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

NIH Biographical Sketch Common Form

Name: Pemberton, Lucy Frances

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0009-0003-9747-1174

Position Title: Associate Professor

Organization and Location:Microbiology, Immunology and Cancer Biology, University of Virginia, Charlottesville, Virginia, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
The Rockefeller University, New York, New York, United States	Postdoctoral Fellow	01/1994	11/1999	Cell and Molecular Biology
Imperial Cancer Research Fund, London, Not Applicable, N/A, United Kingdom	Doctor of Philosophy (PHD)	09/1990	12/1993	Cancer Cell and Molecular Biology
Kings College, University of London, London, Not Applicable, N/A, United Kingdom	Master of Science (MS)	08/1989	06/1990	Immunology
University of Manchester, Manchester, Not Applicable, N/A, United Kingdom	Bachelor of Science (BS)	09/1983	06/1986	Genetics and Cell Biology

Appointments and Positions

2004 - present	Associate Professor , Microbiology, Immunology and Cancer Biology, University of Virginia, Charlottesville, Virginia, United States
2023 - present	Associate Director for Education and Training, UVA Comprehensive Cancer Center, Charlottesville, Virginia, United States
2012 - present	Joint Appointment-Associate Professor , Cell and Developmental Biology, University of Virginia,, Charlottesville, Virginia, United States
1999 - 2004	Assistant Professor, Microbiology, Immunology and Cancer Cell Biology, University of Virginia,, Charlottesville, Virginia, United States

Products

Products Closely Related to the Proposed Project

1. Xue YM, Kowalska AK, Grabowska K, Przybyt K, Cichewicz MA, Del Rosario BC, Pemberton LF. Histone chaperones Nap1 and Vps75 regulate histone acetylation during transcription elongation. Mol Cell Biol. 2013 Apr;33(8):1645-56. PubMed Central PMCID: PMC3624251.
2. Del Rosario BC, Pemberton LF. Nap1 links transcription elongation, chromatin assembly, and messenger RNP complex biogenesis. Mol Cell Biol. 2008 Apr;28(7):2113-24. PubMed Central PMCID: PMC2268417.
3. Mosammaparast N, Ewart CS, Pemberton LF. A role for nucleosome assembly protein 1 in the nuclear transport of histones H2A and H2B. EMBO J. 2002 Dec 2;21(23):6527-38. PubMed Central PMCID: PMC136951.
4. Keck KM, Pemberton LF. Histone chaperones link histone nuclear import and chromatin assembly. Biochim Biophys Acta. 2012 Mar;1819(3-4):277-89. PubMed Central PMCID: PMC3272145.
5. Mosammaparast N, Pemberton LF. Karyopherins: from nuclear-transport mediators to nuclear-function regulators. Trends Cell Biol. 2004 Oct;14(10):547-56. PubMed PMID: 15450977.

Other Significant Products, Whether or Not Related to the Proposed Project

1. Wotton D, Pemberton LF, Merrill-Schools J. SUMO and Chromatin Remodeling. Adv Exp Med Biol. 2017;963:35-50. PubMed PMID: 28197905.
2. Keck KM, Pemberton LF. Interaction with the histone chaperone Vps75 promotes nuclear localization and HAT activity of Rtt109 in vivo. Traffic. 2011 Jul;12(7):826-39. PubMed Central PMCID: PMC3115401.

3. Mosammaparast N, Del Rosario BC, Pemberton LF. Modulation of histone deposition by the karyopherin kap114. Mol Cell Biol. 2005 Mar;25(5):1764-78. PubMed Central PMCID: PMC549354.
4. Mosammaparast N, Guo Y, Shabanowitz J, Hunt DF, Pemberton LF. Pathways mediating the nuclear import of histones H3 and H4 in yeast. J Biol Chem. 2002 Jan 4;277(1):862-8. PubMed PMID: 11694505.
5. Mosammaparast N, Jackson KR, Guo Y, Brame CJ, Shabanowitz J, Hunt DF, Pemberton LF. Nuclear import of histone H2A and H2B is mediated by a network of karyopherins. J Cell Biol. 2001 Apr 16;153(2):251-62. PubMed Central PMCID: PMC2169462.

