NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Antalis, Toni M.

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-0132-6171

Position Title: Professor

Organization and Location: University of Maryland School of Medicine, Baltimore, Maryland, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Baylor College of. Medicine, Houston, Texas, United States	Postdoctoral Fellow	05/1981	09/1982	Cell Biology
Rice University, Houston, Texas, United States	Doctor of Philosophy (PHD)	09/1975	05/1981	Biochemistry
Furman University, Greenville, Texas, United States	Bachelor of Science (BS)	09/1971	05/1975	Chemistry

Appointments and Positions

2004 - present Professor, University of Maryland School of Medicine, Baltimore, Maryland, United States
2014 - present Associate Director of Training and Education, University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, Maryland, United States
2013 - present Research Health Scientist, VA Maryland Health Care System, Baltimore, Maryland, United States
2005 - present Associate Director, Center for Vascular Biology and Inflammatory Diseases, University of Maryland School of Medicine, Baltimore, Baltimore, Maryland, United States

Products

Products Closely Related to the Proposed Project

1. Strong AA, Buzza MS, Antalis TM. Protease-Activated Receptor-2 Promotes Metastasis: An Emerging Therapeutic Target. Mol Cancer Res. 2026 Apr 2;24(4):207-220. PubMed Central PMCID: PMC13040814.
2. Pawar NR, Buzza MS, Duru N, Strong AA, Antalis TM. Matriptase drives dissemination of ovarian cancer spheroids by a PAR-2/PI3K/Akt/MMP9 signaling axis. J Cell Biol. 2023 Nov 6;222(11) PubMed Central PMCID: PMC10515437.
3. Welch DR, Antalis TM, Burnstein K, Vona-Davis L, Jensen RA, Nakshatri H, Riegel AT, Spitz DR, Watson DK, Weiner GJ. Essential Components of Cancer Education. Cancer Res. 2015 Dec 15;75(24):5202-5. PubMed Central PMCID: PMC4681646.
4. Keith , Welch , Agarwal , Blair , Chukwudozie , Shevde , Boise , Burnstein , Antalis , O?Connor , Dalal , Ellis , Nakshatri . Challenges and opportunities in training cancer researchers. Nature Cancer. 2025; 6(2):223-225. DOI: 10.1038/s43018-024-00872-4
5. Duru N, Pawar NR, Martin EW, Buzza MS, Conway GD, Lapidus RG, Liu S, Reader J, Rao GG, Roque DM, Leppla SH, Antalis TM. Selective targeting of metastatic ovarian cancer using an engineered anthrax prodrug activated by membrane-anchored serine proteases. Proc Natl Acad Sci U S A. 2022 Jul 12;119(28):e2201423119. PubMed Central PMCID: PMC9282395.

Other Significant Products Highlighting Contributions to Science

1. Conway GD, Buzza MS, Martin EW, Duru N, Johnson TA, Peroutka RJ, Pawar NR, Antalis TM. PRSS21/testisin inhibits ovarian tumor metastasis and antagonizes proangiogenic angiopoietins ANG2 and ANGPTL4. J Mol Med (Berl). 2019 May;97(5):691-709. PubMed Central PMCID: PMC6513752.
2. Antalis TM, Conway GD, Peroutka RJ, Buzza MS. Membrane-anchored proteases in endothelial cell biology. Curr Opin Hematol. 2016 May;23(3):243-52. PubMed Central PMCID: PMC4882107.
3. Driesbaugh KH, Buzza MS, Martin EW, Conway GD, Kao JP, Antalis TM. Proteolytic activation of the protease-activated receptor (PAR)-2 by the glycosylphosphatidylinositol-anchored serine protease testisin. J Biol Chem. 2015 Feb 6;290(6):3529-

41. PubMed Central PMCID: PMC4319020.

4. Martin E.W., Buzza M.S., Driesbaugh K.H., Liu S., Fortenberry Y.M., Leppla S.H., Antalis T.M.. Targeting the membrane-anchored serine protease testisin with a novel engineered anthrax toxin prodrug to kill tumor cells and reduce tumor burden. Oncotarget. 2015; 6(32):33534-33553. DOI: 10.18632/oncotarget.5214
5. Kessler MD, Pawar NR, Martin SS, Antalis TM, O'Connor TD. Improving Cancer Detection and Treatment with Liquid Biopsies and ptDNA. Trends Cancer. 2018 Sep;4(9):643-654. PubMed Central PMCID: PMC6116552.

