BIOGRAPHICAL SKETCH

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NAME: Carolyn Machamer

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POSITION TITLE: Professor Emerita of Cell Biology

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Bucknell University, Lewisburg PA	BS	05/1975	Biology
Duke University, Durham NC	PhD	02/1983	Microbiology & Immunology
Salk Institute, La Jolla CA	Postdoctoral	02/1987	Molecular Cell Biology

A. Personal Statement

My expertise is in intracellular membrane traffic in mammalian cells, with particular focus on the Golgi complex. The Golgi complex plays a central role in processing and sorting of cargo in the secretory pathway of all eukaryotic cells. We were the first to identify a targeting signal in a Golgi resident protein. We also determined how golgin family members and other Golgi resident proteins are cleaved during apoptosis, leading to Golgi disassembly. The latter project led to the proposal of a novel Golgi stress-sensing pathway, where fragments of golgin proteins enter the nucleus to induce gene transcription to alleviate the stress. In addition to the goal of understanding the structure and function of the Golgi, my laboratory studies the intracellular assembly of coronaviruses. These enveloped viruses target their membrane proteins to the early Golgi and bud into the lumen of the compartment. The mechanism of assembly and exocytosis from infected cells is poorly understood, as is the advantage of intracellular assembly. Coronaviruses are significant human pathogens, and recently emerged novel coronaviruses cause severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and COVID-19.

I was the director of one of the largest graduate programs at Johns Hopkins University School of Medicine from 2006-2018 (the Biochemistry, Cellular and Molecular Biology program). In this role, I spearheaded efforts to improve the way the curriculum is delivered, to increase diversity, and to enhance preparation of our students for the next steps in their careers. I participated in all aspects of the program, including advising all students (an average of 210 per year), directing some of the core courses and organizing career workshops. In my own lab, I have trained 6 postdoctoral fellows, 18 graduate students, 21 undergraduates and 5 high school students. In addition, I served on 183 thesis committees and sat on 209 oral qualifying exam committees. I considered my contributions to the training of the next generation of biomedical scientists to be at least as important as the research in my laboratory.

• Machamer, C.E. 1993. Targeting and retention of Golgi membrane proteins. *Curr. Opin. Cell Biol.* **5**:606-612.

• Hicks, S.W., and C.E. Machamer. 2005. Golgi structure in stress sensing and apoptosis. *Biochim., Biophys. Acta*, **1744**:406-414.

• Ruch, T.R*. and C. E. Machamer. 2012. The coronavirus E protein: assembly and beyond. *Viruses* **4**:363-382. **PMCID: PMC3347032**

• Machamer, C.E. 2013. Accommodation of large cargo within Golgi cisternae. *Histochem. Cell Biol*.,**140**:261-269. **PMCID: PMC3756474**

B. Positions and Honors

Professional Positions:

1975-1976	Research Technician, National Cancer Institute National Institutes of Health
1983	Research Associate, Division of Immunology Duke University Medical Center
1983-1986	Postdoctoral Fellow, The Salk Institute
1987-1988	Associate Research Scientist, Department of Pathology Yale University Medical School
1988-2004	Assistant Professor, Associate Professor; Department of Cell Biology & Anatomy Johns Hopkins University School of Medicine
2004-2022	Professor, Department of Cell Biology Johns Hopkins University School of Medicine
2006-2018	Director, Biochemistry, Cell and Molecular Biology Training Program, Johns Hopkins University School of Medicine
2013-2014	Interim Associate Dean for Graduate Student Affairs Johns Hopkins University School of Medicine
2022-present	Professor Emerita, Department of Cell Biology

Other Experience and Professional Memberships

1993-2020	NIH grant reviewer (CBY-1, CTY-1, PC, ZRG-1, MBPP)
1999-2004	Editorial Board, *Traffic*
2004-2013	Associate Editor, *Traffic*
2010-2022	Editorial Board, *Frontiers in Microbiology*
2013-2020	Editorial Board, *Traffic*
1986-present	Member, American Society for Cell Biology
1988-present	Member, American Association for the Advancement of Science
1990-present	Member, American Society for Microbiology
2002-present	Member, American Society for Virology
2006-present	Member, American Society for Biochemistry and Molecular Biology

Honors

1976	Special Achievement Award, NIH
1984-1986	NIH Individual NRSA, Postdoctoral
1990-1994	Pew Scholar in the Biomedical Sciences
1995	Graduate Student “Teacher of the Year” Award
2005	Professor’s Award for Excellence in Teaching
2006	American Heart Association Donna Garff Marriott Research Award
2014	Graduate Student Teaching Award
2016	Leadership and Mentoring Award, Institute for Excellence in Education
2018	Hopkins SOM125 Hero
2018	Graduate Student Teaching Award

