

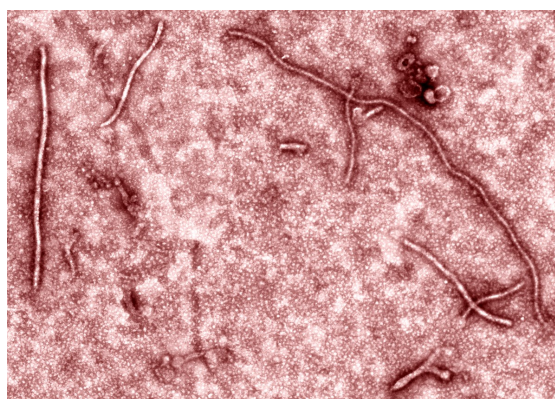
August 2015



Center for Childhood Infections and Vaccines

Ebola Vaccine Contract Awarded to Emory's VTEU and CCIV Investigators

A team of CCIV investigators has taken the lead in a new \$4.5 million contract from NIH to intensively study two Ebola vaccines in humans. The team is led by Evan Anderson, Paul Spearman, Mehul Suthar, Karnail Singh, and Anita McElroy; all working within the Emory Vaccine and Treatment Evaluation Unit (VTEU) led by Mark Mulligan. A number of Emory leaders in systems biology will also contribute to this project, which will study the proteomics, transcriptomics, lipidomics, and metabolomics of a prime-boost regimen of the MVA multi-filovirus vaccine from Bavarian Nordic and the Ad26 Zaire vaccine from Crucell Holland BV. This exciting study has the potential to identify early innate immune responses that can predict later protective responses against Ebola and Marburg viruses. Along the way the investigators are developing new assays to measure cellular and humoral responses to Ebola vaccination that should be useful in global efforts to understand and combat this deadly infection. The team has benefited



Ebolavirus is a filovirus, and forms long filamentous strands covered with viral proteins. Shown are Ebola virus-like particles contributed by Xuemin Chen and Karnail Singh, with negative stain EM image by JJ Wang.

from the experience at Emory in caring for the first Ebola-infected individuals to be treated in the United States. Studies performed by Dr. Anita McElroy working with Rafi Ahmed and colleagues of the Emory Vaccine Center this past year showed that cellular immune responses against Ebola were present early after infection, and documented a very high plasmablast response to Ebola infection. The current vaccine trial represents a unique opportunity to compare immune responses observed in vaccine recipients with the responses observed in Ebola-infected individuals treated at Emory.

-submitted by Paul Spearman, MD

Inside this issue:

Highlight: Mark Prausnitz 2

Highlight: Philip Santangelo 3

Recent Grants 4

Recent Articles 5

Upcoming Events 7

CCIV Social

September 10 at 5:30 pm in ECC 502

Come join fellow CCIV members to welcome new faculty member Bernardo Mainou, PhD



An Interview with CCIV Member Mark Prausnitz, PhD



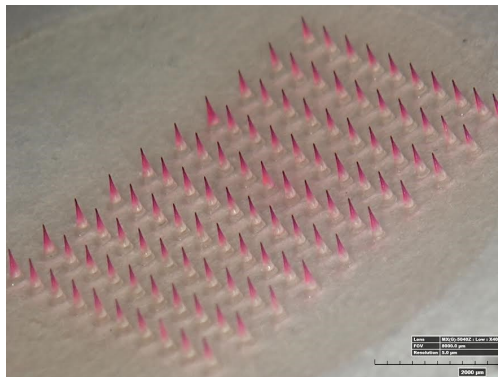
Mark Prausnitz, PhD
Regent's Professor and
Love Family Professor of
Chemical and
Biomolecular Engineering
Georgia Tech

In June, CCIV Faculty Member Mark Prausnitz, PhD sat down with CCIV Program Coordinator Karen Kennedy to discuss his research. Keep reading to learn what Dr. Prausnitz shared about his work on vaccine delivery and microneedles.

How did Dr. Prausnitz's career evolve to focus on vaccine delivery?

In high school Dr. Prausnitz did well in chemistry class, and realizing he was science oriented, decided to study chemistry in college. He also liked the

application of engineering, so he studied chemical engineering. Later realized that the classical applications of chemical engineering was not his area of interest, rather he liked the chemical engineering of molecules and controlling where molecules go in the body. After college, Dr. Prausnitz took a job at a company that worked on patches for transdermal drug delivery, which was the beginning of his interest that grew his graduate school and his own lab's interest in the development of microneedles for drug and vaccine delivery. Initially he didn't work on vaccine delivery, but a visiting scientist position at the NIH in 2002 in vaccine research ultimately led to a collaboration with Emory researcher Richard Compans, PhD, an expert in influenza vaccines. The flu vaccine turned out to be a good match for microneedle technology, and Dr. Prausnitz's interest in developing microneedle technology for vaccine delivery grew. Since his collaboration with Dr. Compans, Dr. Prausnitz has continued his local collaborations, working with multiple Emory and CDC researchers as well as other collaborators at Georgia Tech. While other key collaborations have developed over time, these Atlanta-based teams have been important in the productivity of Dr. Prausnitz's laboratory.



