BIOGRAPHICAL SKETCH

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NAME: Carolyn Coyne

eRA COMMONS USER NAME (credential, e.g., agency login): COYNECAR

POSITION TITLE: Professor, Department of Pediatrics

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
Florida State University	B.S.	05/98	Biochemistry
University of North Carolina-Chapel Hill	Ph.D.	04/03	Pharmacology
University of Pennsylvania/Children's Hospital of Philadelphia	Post-doctoral	04/07	Microbiology

A. Personal Statement

Viruses are in a constant battle with the host cells they infect. My research employs cell biology, immunology, and microbiology to dissect the complex dialogue that occurs between virus and host during the course of viral infections and to identify potential therapeutic targets that might limit viral-induced human disease. I am recognized as a leader in the field of virus infection of cellular barriers, primarily focusing on the gastrointestinal (GI) tract and the human placenta.

Two major areas of research in my laboratory are *(1)* defining the mechanisms by which viruses, and other microorganisms, cross the placental barrier to be transmitted vertically during pregnancy and *(2)* defining the mechanisms by which enteroviruses bypass the GI epithelium. Through these studies, we have defined how some viruses bypass key cellular barriers, which have provided insights into viral pathogenesis and into pathways that can be targeted to circumvent viral-induced disease and/or spread. I am a recognized leader in the field of enterovirus-GI cell interactions and my work is frequently recognized for its innovation and impact.

B. Positions and Honors

Positions

1998-2003 Graduate Student, Department of Pharmacology, University of North Carolina at Chapel Hill, Chapel Hill, NC
2003-2007 Post-doctoral Fellow, Department of Microbiology, University of Pennsylvania, Philadelphia, PA
2007- 2013 Assistant Professor, Department of Microbiology and Molecular Genetics, University of Pittsburgh, Pittsburgh, PA
2013-2017 Associate Professor, Department of Microbiology and Molecular Genetics, University of Pittsburgh, Pittsburgh, PA
2017-2019 Associate Professor, Department of Pediatrics, University of Pittsburgh, Pittsburgh, PA
2017-present Director, Center for Microbial Pathogenesis, UPMC Children's Hospital of Pittsburgh
2018-present Associate Director, Richard King Mellon Pediatric Research Institute, UPMC Children's Hospital of Pittsburgh
2019-present Professor, Department of Pediatrics, University of Pittsburgh, Pittsburgh, PA

Other Experience and Professional Memberships

2017-present Editorial board, *mBio*

2015-present Mini-review Editor, *Journal of Virology*
2015-present Opinions Editor, *PLoS Pathogens*
2010-present Editorial board, *Journal of Virology*
2013-present Editorial board, *Virology*
2015-2021 Standing member, NIH Study Section, NIAID VIRA
2015-2017 Senior Editor, *mSphere*
2014-2016 Associate Editor, RNA viruses, *PLoS Pathogens*
2009-2017 Faculty Member, Faculty of 1000 (Virology)
2018-present Board of Reviewing editors, *Science*

Member, American Society for Virology
Member, American Society for Microbiology
Member, American Association for the Advancement of Science

Honors

2019 Elected Fellow, American Academy of Microbiology, American Society of Microbiology
2014 Recipient, Cozzarelli Prize for best 2013 Biomedical Sciences Publication in the *Proceedings of the National Academy of Sciences*
2012 Awardee, Burroughs Wellcome Fund, Investigators in the Pathogenesis of Infectious Disease Grant Program
2006 American Heart Association Pennsylvania/Delaware Affiliate Excellence Award
2006 Outstanding Presentation in Basic Research Award, Fellow's Research Poster Day, Children's Hospital of Philadelphia
2005 American Heart Association Postdoctoral Research Fellowship
2005 Postdoctoral Ruth L. Kirschstein National Research Service Award (NRSA)

C. Contributions to Science

1. Enteroviral infections. The human gastrointestinal (GI) tract is a complex organ, with an epithelial surface that must provide a protective and immunological barrier in a complex and diverse microbial environment. Enteroviruses are leading causes of human infections worldwide, particularly in infants and children, and infect primarily via the fecal-oral route. These viruses, which include poliovirus, coxsackievirus, echovirus, enterovirus D68 (EV-D68), and enterovirus 71 (EV71), are small, single-stranded RNA viruses belonging to the Picornaviridae family. The events that surround enterovirus infections of the human GI epithelium remain poorly understood. My laboratory defines the mechanisms by which enteroviruses bypass the GI barrier to initiate infection using novel organotypic cell models developed in my laboratory, with a specific focus on the cell biological and immunological events associated with enterovirus infections of the GI tract. Our work in this area has established new paradigms in our understanding of how enteroviruses enter and replicate in the human GI tract. We were the first group to apply stem cell-derived enteroids models to the study of enterovirus infections, which revealed the cell type-specific nature of enteroviruses infections in the GI tract and important differences in how the GI epithelium responds to infection in a virus type-specific manner. Recently, we also identified the receptor for echoviruses as the neonatal Fc receptor (FcRn), which will allow us to interrogate fundamental aspects of echovirus infection and pathogenesis. Key publications from these studies include:

1. Morosky S, Wells A, Lemon K, Evans E, Schamus S, Bakkenist CJ, **Coyne CB**. The neonatal Fc receptor is a pan-echovirus receptor. *Proceedings of the National Academy of Science*, 2019 2019 Feb 26;116(9):3758-3763. PMID: 30808762.
2. Good CA, Wells AI, and **Coyne CB**. Type III interferon signaling restricts enterovirus 71 infection of goblet cells. *Science Advances* 2019 Mar 6;5(3). PMID: 30854425.
3. Drummond CG, Bolock AM, Ma C, Luke CJ, Good M, **Coyne CB**. Enteroviruses infect human enteroids and induce antiviral signaling in a cell lineage-specific manner. Proc Natl Acad Sci U S A. 2017;114(7):1672-7. Epub 2017/02/01. doi: 10.1073/pnas.1617363114. PubMed PMID: 28137842; PMCID: PMC5320971.
4. Harris KG, Morosky SA, Drummond CG, Patel M, Kim C, Stolz, DB, Bergelson JM, Cherry S, and **Coyne CB**. RIP3 Regulates Autophagy and Promotes Coxsackievirus B3 Infection of Intestinal Epithelial Cells. *Cell Host & Microbe*, Volume 18, Issue 2, p221–232, 2015. PMID: 26269957

2. Cellular pathways targeted by RNA viruses to promote their replication. RNA viruses usurp a variety of host cell pathways to facilitate their replication. My laboratory has identified pathways targeted by RNA viruses (including enteroviruses and flaviviruses) to promote their replication and spread. An obligate step in the life cycle of positive sense RNA viruses is the formation of membrane-enriched organelles, termed replication organelles, that provide the structural support for viral replication. Multiple mechanisms have been proposed for the generation of these membranes, including manipulation of the host autophagic pathway, a process that removes damaged organelles via the formation of double membrane bound vesicles. Our studies have focused on the identification and characterization of novel regulators of host cell autophagy and on the identification of mechanisms employed by RNA viruses to specifically modulate the host autophagic pathway. In addition, our studies have identified novel host associated effectors, including interferon stimulated genes (ISGs), that target RNA viruses to restrict their replication. Key publications from these studies include:

1. Lennemann NJ, **Coyne CB**. Dengue and Zika viruses subvert reticulophagy by NS2B3-mediated cleavage of FAM134B. Autophagy. 2017;13(2):322-32. Epub 2017/01/20. doi: 10.1080/15548627.2016.1265192. PubMed PMID: 28102736; PMCID: PMC5324851.
2. Shu Q, Lennemann NJ, Sarkar SN, Sadovsky Y, **Coyne CB**. ADAP2 Is an Interferon Stimulated Gene That Restricts RNA Virus Entry. PLoS Pathog. 2015;11(9):e1005150. Epub 2015/09/16. doi: 10.1371/journal.ppat.1005150. PubMed PMID: 26372645; PMCID: PMC4570769.
3. Delorme-Axford E, Morosky S, Bomberger J, Stolz DB, Jackson WT, **Coyne CB**. BPIFB3 regulates autophagy and coxsackievirus B replication through a noncanonical pathway independent of the core initiation machinery. MBio. 2014;5(6):e02147. Epub 2014/12/11. doi: 10.1128/mBio.02147-14. PubMed PMID: 25491355; PMCID: PMC4324245.
4. Bozym RA, Delorme-Axford E, Harris K, Morosky S, Ikizler M, Dermody TS, Sarkar SN, **Coyne CB**. Focal adhesion kinase is a component of antiviral RIG-I-like receptor signaling. Cell Host Microbe. 2012;11(2):153-66. Epub 2012/02/22. doi: 10.1016/j.chom.2012.01.008. PubMed PMID: 22341464; PMCID: PMC3995454.