C. Contribution to Science

1. Targeting of Golgi membrane proteins. We were the first to identify a targeting signal in a Golgi resident protein, the coronavirus M protein. The targeting signal is present in a transmembrane domain, which while surprising at the time, is now known to be a common mechanism for membrane protein targeting to this organelle. We found that one face of the predicted alpha-helix (containing uncharged polar residues) was critical for Golgi localization, and directed formation of large oligomers as the protein reaches the Golgi complex. We proposed that Golgi localization depended on retention rather than retrieval from a more distant compartment. [*trainees, **URM trainees]

• Machamer, C.E. and J.K. Rose. 1987. A specific membrane-spanning domain of a coronavirus E1 glycoprotein is required for its retention in the Golgi region. *J. Cell Biol.* **105**:1205-1214. **PMC2114809**

• Swift, A.M., and C.E. Machamer. 1991. A Golgi retention signal in a membrane-spanning domain of coronavirus E1 protein. *J. Cell Biol*. **115**:19-30. **PMC2289920**

• Machamer, C.E**.**, M.G. Grim, A. Esquela**, S.W. Chung, M. Rolls*, K. Ryan*, and A.M. Swift. 1993. Retention of a *cis* Golgi protein requires polar residues on one face of a predicted a-helix in the transmembrane domain. *Molec. Biol. Cell* **4**:695-704. **PMC300979**

• Weisz, O.A*., A.M. Swift, and C.E. Machamer. 1993. Oligomerization of a membrane protein correlates with its retention in the Golgi complex. *J. Cell Biol.* **122**:1185-1196. **PMC2119850**

2. Identification of a potential stress sensing pathway at the Golgi complex. Golgins are peripheral membrane proteins with long coiled-coil domains that have important roles in Golgi structure and vesicle tethering. We found that certain golgins as well as other Golgi resident proteins are cleaved early during apoptosis, leading to Golgi disassembly. Some cleavage occurs by caspases and inactivates the cleaved protein and/or generates fragments that enter the nucleus. We proposed that nuclear targeting of golgin fragments leads to gene expression to correct the stress. This is a novel pathway that is predicted to respond to secretory pathway stress and does not activate the unfolded protein response in the endoplasmic reticulum. We attempted to identify the genes regulated and the types of stress that induce the pathway. [*trainees, **URM trainees]

• Mancini, M*., C.E. Machamer, S. Roy, D.W. Nicholson, N.A. Thornberry, L.A. Casciola-Rosen, and A. Rosen. 2000. Caspase-2 is localized at the Golgi complex and cleaves golgin-160 during apoptosis. *J. Cell Biol*.**149**:603-612. **PMC2174848**

• Hicks, S.W*. and C.E. Machamer. 2002. The N-terminal domain of golgin-160 contains both Golgi and nuclear targeting information. *J. Biol. Chem* **277**:35833-35839*.*

• Maag, R., M*. Mancini,R*, A. Rosen and C. E. Machamer**.** 2005. Caspase-resistant golgin-160 disrupts apoptosis induced by secretory pathway stress and ligation of death receptors. *Molec. Biol. Cell* **16**:3019-2027*.* **PMC1142444**

• Chandran, S*. and C.E. Machamer. 2008. Acute perturbations in Golgi organization impact de novo sphingomyelin synthesis. *Traffic* **9**:1894-1904. **PMC2862547**

3. Function of golgin-160 in cargo trafficking. Golgin-160 is a vertebrate-specific golgin that is cleaved early during pro-apoptotic stress. We found that unlike most other golgins that are important for Golgi structure and vesicle tethering, golgin-160 promotes efficient trafficking of specific cargo molecules, including the GLUT4 glucose transporter and the beta-1 adrenergic receptor. Interestingly, golgin-160 is enriched on the *cis* side of the Golgi at steady state, but promotes a late Golgi or post-Golgi trafficking step. The mechanism by which this occurs is not known. Golgin-160 cleavage during stress is predicted to reduce trafficking of key plasma membrane molecules. [*trainees, **URM trainees]

• Hicks, S.W*., T.A. Horn*, J.M. McCaffery, D.M. Zuckerman*, and C.E. Machamer. 2006. Golgin-160 promotes cell surface expression of the beta-1-adrenergic receptor. *Traffic* 7:1666-1677.