Dr. Prausnitz described the basics of microneedles.

A goal of the microneedles is to deliver medicine or vaccines. For vaccine delivery, the microneedles need to encapsulate the vaccine and keep it stable over time, preferably without special storage needs. The needles must be able to puncture the skin and then dissolve into the skin quickly to safely deliver the vaccine without sharps waste. This is an optimization problem, and manufacturability is a concern throughout development. Being a trained engineer, Dr. Prausnitz knows the importance of considering how the microneedles should be developed for large-scale production.

What are the biggest challenges to new vaccine delivery technology?

Dr. Prausnitz noted that unlike other pharmaceutical developments, there is no "microneedle behemoth." This means there is no large backer of research in development of microneedles for various needs. Big pharmaceutical companies prefer that smaller companies develop this technology for a specific drug or vaccine, then they will acquire the very specific technology. However it is

unattractive for these companies to support more general microneedle development because the technology has such diverse applications so the company cannot get the full realization of the technology. Another challenge is that vaccines are delivered to healthy people, including babies and children, so safety standards are very high. Vaccines are also widely administered, meaning they must be cheap. Without the support of a large microneedle backer, these requirements can be burdensome, but not insurmountable, as Dr. Prausnitz has shown.

Continued on page 3



CCIV Faculty Highlight: Philip Santangelo



Philip Santangelo, PhD
Associate Professor
Department of Biomedical
Engineering
Georgia Tech

Dr. Philip Santangelo is concerned about the lack of treatment and cures for a number of important infectious agents. Dr. Santangelo is attempting to address this through the development and engineering of new molecular imaging technology for uncovering biological mechanisms.

Molecular imaging provides both spatial and temporal information, at the single molecule, cell or organism level, which cannot often be obtained

via biochemical assays; these tools have the potential to reveal new mechanisms and drug targets.

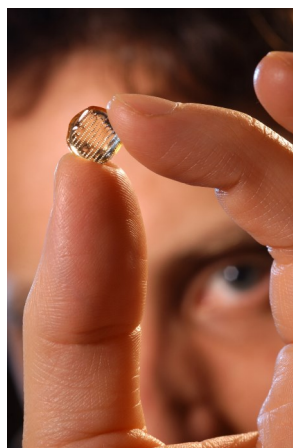
Every year one out of 100-200 children end up in the hospital with severe respiratory syncytial virus (RSV) infections. Currently there is no vaccine for RSV and few treatments. Dr. Santangelo is addressing this through the development of new imaging agents to reveal the mechanisms of the RSV virion assembly, entry, and replication in live cells, with the goal of

identifying virus specific mechanisms as new drug targets. The lab has developed single molecule-sensitive probes for imaging ribonucleic acid (RNA) molecules, which allow for the study of RNA regulation, an important part of gene expression, and the replication and assembly of RNA viruses such as RSV. We have also developed, based on these probes, a method for detecting RNA-protein interactions in situ, with single interaction sensitivity, which should aid in revealing interactions associated with RSV mechanisms.

Another area of interest to him is HIV infection. In order to cure HIV, it is critical to understand where the virus is “hiding” during treatment, and how treatments affect the virus at different locations within the body. To confront this issue, the Santangelo lab, in conjunction with the Villinger lab at Emory, has developed positron-emission tomography (PET) probes, which utilize antibodies and radioactive atoms to target SIV in the macaque model and enable whole body scans for the virus. This type of probe should be easily adapted to HIV in humans. The hope is that the tool will contribute to the discovery of new treatments and possibly even a cure for HIV.

-submitted by Philip Santangelo, PhD

Mark Prausnitz Interview *continued from page 2*

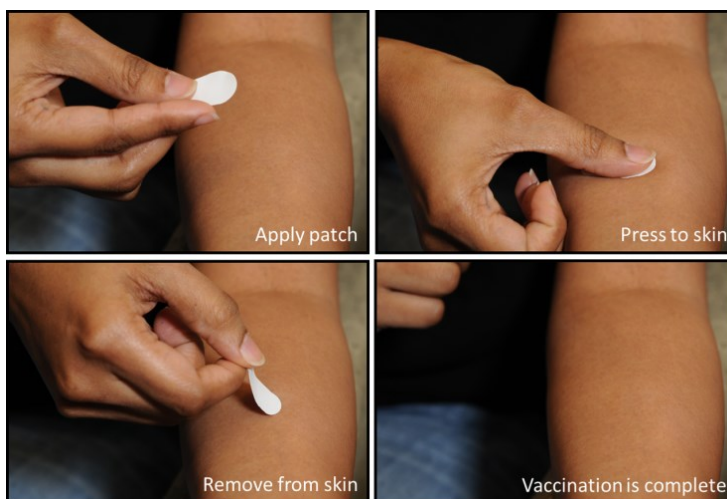


What is the most exciting/new thing on the horizon?

Dr. Prausnitz is very excited that microneedles are opening new avenues to bring necessary medicines/ vaccines to people who need them while lowering logistical barriers. There are two microneedle vaccine clinical trials in the pipeline in which Dr. Prausnitz is involved. First there is a flu vaccine trial starting this year. Next

year there will be a trial with a polio vaccine, which will include children in the later phase II studies.