3. The mechanisms employed by human placental trophoblasts to combat microbial infections. My research program asks two central questions: *(1)* what are the mechanisms by which the placenta restricts the vertical transmission of microorganisms, and *(2)* how do microorganisms associated with congenital disease breach the placental barrier? To answer these questions, we have established models of mid- and late-gestation human placental trophoblasts that fully recapitulate the highly complex cellular composition of the human placenta at various gestational stages. In addition, we have pioneered the development of tractable *in vitro* cell-line based organotypic models of placental trophoblasts that can be used to elucidate placental defense mechanisms. Our work in this area has established a new and important paradigm – that in addition to its role as a physical barrier, the placenta is a dynamic and highly reactive chemical barrier that uses multiple classes of molecules, including type III interferons and microRNAs, to protect the fetus and maternal host from viral infections. Collectively, our work has provided transformative insights into the pathways by which the human placenta restricts microbial access to the intrauterine compartment, which will guide development of therapeutic approaches to limit vertical transmission and fetal disease. Key publications from these studies include:

1. Ander SE, Rudzki EN, Arora N, Sadovsky Y, **Coyne CB***, Boyle JP*. Human Placental Syncytiotrophoblasts Restrict Toxoplasma gondii Attachment and Replication and Respond to Infection by Producing Immunomodulatory Chemokines. MBio. 2018;9(1). Epub 2018/01/11. doi: 10.1128/mBio.01678-17. PubMed PMID: 29317509; PMCID: PMC5760739. *co-corresponding
2. Corry J, Arora N, Good CA, Sadovsky Y, **Coyne CB**. Organotypic models of type III interferon-mediated protection from Zika virus infections at the maternal-fetal interface. Proc Natl Acad Sci U S A. 2017;114(35):9433-8. Epub 2017/08/09. doi: 10.1073/pnas.1707513114. PubMed PMID: 28784796; PMCID: PMC5584447.
3. Bayer A, Lennemann NJ, Ouyang Y, Bramley JC, Morosky S, Marques ET, Jr., Cherry S, Sadovsky Y, **Coyne CB**. Type III Interferons Produced by Human Placental Trophoblasts Confer Protection against Zika Virus Infection. Cell Host Microbe. 2016;19(5):705-12. Epub 2016/04/14. doi: 10.1016/j.chom.2016.03.008. PubMed PMID: 27066743; PMCID: PMC4866896.
4. Delorme-Axford E, Donker RB, Mouillet JF, Chu T, Bayer A, Ouyang Y, Wang T, Stolz DB, Sarkar SN, Morelli AE, Sadovsky Y, **Coyne CB**. Human placental trophoblasts confer viral resistance to recipient

cells. Proc Natl Acad Sci U S A. 2013;110(29):12048-53. Epub 2013/07/03. doi: 10.1073/pnas.1304718110. PubMed PMID: 23818581; PMCID: PMC3718097. **Recipient of the Cozzarelli Prize for the best biomedical sciences publication in PNAS in 2013.*

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/carolyn.coyne.1/bibliography/public/

Patents:
Use of the chromosome 19 microRNA cluster (C19MC) for treating microbial disease and promoting autophagy. Patent No. 10,000,755, issued June 19, 2018

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

R01 AI150151 Coyne (PI) 1/20-12/25
"The role of FcRn in echovirus entry and pathogenesis"
The goal of this project is to define the role of the neonatal Fc receptor (FcRn) in the entry of echoviruses into the intestinal epithelium using *in vitro* stem cell-derived models and the role of this receptor in pathogenesis using *in vivo* mouse models.

R01 AI145828 Coyne (PI, MPI) 07/19-06/24
"Innate immune signaling in placental antiviral defenses"
The goal of this MPI project with the Diamond laboratory is to define the role of placental cell-type specific innate immune signaling in placental antiviral defenses.

R01 AI145296 Coyne (PI, MPI) 04/19-03/24
"*Innate Immune Regulation of Zika Virus Infection***"**
The goal of this MPI project with the Gale and Diamond laboratories is to define the role of innate immune signaling in the defense against Zika virus (ZIKV) infections at the maternal-fetal interface.

R37 HD086916 Coyne (co-I) 02/17-01/22
"*Exosome based placental maternal communication***"**
The goal of this project is to characterize the mechanisms by which placental-derived microvesicles communicate with the maternal host to alter cell function and response to viral infections.

R21 HD097400 Coyne (PI) 10/18-09/20
"The role of placental secreted factors in teratogenic virus infections"
The goal of this project is to define the role of placental secreted factors in the sensitization of maternal immune cells to teratogenic viruses and to identify the antiviral activity of placental-enriched interferon stimulated genes (ISGs).

R21 AI139576 Coyne (PI, MPI) 07/18-06/20
"Molecular mechanisms of Toxoplasma-placenta interactions"
The goal of this project with the Boyle laboratory is to characterize the mechanisms by which Toxoplasma gondii infection of human primary placental trophoblasts induces inflammatory signaling.

R56 AI081759 Coyne (PI) 03/19-02/20
"Enterovirus infection of polarized epithelial cells"
The goal of this project is to characterize the signaling pathways by which coxsackievirus B (CVB) induces host cell death in polarized intestinal epithelial cells and the cell biological consequences of this signaling.