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 Antalis, Toni M. in SciENcv on 2026-05-11 11:06:38

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Antalis, Toni M.

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-0132-6171

Position Title: Professor

Organization and Location: University of Maryland School of Medicine, Baltimore, Maryland, United States

Personal Statement

I bring the leadership, experimental expertise, and sustained commitment to training necessary to lead the Cancer Research Training and Education Coordination (CRTEC) Core within the University of Maryland Greenbaum Cancer Center Support Grant (CCSG). My research program integrates fundamental mechanistic discovery with translational innovation, while maintaining a strong emphasis on rigorous experimental design and trainee development.

Scientifically, my work centers on tumor metastasis and vascular biology, with a particular focus on protease-induced signaling pathways in cancer progression. My laboratory investigates membrane-anchored serine proteases (MASPs) and their inhibitors as key regulators of cellular signaling in normal physiology and disease. We were among the first to define the functional significance of multi-domain serine proteases anchored to the plasma membrane via transmembrane domains or GPI anchors. Our studies demonstrated that specific MASPs disrupt cell–cell adhesion to promote pro-metastatic spheroid formation, mesothelial adhesion, and sub-mesothelial invasion through activation of matriptase-PAR-2 signaling. More recently, we discovered that chemotherapy can inadvertently stimulate MASP activation, enhancing metastatic dissemination—revealing an important and previously unrecognized gap in our understanding of anti-mitotic chemotherapeutics. These mechanistic insights have enabled translational advances, including the development of MASP-activated prodrug biologics, resulting in two U.S. patents and peer-reviewed publications.

Equally central to my career is a sustained and demonstrated commitment to mentoring and workforce development. As Associate Director of CRTEC since its inception, I oversee initiatives that promote rigorous, reproducible research training across educational levels. I am also co-director of a long-standing, 14-year NCI–funded T32 Training Program in Cancer Biology. Through these activities, I have developed structured mentoring frameworks that emphasize experimental rigor, professional development, and career advancement.

I have directly mentored over 40 trainees, including undergraduate students, graduate students, postdoctoral fellows, and junior faculty. Many of these individuals have secured competitive funding, obtained academic appointments, or advanced into leadership positions in research-intensive careers. My mentoring philosophy emphasizes scientific independence, critical thinking, and reproducibility, ensuring that trainees are well prepared to lead their own programs.

My national leadership experience further supports my role in leading the CRTEC office. I have served as a member of the Board for the Cancer Biology Training Consortium (CABTRAC) and as former President of CABTRAC. I was elected President (2020–2022) and subsequently Past-President (2022–2024) of the 13,000 member American Society for Biochemistry and Molecular Biology (ASBMB), where I led initiatives in scientific advocacy, training, workforce development and community building. I have also served extensively as a reviewer and panel member for the National Institutes of Health, on journal editorial boards, and on conference organizing committees in the field of proteolysis.

Together, my scientific expertise in cancer biology and metastasis, my translational experience, and my sustained leadership in training and mentoring position me to effectively lead and further develop CRTEC within our Cancer Center.

Honors

2025	Keynote Speaker, ASBMB Conference - Nucleophilic Proteases: Structure, function, regulation and disease
2025	Study Section Reviewer, NIH Mechanisms of Cancer Therapeutics (C) Study Section (MCTC)
2024	Fellow of the ASBMB, American Society for Molecular Biology and Biochemistry
2024	Keynote Speaker, 18th Annual Earl W. Davie Symposium, Centre for Blood Research, University of British Columbia
2022	Voting Member (current), Federation of American Societies for Experimental Biology (FASEB) Finance Committee

