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

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Cross, Janet V

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-9528-0812

Position Title: Associate Dean for Graduate and Medical Scientist Programs

Organization and Location: University of Virginia School of Medicine, Charlottesville, Virginia, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Case Western Reserve University, Cleveland, Ohio, United States	Postdoctoral Fellow	05/2000	02/2002	Cancer Biology
Case Western Reserve University, Cleveland, Ohio, United States	Doctor of Philosophy (PHD)	08/1992	05/2000	Molecular Biology and Microbiology
State University of New York College at Fredonia, Fredonia, New York, United States	Bachelor of Science (BS)	08/1990	05/1992	Recombinant Gene Technology, Medical Technology
Jefferson Community College, Watertown, New York, United States	Associate in Applied Science (AAS)	08/1988	05/1990	Medical Laboratory Technology

Appointments and Positions

2020 - present	Associate Dean for Graduate and Medical Scientist Programs, University of Virginia School of Medicine, Charlottesville, Virginia, United States
2020 - present	Harrison Distinguished Associate Professor of Medical Education and Pathology, University of Virginia Shool of Medicine, Charlottesville, Virginia, United States
2016 - 2020	Assistant Dean for Graduate Research and Training, University of Virginia School of Medicine, Charlottesville, Virginia, United States
2015 - 2016	Interim Assistant Dean for Graduate Research and Training, University of Virginia School of Medicine, Charlottesville , Virginia, United States
2014 - present	Associate Professor of Pathology, University of Virginia School of Medicine, Charlottesville, Virginia, United States
2010 - 2020	Director of Graduate Studies, Experimental Pathology PhD Program, University of Virginia School of Medicine/Pathology, Charlottesville, Virginia, United States
2008 - 2014	Assistant Professor, University of Virginia School of Medicine/Pathology, Charlottesville , Virginia, United States
2004 - 2007	Assistant Professor of Research, University of Virginia School of Medicine/Pathology, Charlottesville, Virginia, United States
2003 - 2004	Senior Scientist, University of Virginia School of Medicine/Pathology, Charlottesville , Virginia, United States
2002 - 2003	Research Associate, University of Virginia School of Medicine/Pathology, Charlottesville, Virginia, United States

Products

Products Closely Related to the Proposed Project

1. Balogh KN, Templeton DJ, Cross JV. Macrophage Migration Inhibitory Factor protects cancer cells from immunogenic cell death and impairs anti-tumor immune responses. PLoS One. 2018;13(6):e0197702. PubMed Central PMCID: PMC5986154.
2. Simpson KD, Templeton DJ, Cross JV. Macrophage migration inhibitory factor promotes tumor growth and metastasis by inducing myeloid-derived suppressor cells in the tumor microenvironment. J Immunol. 2012 Dec 15;189(12):5533-40. PubMed Central PMCID: PMC3518629.
3. Cross JV, Rady JM, Foss FW, Lyons CE, Macdonald TL, Templeton DJ. Nutrient isothiocyanates covalently modify and inhibit the inflammatory cytokine macrophage migration inhibitory factor (MIF). Biochem J. 2009 Oct 12;423(3):315-21.

PubMed Central PMCID: PMC2858637.

4. Simpson KD, Cross JV. MIF: metastasis/MDSC-inducing factor?. Oncoimmunology. 2013 Mar 1;2(3):e23337. PubMed Central PMCID: PMC3661162.
5. Cross JV, Foss FW, Rady JM, Macdonald TL, Templeton DJ. The isothiocyanate class of bioactive nutrients covalently inhibit the MEKK1 protein kinase. BMC Cancer. 2007 Sep 25;7:183. PubMed Central PMCID: PMC2071920.

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 Cross, Janet V in SciENcv on 2026-06-02 10:32:31

NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Cross, Janet V

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-9528-0812

Position Title: Associate Dean for Graduate and Medical Scientist Programs

Organization and Location: University of Virginia School of Medicine, Charlottesville, Virginia, United States

