Publications

Bochkov, Y. A., Watters, K., Ashraf, S., **Griggs, T. F.**, Devries, M. K., Jackson, D. J., ... & Gern, J. E. (2015). Cadherin-related family member 3, a childhood asthma susceptibility gene product, mediates rhinovirus C binding and replication. Proceedings of the National Academy of Sciences, 201421178.

Griggs, T. F., Bochkov, Y. A., Nakagome, K., Palmenberg, A. C., & Gern, J. E. (2015). Production, purification, and capsid stability of rhinovirus C types. Journal of virological methods, 217, 18-23.

Johnson, C.R., **Griggs, T.F.**, Gnanandarajah, J., Murtaugh, M.P. (2011). Novel structural protein in porcine reproductive and respiratory syndrome virus encoded by an alternative ORF5 present in all arteriviruses. J. Gen Virol. 92, 1107-16.

Puvanendiran, S., Stone, S., Yu, W., Johnson, C.R., Abrahante, J., Jimenez, L.G., **Griggs, T.**, Haley, C., Wagner, B., Murtaugh, M.P. (2011). Absence of porcine circovirus type 1 (PCV1) and high prevalence of PCV 2 exposure and infection in swine finisher herds. Virus Res. 157, 92-8.

Puvanendiran, S., Stone, S., Yu, W., Johnson, C., Jimenez, L. G., **Griggs, T.**, Fuentes, M., Murtaugh, M. P. (2008). Differentiating PCV1 and PCV2 infections in swine. Proceedings of the 39th American Association of Swine Veterinarians meeting.

Recent Presentations

"Rhinovirus C Infects a Subset of Ciliated Bronchial Epithelial Cells" (Poster, April 2015) - *Medical Scientist Training Program Annual Symposium, University of Wisconsin*

"RV-C Infects Ciliated Bronchial Epithelial Cells" (March, 2015) - *Cellular & Molecular Pathology Student Seminar, University of Wisconsin School of Medicine*

"Rhinovirus C Infects a Subset of Ciliated Bronchial Epithelial Cells" (Poster, October 2014) - *Asthma and Allergic Diseases Cooperative Research Centers Steering Committee Meeting, Rockville, MD*

"Rhinovirus C Infects Ciliated Bronchial Epithelial Cells" (Poster, August 2014) - *Michael N. Hart Pathology Research Day, University of Wisconsin*

"Stability Characteristics & Methods for Purification of Rhinovirus C" (Poster, April 2014) - *Medical Scientist Training Program Annual Symposium, University of Wisconsin*

"Purifying Rhinovirus C" (Talk, April 2014) - *Cellular & Molecular Pathology Student Seminar, University of Wisconsin School of Medicine*

"Development of a method to purify all Rhinovirus species, and mechanisms of Rhinovirus C Instability" (Talk, October 2013) – *University of Wisconsin*

Cellular and Molecular Pathology Graduate Program, Joanne Thornton, 3170-10K MFCB, 1685 Highland Avenue, Madison, WI 53705

CMP Cellular and Molecular Pathology

Theodor F. Griggs

Program of the Dissertation Defense Seminar
for the Degree of Doctor of Philosophy
in Cellular and Molecular Pathology

"THE RHINOVIRUS C: CAPSID STABILITY, VIRION PURIFICATION, AND IDENTIFICATION OF CELLULAR AND TISSUE TROPISM"

CLINICAL SCIENCES CENTER

Wednesday, June 24, 2015

9:00am Room G5/113

Research conducted in the lab of
James Gern, PhD
Department of Pediatrics

UNIVERSITY OF WISCONSIN – MADISON

Ted Griggs

Education

University of Wisconsin-Madison
PhD in Cellular and Molecular Pathology

University of Minnesota, St. Paul, MN
Bachelor of Science
Majors: Biochemistry, Microbiology

Research Experience

James E. Gern (MD) Laboratory (July 2012-Present) – Madison, WI: Elucidation of rhinovirus C cellular tropism in bronchial epithelium. Characterization and purification of the rhinovirus C.

Michael P. Murtaugh (PhD) Laboratory (October 2006- August 2010) – St. Paul, MN: Discovering and characterization of a novel structural protein in porcine reproductive and respiratory syndrome virus encoded by an alternative ORF5 present in all arteriviruses**.** Differentiating PCV1 and PCV2 infections in swine.

Stephen J. Russell (MD, PhD) Laboratory (Summer 2009) – Rochester, MN: Investigated the selection of fusogenic measles virus (MV) by studying: host innate immunity in cell-cell fusing and non-fusing conditions with and without MV infection; effect on viral infectivity in the presence of immunized human serum; and active ribosome, nuclear, and viral protein localization within syncytia.

Honors & Awards

University of Wisconsin, Medical Scientist Training Program (MSTP): Nominated and Elected as MSTP Co-President (Spring 2013 – 5)

University of Wisconsin, Cellular and Molecular Pathology Graduate Program: CMP T32 Training Grant (July 1, 2014 – June 30, 2015), Travel Grant (2013)

Mayo Graduate School: Summer Undergraduate Research Fellowship (2009)

University of Minnesota: Suma Cum Laude with Distinction (2010), Phi Beta Kappa (2010-Present), Richard C. Nelson Endowed Scholarship in Biochemistry (2009), Juliamarie Andreen Grilly Undergraduate Research Scholarship in Molecular Biology (2008), Dean's List (2006-10), National Residence Hall Honorary (2007), Golden Key International Honour Society (2007-Present)

DISSERTATION ABSTRACT

The common cold is the most prevalent infectious disease in humans, and the rhinovirus (RV) is the main pathogen responsible. While most RV infections result in mild illness, young and old patients and those with chronic airway inflammatory diseases, cystic fibrosis (CF), and immunodeficiencies are predisposed to higher symptom burdens and respiratory distress. Many studies have demonstrated an increased disease severity with the RV-C species in all of these populations, however there is still very little known about RV-C molecular biology and the mechanism by which they are able to cause more severe respiratory disease. Our knowledge of RV-C structure and biology is further limited by the lack of a robust culture system and purification method for their study. Furthermore, there are no data in the literature on the cellular tropism of the RV-C, an important consideration to fully understand the mechanism of RV-C entry and interactions with the host. Thus, there were two primary goals of this dissertation: the first was to develop a more robust growth and purification protocol for all RV-C clones; and the second was to identify the cellular and tissue targets of the RV-C in respiratory epithelium, and additionally determine the relationship of CDHR3 expression with RV-C tropism.

In this dissertation, we address the need for an improved purification protocol for multiple isolates of the RV-C, refute the hypothesis that RV-C capsids are intrinsically less stable than those of other species, and present a revised purification protocol that results in high levels of purified virus materials. We also identified an increased sensitivity to low pH in all RV-C genotypes examined, and demonstrated an increased capacity for virion production in Wis.L cells (embryonic fibroblasts). We further identify the ciliated respiratory epithelial cell as the primary target of the RV-C by multiple methods and demonstrate that the majority and highest levels of CDHR3 expression occurs in the ciliated cell population. Our data also indicate that RV-C infection results in cell shedding, diminished CDHR3+ populations, and decreased CDHR3 expression in individually infected cells. We then present preliminary evidence that the RV-C target pharyngeal but not palatine tonsillar epithelium. The work presented in this thesis demonstrates foundational experiments that answered multiple important questions regarding basic RV-C capsid biology and tissue tropism and will serve as a springboard for future studies into RV-C structure, biochemistry, and interactions with the human host.

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