Certification:

I certify that the information provided is current, accurate, and complete. This includes but is not limited to information related to domestic and foreign appointments and positions.

I also certify that, at the time of submission, I am not a party to a malign foreign talent recruitment program.

I also certify that, as senior/key personnel listed within this application, I have taken the required research security training consistent and in compliance with Section 10634 of the CHIPS and Science Act of 2022.

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.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Pemberton, Lucy Frances

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0009-0003-9747-1174

Position Title: Associate Professor

Organization and Location: Microbiology, Immunology and Cancer Biology, University of Virginia, Charlottesville, Virginia, United States

Personal Statement

My experience up to this point illustrates my dedication to the educational mission at UVA. I have served as the Director of Graduate Studies for Microbiology, Immunology and Cancer Biology (MIC) and an Admission Co-Chair for the UVA School of Medicine (SOM) Biomedical Sciences Graduate Program since 2013. I currently serve as the Associate Director for Education and Training for the UVA Comprehensive Cancer Center (UVACCC) and I am a member of the UVACCC Senior Leadership Group and Executive Committee. Throughout my career, I have been strongly committed to mentorship and education. I have mentored numerous students at various academic levels, including four PhD students, six master's students, two postdoctoral fellows, and countless undergraduates in my own laboratory. This training and experience prepares me for my role on the Executive Committee and well positions me to coordinate activities, programs and training opportunities between the UVACCC and the T32 Training Program. My former research activities indicate a longstanding interest in cancer research. I performed my PhD research in cancer cell biology at the Imperial Cancer Research Fund, UK (now Cancer Research, UK) and undertook my postdoctoral research at The Rockefeller University with Dr. Günter Blobel. As an Assistant and then Associate Professor of Microbiology, Immunology and Cancer Biology at UVA I have more than 20 years' experience studying nucleo-cytoplasmic transport and chromatin structure. These studies have provided insights into the early steps of nucleosome biogenesis and the overall regulation of chromatin dynamics and integrity. My laboratory research focused on the regulation and transport of proteins that assemble and modify chromatin, and the study of chromatin structure during transcription and metastasis. This research has allowed me to create a strong training environment and has been funded by NIGMS and NCI. I have served in the educational mission of the UVA in the following capacities: • Director of Graduate Studies for Microbiology, Immunology and Cancer (MIC) for the last eleven years, advising around seventy students per year. • Co-Chair of Biomedical Sciences Graduate Program Admission Committee. This role includes overseeing the recruitment of cancer biology interested applicants. • I serve on numerous committees including Chair of the MIC Academic Advisory Committee and Graduate Student First Year Advisory Committee and the Academic Progress and Achievement Committee. • I have taught in several courses in the School of Medicine. • I serve on the Executive Committee of three T32 Training Grants; Cancer Research (NCI), Surgical Oncology (NCI) and Cell and Molecular Biology (NIGMS). • As the Associate Director for Education and Training in the UVACCC, I have focused on both strengthening current, and developing new, cancer-related training and education activities across the full spectrum of learners from grade school through junior faculty. This includes PI of the American Cancer Society (ACS) Cancer Research Postbaccalaureate Fellows Program, Director of the Short-Term Research Initiative for Visiting Educators and Chair of UVACCC Travel and Fellowship Award Committees. • I Co-Chaired the 2023 Commonwealth of Virginia Cancer Research Conference, 2025 Elements of Excellence: DMV-ACS Cancer Research Intern Retreat, Baltimore, MD and the 2025 Cancer Biology Training Consortium Retreat, Richmond VA.

Honors

2025	Co-host, Cancer Biology Training Consortium, Annual Retreat
2025	Co-host, Elements of Excellence: DMV-ACS Cancer Research Intern Retreat
2023	Co-Chair, Commonwealth of Virginia Cancer Research Conference
2003	Chair of Nucleocytoplasmic Minisymposium , ASCB Meeting
2001	Basil O'Connor Scholar Award, March of Dimes Foundation
2000 - 2020	Editorial Board, , Traffic