Personal Statement

The central objective of my research program has been to understand how the host immune response is reprogrammed by tumors to promote growth and metastasis, focused on the study of mechanisms that contribute to tumor development. Early on, my work centered on the regulation of cell signaling pathways and the aberrations in these networks that promote cell growth, prevent cell death, or otherwise contribute to cancer. We identified an inflammatory cytokine, the Macrophage Migration Inhibitory Factor (MIF), as the major target of the isothiocyanate chemopreventives, a discovery that ultimately led to our published study demonstrating the critical importance of MIF in tumor growth and metastasis through regulation of myeloid derived suppressor cells (MDSCs) and our subsequent study demonstrating the role of MIF in preventing Immunogenic Cell Death (ICD) at the very early stages of tumor growth This further advanced our understanding of the role of MIF in mediating tumor/ immune interactions. Our findings provide foundations for efforts to dissect the role of MIF in the tumor microenvironment and evaluate MIF inhibition as an approach for prevention of cancer progression.
My interest in and passion for training the next generation of scientists is evidenced through my mentoring of individual trainees in my research lab, my extensive participation in the teaching mission of the institution, my directorship of the Molecular and Cellular Basis of Disease/Experimental Pathology graduate program, my term as Director of the Summer Research Internship Program and Summer Medical Research Internship, my leadership roles in the Cancer Training Program and at the helm of the School of Medicine Biomedical Sciences (BIMS) graduate program, where I oversee curriculum development, admissions and recruiting, and all fiscal, administrative and student affairs functions of the Graduate Programs Office as the Associate Dean for Graduate and Medical Scientist Programs. Through all of these different roles, I have developed substantial expertise in every facet of graduate education, as well as embracing every opportunity to enhance the training environment for our students towards a goal of equipping them for ultimate success. In my current position as Associate Dean, I am responsible for strategic decision-making for the graduate and summer programs administered through our office, as well as oversight of the substantial budget of the graduate program and the Medical Scientist Training Program. I also directly or indirectly supervise a staff of 13 dedicated individuals who ensure the smooth operations of our programs. Based on my experience, I believe that I am uniquely positioned to advise the leadership of this successful T32-supported program to ensure its continued excellence through participation on the External Advisory Board.

Honors

2025 - 2027	President-elect, President, Immediate Past President, Cancer Biology Training Consortium
2024	Trained Facilitator, Culturally Aware Mentoring Curriculum, Center for the Improvement of Mentored Experiences in Research (CIMER)
2023 - 2026	Chair, Committee on Improving Mentor-Mentee Relationships, Cancer Biology Training Consortium
2023 - 2026	Member, Outreach Committee, AAMC Group on Research Education and Training (GREAT)
2022	Certified Facilitator for "Entering Mentoring" Curriculum, Center for the Improvement of Mentored Experiences in Research (CIMER)
2021 - 2024	Board of Directors, Cancer Biology Training Consortium
2019 - 2019	Significant Contributions to Teaching Mission, University of Virginia Center for Teaching Excellence
2018 - 2023	Chair, Enhancing Diversity Committee, Cancer Biology Training Consortium
2017 - 2021	F09 Fellowship Study Section Member (June 2017, March and November 2018, March 2019, March 2020, March 2021), National Cancer Institute, National Institutes of Health
2017 - 2017	F09CY(20)L Fellowship Special Emphasis Panel, Member and Acting Chair, National Institutes of Health
2016 - 2016	R25 Training Grant Study Section, National Heart, Lung and Blood Institute, National Institutes of Health
2014 - 2015	BRCP Review Panel/Study Section (two panels), Department of Defense
2012 - 2012	Special Emphasis Panel, Study Section, National Center for Complementary and Alternative Medicine, National Institutes of Health

2011 - 2011 Dean's Excellence in Teaching Award and Election to University of Virginia Academy of Distinguished Educators, University of Virginia School of Medicine

Contributions to Science

1. Identification of the Macrophage Migration Inhibitory Factor (MIF) as an important mediator of metastasis through influence over the immune response. MIF is overexpressed in many cancers, and the degree of overexpression correlates with tumor aggressiveness and metastatic potential. This observation, along with our identification of MIF as a target of the cancer chemopreventive isothiocyanates (see Contribution to Science 2 below), supported our efforts to determine how MIF might contribute to cancer. We established that MIF promotes tumor growth and is required for tumor metastasis and demonstrated that MIF carries out its pro-tumor effects through influence over the host immune system, rather than by altering an intrinsic property of the tumor cells. Specifically, we discovered that MIF regulates the abundance of a class of immunosuppressive cells within the tumor microenvironment—monocytic Myeloid Derived Suppressor Cells (Mo-MDSCs)—that suppress T cell mediated immune responses, protecting the tumor from immune destruction. We showed that our MIF inhibitory drug reduces the abundance of Mo-MDSCs in the tumors, suggesting that we may be able to target MIF therapeutically to inhibit tumor progression through manipulation of the host immune response. In follow up studies, we demonstrated that MIF is responsible for preventing immunogenic cell death and that, in its absence, the tumor becomes susceptible to an enhanced T cell mediated immune response. Our hope is that this work will form the foundation for future efforts to further explore the mechanism(s) behind this significant finding, as well as to further evaluate whether MIF inhibition may represent a clinically translatable approach to overcome the immunosuppressive tumor microenvironment to promote tumor control, either alone or in combination with immunotherapy approaches.

