5/8 and PI3K/Akt to inhibit endothelial cell migration, and the interaction with beta-arrestin2 resulting in receptor internalization, downregulation of ERK signaling to inhibit endothelial cell migration. We have also established that endoglin interacts with alpha5beta1 integrin to regulating its trafficking, with the crosstalk between these pathways regulating TGF-beta1 responses and developmental angiogenesis. Finally, we have established how ALK-1 is regulated, including regulation by interaction with LXRbeta and CK2beta.

4. **Defined roles for heparan sulfate proteoglycan co-receptors, including TbetaRIII, glypicans and syndecans as promoters of FGF-mediated neuroblast differentiation, and heparin derivatives as novel differentiating agents for neuroblastoma patients.** Neuroblastoma is a common and deadly pediatric cancer. While increased stromal content was known to indicate a better prognosis for neuroblastoma patients and to promote the differentiation of neuroblastoma cells, the mechanism for these effects was unknown. My laboratory established that expression of heparan sulfate proteoglycan co-receptors, including TbetaRIII, glypicans and syndecans, was suppressed in neuroblastoma, but that these were abundantly expressed in the stroma. We further established that the shed extracellular domains of these proteins functioned to increase FGF-mediated neuroblast differentiation, and decrease neuroblastoma growth and progression in preclinical models. Finally, we defined desulfated heparin analogues that could mimic the effect of heparan sulfate proteoglycan co-receptors on FGF signaling and neuroblastoma differentiation, thus suppressing tumor growth and metastasis without anticoagulation. These studies provide a rationale for using a heparin analogue as a differentiating agent in neuroblastoma patients. (Knelson, JCI 2013; Knelson, JCI 2014)

5. **Defined the role of a cancer cell's biomechanical properties in dictating its migratory and invasive properties.** While it was known that tumor tissue is stiffer than normal tissue, while tumor cells are less stiff than their normal counterparts, in a multi-disciplinary collaboration with the Rich Superfine laboratory at UNC-Chapel Hill, we were the first to demonstrate that cancer cells have a range of mechanical stiffness, with their stiffness inversely correlating with their invasive and metastatic potential. These studies demonstrated that mechanical phenotypes can be used to grade the metastatic potential of cell populations with the potential for single cell grading. We further demonstrated that during epithelial-to-mesenchymal transition (EMT), the mechanical stiffness and response to force of cancer cells decreased, with these effects mediated by suppression of the RhoA guanine nucleotide exchange factors (GEFs) LARG and GEF-H1.

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