2020 - 2024	President, Past President, American Society for Molecular Biology and Biochemistry (ASBMB)
2019	Study Section Reviewer, NCI SEP ZCA1 RTRB-U
2018	Study Section Reviewer, DoD CDMRP Ovarian Cancer Research Program
2018	Voting Member (current), Veterans Administration Baltimore Research and Development Committee
2017	Keynote Speaker, ASBMB Special Symposia on Membrane Anchored Serine Proteases
2017	Study Section Reviewer, HEMA, Veterans Administration
2017 - 2022	Study Section Reviewer, NHLBI Institutional Training Mechanism Review Committee – T32 (NITMR)
2011	co-Director, T32 Training Program in Cancer Biology - NIH/NCI T32CA154274 (current), NIH
2010	President (2014-2015); Board of Directors, Chair CRTEC Committee (current), Cancer Biology Training Consortium (CABTRAC)
2010 - 2023	Director, Graduate Program in Molecular Medicine, University of Maryland Baltimore

Contributions to Science

1. **Membrane anchored serine proteases (MASPs) in ovarian cancer -**

   These studies focus on proteolytic cascades that regulate inflammation, vascular biology, angiogenesis, and cancer. This work has revealed novel insights into proteolytic mechanisms that control cell-cell interactions and is leading to a more complete understanding of blood vessel formation, angiogenesis and tumor metastasis. My laboratory originally cloned and characterized testisin (PRSS21) as a unique, glycosyl-phosphatidylinositol (GPI) membrane anchored, trypsin-like serine protease overexpressed in ovarian cancers. We succeeded in producing the first testisin gene knockout mouse model and showed that testisin deficiency results in damaged spermatocytes, fragile sperm, and impairments in male fertility. Testisin has the characteristics of a cancer/testis antigen, a group of proteins whose expression is normally restricted to testis but are frequently aberrantly activated in tumors. A proteolytic target of testisin is the G-protein coupled, seven transmembrane receptor, protease activated receptor type 2 (PAR-2). Testisin uniquely induces the loss of cell surface PAR-2 and and alters PAR-2 biased signaling. This was the first demonstration of the activation of a PAR by a serine protease GPI-linked to the cell surface. I serve as the principal investigator in these efforts.

2. **Selective targeting of metastatic ovarian cancer using an engineered anthrax prodrug activated by membrane-anchored serine proteases –**

   Treatments for advanced and recurrent ovarian cancer remain a challenge due to a lack of potent, selective, and effective therapeutics. We are developing therapies based on the pro-metastatic activities of membrane-anchored serine proteases (MASPs). We have engineered a potentially transformative anticancer strategy based on anthrax toxin that is selectively activated by the catalytic power of zymogen-activating proteases on the surface of malignant tumor cells to induce cell death. Exposure to the engineered toxin is cytotoxic to ovarian tumor cell lines and ovarian tumor spheroids derived from patient ascites. Preclinical studies demonstrate that toxin treatment induces tumor regression in several in vivo ovarian cancer models, including patient-derived xenografts, without adverse side effects, supportive of progression toward clinical evaluation. These data lay the groundwork for developing therapeutics for treating women with late-stage and recurrent ovarian cancers, utilizing a mechanism distinct from current anticancer therapies. I serve as the principal investigator in these efforts.

3. **MASPs in epithelial and endothelial barrier functions and angiogenesis -**

   This research is focused on determining how protease-mediated signaling maintains the function of epithelial and endothelial barriers, thereby regulating inflammation and cancer metastasis. Our studies have revealed that matriptase, a MASP encoded by the suppression of tumorigenicity-14 (ST14) gene, is required for epithelial barrier homeostasis. These studies, using the ST14 hypomorphic mouse model of matriptase deficiency, have uncovered that the matriptase barrier forming pathway is down-regulated at the transcriptional and protein levels by cytokines produced during inflammatory colitis. Further, matriptase acts downstream of prostasin in a protease catalytic cascade to mediate barrier formation, and we find that both proteases are coordinately regulated. We demonstrated for the first time that matriptase and not prostasin is the primary effector protease of tight junction assembly in simple columnar epithelia, highlighting a novel spatial and tissue-specific aspect of cell surface proteolytic cascades. In addition we discovered novel roles for the glycosylphosphatidylinositol (GPI)-anchored serine protease testisin in the regulation of pericellular hemostasis. We found that the expression of catalytically active testisin on the cell surface accelerates thrombin-dependent fibrin polymerization, and intriguingly, that it subsequently promotes accelerated fibrinolysis. This work has implications for angiogenesis, cancer biology, and male fertility. The idea of MASPs as essential for formation of epithelial and endothelial barrier functions is innovative because proteases are traditionally recognized as barrier disrupting enzymes. I serve as the principal investigator in these efforts.