• Williams, D., S.W. Hicks*, C.E. Machamer, and J.E. Pessin. 2006. Golgin-160 is required for the Golgi membrane sorting of the insulin-responsive glucose transporter GLUT4 in adipocytes., *Molec. Biol. Cell* 17:5346-5355. **PMC1679696**

• Zuckerman, D.M*. S.W. Hicks*, G. Charron, H.C. Hang, and C.E. Machamer. 2011. Differential regulation of two palmitoylation sites in the cytoplasmic tail of the beta-1 adrenergic receptor. *J. Biol. Chem*. **286**:19014-23. **PMC3099716**

• Gilbert, C.E*., D.M. Zuckerman*, P.L. Currier*, and C.E. Machamer. 2014. Three basic residues of intracellular loop 3 of the beta-1 adrenergic receptor are required for golgin-160-dependent trafficking. *Int. J. Mol. Sci*.**15**:2929-45. **PMC3958891**

4. Mechanism of assembly of coronaviruses at Golgi membranes. Coronaviruses are significant human pathogens that caused the SARS, MERS and COVID-19 outbreaks. These enveloped viruses have the curious property of assembling by budding into the early Golgi lumen, and must then be exocytosed. The advantage of intracellular assembly is unknown, but we have proposed that disrupting this pathway would be an excellent target for novel anti-viral therapeutics. Using infectious bronchitis virus as a model system, as well as the envelope proteins from the SARS coronavirus, we have determined how the envelope proteins are targeted to the assembly site and interact with each other to induce budding. This information lays the groundwork for future work directed towards interfering with assembly. [*trainees, **URM trainees]

• Corse, E*. and C.E. Machamer. 2000. Infectious bronchitis virus E protein is targeted to the Golgi complex and directs release of virus-like particles. *J. Virol* **74:**4319-4326. **PMC111949**

• Lontok, E**., E. Corse*, and C.E. Machamer**.** 2004. Intracellular targeting signals contribute to localization of coronavirus spike proteins near the virus assembly site. *J. Virol*. **78:**5913-5922. **PMC415842**

• McBride, C.E**., J. Li*, and C.E. Machamer. 2007. The cytoplasmic tail of the spike protein of the severe acute respiratory syndrome coronavirus contains a novel endoplasmic reticulum retrieval signal that binds COPI and promotes interaction with membrane protein. *J. Virol.* **81**:2418-2428. **PMC186591**

• Cohen, J.R**., L.D. Lin* and C.E. Machamer. 2011. Identification of a Golgi targeting signal in the cytoplasmic tail of the severe acute respiratory syndrome coronavirus envelope protein. *J. Virol.* **85**:5794-5803. **PMC3126292**

5. Accommodation of large cargo within Golgi cisternae. Our coronavirus model led to some interesting observations about how large cargo fits inside flat Golgi cisternae, and how cells handle exocytosis of the cargo. We found that one of the viral envelope proteins plays a second role (in addition to assembly) in promoting efficient exocytosis of infectious virions. The coronavirus E protein forms a cation-specific ion channel *in vitro*, and we have proposed that it is required to increase the pH in late secretory compartments to protect slowly exocytosed large cargo from proteolytic damage. We also examined a potential egress pathway that moves virions from the budding compartment directly to endosomal compartments. [*trainees, **URM trainees]

• Ruch*, T.R. and C.E. Machamer. 2011. The hydrophobic domain of the infectious bronchitis virus E protein alters the host secretory pathway and is important for release of infectious virus. J. Virol. 85:675-685. **PMC3020032**

• Ruch, T.R*. and C.E. Machamer. 2012. A single polar residue and distinct membrane topologies impact the function of the infectious bronchitis coronavirus E protein. *PLoS Pathogens* 8(5):e1002674. **PMCID: PMC3343006**

• Westerbeck, J.W*. and **C.E. Machamer**. 2015. A coronavirus E protein is present in two distinct pools with different effects on assembly and the secretory pathway. *J. Virol.*, **89**:9313-9323. PMCID: **PMC4542375**

• Westerbeck, J.W*. and C.E. Machamer. 2019. The infectious bronchitis virus coronavirus envelope protein alters Golgi pH to protect spike protein and promote release of infectious virus. J. Virol.93(11):1-15. **PMCID: PMC6532078**

- Saraste, J, M. Enyioko, H. Dale, K. Prydz, **C. Machamer**. 2022. Evidence for the role of Rab11-positive recycling endosomes as intermediates in coronavirus egress from epithelial cells. Histochem. Cell Biol. 158:241-251. PMCID: PMC9124743

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/carolyn.machamer.1/bibliography/40820545/public/?sort=date&direction=descending