Contribution to Science

1. Analysis of histone nuclear import and the role of acetylation: Shortly after starting my independent laboratory, I continued to analyze the mechanism by which proteins gained access to the nucleus. I focused my attention on proteins that regulate chromatin structure such as histones as although small enough to diffuse into the nucleus previous studies suggested they were

actively transported. I applied biochemical, cell biological and genetic methods to define nuclear transport pathways for each of the core histones and the variant histone H2A.Z in S. cerevisiae. I used biochemical purification and Mass Spectrometry (MS) to define proteins that interact with histones prior to their assembly into nucleosomes; these proteins include histone chaperones and histone modifying proteins. Mass spec analysis of evolutionarily conserved acetylation sites on the histone tails uncovered links between acetylation, nuclear transport and histone chaperone function that have given me a unique perspective into the overall regulation of chromatin dynamics and integrity, the dysregulation of which is central driver of cancer.

2. Histone chaperones and nuclear transport: Nap1 is a protein that is abundant in the cytoplasm and previous studies suggested this protein was a chromatin binding protein and cell cycle regulator. Using biochemical and genetic techniques, we were the first to show that the histone chaperone Nap1 formed a cytoplasmic nuclear import complex with histones and nuclear transport factors prior to nuclear import. We were able to determine that interaction with transport factors decreased the ability of Nap1 to assemble chromatin suggesting there maybe be different functional Nap1 complexes. By examining nuclear import, we demonstrated that a previously undocumented role of this histone chaperones was to mediate histone nuclear import and maintain a soluble pool of histones. We also showed that Nap1 could play a similar role with the variant histone, H2A.Z. To carry out this role histone chaperones must be able to continuously shuttle between the nucleus and cytoplasm, and we showed that Nap1 contains a canonical nuclear export sequence. We could extend the transport paradigm to other histone chaperones, and we defined a role for the histone chaperone Vps75 in the import of the histone acetyl transferase, Rtt109 and in the acetylation of H3. We have also published a review that focuses on our unique insights into the links between histone acetylation, histone chaperones, nuclear transport and the early steps in nucleosome biogenesis. These interconnected processes help regulate genome stability and transcription which are key for tumorigenesis.
3. Histone chaperones regulate transcription elongation: An understanding of the precise function of histone chaperones in the nucleus has proven elusive. We were the first to show the importance of histone chaperones as general regulators of transcription elongation. We showed that Nap1 provides a connection between transcription elongation, chromatin assembly, and messenger RNP complex biogenesis. Generally, factors involved in pre-mRNA processing are recruited by the RNAP II C-terminal domain, and the Nap1- messenger RNP complex interaction would demonstrate a unique mechanism of recruitment of a histone chaperone to an actively transcribed gene. We also demonstrated by ChIP and mRNA analysis that in S. cerevisiae Nap1 is recruited to chromatin in a transcription dependent manner, where it facilitates chromatin remodeling. We showed that histone chaperones work with histone acetyl transferases to regulate elongation using a cryptic transcription assays and ChIp for different histone modifications. Nap1 is a paradigm for other histone chaperones and we have confirmed our findings by analysis of other chaperones such as Asf1, Vps75. Our work has shown that histone chaperones can orchestrate changes in chromatin acetylation, likely through their roles in chromatin assembly and exchange, and so play important roles in the regulation of transcription elongation. Changes in gene expression can drive uncontrolled cell growth and proliferation leading to cancer.
4. Purification and Function of nuclear transport factors and chromatin protein complexes: I have developed methods for the effective purification of protein complexes from different cellular compartments including cytoplasm, nuclei and nuclear envelope fractions. This training and experience is particularly relevant for the success of the experiments in this proposal. This allowed the identification of nuclear transport factors and functional analysis of their interactions with components of the Ran pathway, which includes, Ran, the GTPase RanGAP and the Ran GEF, RCC1. We have also been able to take high throughput approaches and determine the full repertoire of interactors for a given protein such as transport factors or histone chaperones and histones, using Mass Spectrometry. We have also developed approaches in collaboration with Don Hunt's lab that have allowed us to identify all the phosphorylation sites on Nap1, and the acetylation and methylation sites on histones, so giving us tools to understand their regulation. We have also optimized tools for imaging cells both by multispectral flow cytometry and live cell imaging. Together, these tools will help determine how these factors and protein complexes influence cancer development and progression.

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