4. Discovery and elucidation of the biological functions of plasminogen activator inhibitor-2 (PAI-2) during venous thrombus resolution -

   Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is an exceedingly common and serious problem with complications that are a significant source of morbidity and mortality . Maladaptive thrombus resolution and its complications frequently lead to post-thrombotic syndrome (PTS), which causes pain, swelling and ulceration in 25-60% of DVT patients. Current therapies rely on anticoagulants, which do not enhance resolution of existing clots, but only prevent further clot development. There is an urgent unmet need for new therapies based on a better understanding of this process. The pathological course of DVT resolution is modulated by inflammation, through the activation of endothelial cells, platelets, and leukocytes, including neutrophils, monocytes, macrophages and T-cells. We have discovered several novel interacting cell and molecular pathways that are involved in venous thrombus resolution with potential to be developed into therapies to accelerate this process. Of unique significance, we discovered a function for PAI-2 as a critical modulator of venous thrombus resolution. PAI-2 deficiency increases the levels of active urokinase-plasminogen activator in venous thrombi by over 12-fold, enabling significant fibrinolysis required for thrombus resolution. The mechanism we have uncovered involves aseptic neutrophil functions that are underappreciated in this field. Our overall strategy is based on antagonism of natural inhibitors of thrombus resolution, and promises to be highly effective to accelerate the process to prevent and/or limit valvular damage. and enable novel pharmacologic targets that can reduce the risk of PTS and recurrent thromboembolism - clinical problems highly significant to patients. I serve as the principal investigator in these efforts.

5. Synthesizing progress and knowledge in the protease field through invited review articles- Our laboratory is regularly solicited to comment on progress in this burgeoning field of membrane anchored serine proteases through review articles and commentaries that are peer-reviewed. Examples include:

   a. Hooper JD, Clements JA, Quigley JP, Antalis TM. Type II transmembrane serine proteases. Insights into an emerging class of cell surface proteolytic enzymes. J Biol Chem. 2001;276(2):857–60. PubMed PMID: 11060317.

   b. Antalis TM, Buzza MS, Hodge KM, Hooper JD, Netzel-Arnett S. The cutting edge: membrane-anchored serine protease activities in the pericellular microenvironment. Biochem J. 2010 Jun 15;428(3):325–46. PubMed PMID: 20507279; PMCID: PMC3680374.

   c. Pawar NR, Buzza MS, Antalis TM. Membrane-Anchored Serine Proteases and Protease-Activated Receptor-2-Mediated Signaling: Co-Conspirators in Cancer Progression. Cancer Res. 2019 Jan 15;79(2):301-310. Review. PubMed PMID: 30610085; PMCID: PMC6335149.

   d. Antalis TM, Buzza MS, Pawar N. Extracellular: Plasma Membrane Proteases – Serine Proteases. MS. 10076. In: Ralph A Bradshaw, Gerald W Hart and Philip D Stahl (Editors-in-Chief), Encyclopedia of Cell Biology, 2021, Vol 1, Waltham, MA: Academic Press.

   e. Strong, AA, Buzza, MS, Antalis TM. Protease activated Receptor-2 (PAR-2) – a target for anti-metastasis therapies. under review.

   PATENTS

   • U.S. Patent Number 10,568,929 “Engineered Anthrax Protective Antigen Proteins for Cancer Therapy” issued on February 25, 2020. Inventors: T.M. Antalis, E Martin.

   • US Patent Number 11,013,784 “Engineered Anthrax Protective Antigen Proteins for Cancer Therapy” issued on May 25, 2021. Inventors: T.M. Antalis, E Martin.(US Div)

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