Furthermore, Dr. Prausnitz underscored the excitement he has the Atlanta research community—his collaborators at Georgia Tech, Emory and the CDC have provided the critical mix of engineering and biomedical expertise to make these and future project possible.



Thank you to Dr. Prausnitz for the images, obtained from http://drugdelivery.chbe.gatech.edu/gallery_index.html

Recent Funding Awards to CCIV Members

Investigator	Title	Sponsor
Evan Anderson	An Observational, Non-Interventional Study in the United States to Characterize	UNITED BIOSCIENCE CORPORATION
Evan Anderson	Merck V210-063-0001: A Phase III Double Blind, Randomized, Multicenter	COVANCE
Evan Anderson	Clinical Evaluation of an Improved BinaxNOW Influenza A&B Card	ALERE SCARBOROUGH
Evan Anderson	PXVX-VC-200-004	PAXVAX INC
Evan Anderson	PXVX-VC-200-005	PAXVAX INC
Evan Anderson	V118-05, A Phase III, Stratified, Randomized, Observer Blind, Controlled	ICON CLINICAL RESEARCH
Andres Camacho-Gonzalez	The MACARTI trial with linkage to care and counseling	CDC
Andres Camacho-Gonzalez	A1424452: A Prospective Single Arm, Open-label, International, Multicenter	BMS
Ann Chahroudi	Vitamin D, drug metabolism, and cardiovascular complications in pediatric HIV	CASE WESTERN RESERVE UNIVERSITY
Rana Chakraborty	GS-US-183-0160	GILEAD SCIENCES
Rana Chakraborty	GS-US-216-0128	GILEAD SCIENCES
Rana Chakraborty	GS-US-292-0106	GILEAD SCIENCES
Joseph Hilinski	IRB 48991 Pfizer 1015 Arm A and B, MCV4 Tdap and rLP2086 Vaccine 10 to 13 years	PFIZER
Lisa Kobrynski	170904 - A CLINICAL STUDY OF IMMUNE GLOBULIN SUBCUTANEOUS (HUMAN), 20% SOLU	BAXTER HEALTHCARE CORPORATION
Tracey Lamb	Ephrin Ligands as Novel Targets for an Adjunct Therapy in Cerebral Malaria	NIH
Gregory Melikian	Biophysics of Protein-Mediated Membrane Fusion	NIH
Gregory Melikian	Entry mechanisms used by a model retrovirus	NIH
Martin Moore	R2222-RSV-1332 Regeneron Pharmaceuticals Laboratory Services Agreement	REGENERON PHARMACEUTICALS
Andi Shane	DMID 11-0070 Herpes Simplex Virus-GeneXpert-401	UAB
Andi Shane	DMID 11-0068 CMX 001 Neonatal Herpes HSV-402	UAB
Paul Spearman	Mucosal Protection Against HIV Generated by PIV5 Priming and VLP Boosting	NIH
Paul Spearman	IRB00055834 GSK IV Zanamivir	GLAXOSMITHKLINE
Paul Spearman	Pediatric and Adolescent HIV/AIDS research program at Emory University School of M	WESTAT
Paul Spearman & Evan Anderson	VTEU Ebola Contract	NIH
Mehul Suthar	Identifying host genetic determinants that regulate dendritic cell activation	NIH

Note: If you have an awarded grant that you would like included in the next CCIV newsletter, please contact kmurra5@emory.edu

Recent Publications by CCIV Members

- Anderson EJ, Shippee DB, Tate JE, Larkin B, Bregger MD, Katz BZ, Noskin GA, Sederdahl BK, Shane AL, Parashar UD, Yogev R. Clinical characteristics and genotypes of rotavirus in adults. *J Infect.* 2015 Jun;70(6):683-7. PMID: 25481405.
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Recent Publications continued

Continued from page 5

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Note: If you have a publication that you would like included in the next CCIV newsletter, please contact kmurra5@emory.edu

Keep in Touch

Visit our website: www.pedsresearch.org/centers/detail/immunology-vaccines

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Emory+Children's Pediatric Research Center

An Atlanta-based research alliance



Upcoming Events

Pediatric ID Seminar Series

Meets each Thursday at 1 pm in the Emory-Children's Center Room 202

September 3: Elizabeth Wright

September 10: Zunlong Ke (Wright Lab) and Jason Hammonds (Spearman Lab)

September 17: Nate Jacobs (Lamb Lab) and Mingli Qi (Spearman Lab)

September 24: Karnail Singh (Spearman Lab) and Siddhartha Bhaumik (Kaja Lab)

October 1: Jens Wrammert

October 8: Sujin Lee (Moore Lab) and Chetan Sood (Melikian Lab)

October 15: Thayer King (Lamb Lab) and Tanay Desay (Melikian Lab)

October 22: JJ Wang (Spearman Lab) and Patrice Mimche (Lamb Lab)

Wednesday, November 18, **Raymond Pickles** from UNC will be visiting, visit www.pedsresearch.org for more details in November