2. Understanding the molecular mechanisms by which chemopreventives exert their anti-cancer effects. Decades of research established that the isothiocyanate (ITC) class of compounds prevalent in cruciferous vegetables protect against cancer in animal models of carcinogenesis, as well as in xenograft and genetic models of cancer. However, the underlying molecular mechanism(s) through which they mediate these effects remained elusive, with available models insufficient to explain all of the observed anti-cancer activities. My early studies on the MEKK1 protein kinase confirmed that these electrophilic chemicals could covalently modify protein targets and alter their activity. The inhibition of MEKK1 by ITCs led to our hypothesis that the anti-cancer effects may be mediated through modification of significant protein targets, leading to alterations of cell signaling responses. This motivated my effort to develop an affinity reagent to probe these interactions. My validation of this reagent led to a novel proteomics screen and identification of the second covalent target of modification, the inflammatory cytokine MIF. I further demonstrated that ITC modification of MIF inhibited an enzymatic activity of the protein with an IC50 within the physiologically attainable concentration range observed in the plasma of human subject who consumed a broccoli sprout meal. We continue to pursue the significance of MIF in the chemoprevention phenomenon and examine the potential utility of the ITCs as anti-cancer and anti-inflammatory agents by virtue of their ability to inhibit this important inflammatory mediator. This work provided the foundation for our effort to characterize the tumor promoting effects of MIF mediated by its influence over the immune response, with the ITCs playing a significant role.

3. Dissection of the molecular mechanisms by which oxidative stress events impact cell signaling. Cell signaling responses are fine-tuned through a number of post-translational modifications on signaling proteins. The prototype of this is protein phosphorylation, which has been studied for decades as an essential mediator. One other significant means of regulation involves oxidative modification of proteins on cysteine residues mediated by reactive oxygen species, which are generated during many cell signaling responses. The study of these modifications has lagged behind, due to the difficulties inherent in studying these unstable modifications in an oxygen environment. In addition to characterizing specific protein targets that are regulated by these modifications, we also tackled one of the major technical hurdles in the field, developing a protocol (PROP – purification of reversibly oxidized proteins) that supports identification of targets of redox modification. We have applied this approach to characterizing specific targets, as well as to proteomics-based approaches to uncover novel targets in an unbiased manner.

4. Furthering our understanding of the regulation of the MEKK1 protein kinase. We contributed significant advances to our understanding of how this central MAPK3K in this stress signaling pathway is regulated. Specifically, our work uncovered a novel means of regulating the MEKK1 protein kinase through caspase-mediated proteolytic cleavage at a specific site in the N terminus. This cleavage frees the C terminal catalytic domain from the N terminal regulatory domain, leading to altered subcellular localization of the protein and concomitant effects on downstream signaling responses. In an effort to further understand these signaling responses, we collaborated with Kevan Shokat to develop a MEKK1 mutant that would accept his synthetic “bumped” ATP analogs. The ultimate goal of these studies was to search for additional substrates for this protein kinase. In the process, we discovered that it was necessary to mutate an additional site in MEKK1, beyond that predicted by the original sequence analysis. This allowed us to contribute to a collaborative paper on these second site mutations. Moreover, the necessary second site of mutation proved to be a cysteine residue, which serendipitously led us to discover the redox regulation of MEKK1 discussed in section 3 above. Finally, in a yeast two hybrid screen, we identified the NADPH quinone oxidoreductase (NQO1) as an interacting partner of MEKK1. Using a number of inhibitors of NQO1, we demonstrated a role for these enzymes in regulating stress signaling pathways, with downstream impacts on stress signaling and NF-kappaB pathways.

5. Characterization of the role of SAPK/JNK stress signaling pathway in cell cycle regulation. Stress signaling pathways have been implicated in controlling cellular responses ranging from proliferation to differentiation to death. Central among this pathway is the SAPK protein kinase, which is also known as JNK. Work in my early career focused on dissecting how these pathways are regulated, as well as how they contribute to significant outcomes for the cells. In the course of these studies, we determined that SAPK plays a significant role in cell cycle progression, through its ability to directly phosphorylate a specific residue in the cell cycle phosphatase cdc25c. The expertise and reagents that we developed allowed us to contribute to subsequent collaborative work that further dissected the role of this signaling event and implicated SAPK/JNK in regulation of the DNA damage response.

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