



Center for Tropical &
Emerging Global Diseases
UNIVERSITY OF GEORGIA



Global Health Through Research

Director's Corner

As the Center for Tropical and Emerging Global Diseases enters its 20th year in existence, we have much to be excited about with the start of the new academic year. Our faculty, postdocs, students, and staff have been very productive and many new initiatives are underway.



One of my favorite activities, the Research In Progress (RIP) series is starting again and I look forward to hearing about the latest progress in research on parasitic diseases. We also welcome a new group of PhD students in the ILS program that undoubtedly will be seeking to secure slots in the CTEGD laboratories. A good way for these students to learn about CTEGD research is by participating in the RIP seminars every Monday morning at 8:30 in Coverdell 175! Finally I want to congratulate the new trainees in the NIH supported T32 training program. There were so many high quality applicants the review committee had a difficult time selecting these students. We certainly have many more deserving students than slots in the training program, yet all the trainees in CTEGD benefit from the NIH supported program. Watch out for an announcement for trainees to learn more about fellowship opportunities on October 12th.

Research in Progress Schedule:

Aug. 13 - Tarleton Lab; Nicole Holderman, Nicole Solano
Aug. 20 - Docampo Lab; Joshua Butler, Michelle Evans
Aug. 27 - Cassera Lab; Brain Mantilla, David Cobb
Sept. 17 - Strand Lab; Evgeniy Potapenko
Sept. 24 - Peterson Lab; Vanessa Morase
Oct. 1 - Mensa-Wilmot Lab; Vivian Padin-Irizarry
Oct. 8 - Kyle Lab; Luca Valzania
Oct. 15 - Harn Lab; Steve Maher
Oct. 22 - Brown Lab; Amrita Sharma, Karla Marquez-Noqueras
Nov. 5 - Moreno Lab; Ruby Harrison, Natasha Perumal
Nov. 12 - Colley Lab; Flavia Zimbres, Rodrigo Baptista
Nov. 26 - Wolstenholme Lab; Srinivasan Ramakrishnan, Bret Boyd
Dec. 3 - Etheridge Lab; Stephen Vella, Manuel Fierro
Jan. 14 - Muralidharan Lab; Nuria Negrao, Nathan Chasen
Jan. 28 - Tarleton Lab; Ana Lisa Valenciano, Heather Bishop
Feb. 4 - Murdock Lab; Ellen Martinson, Michael Arvin
Feb. 11 - Hajduk Lab; Connor O'Neill, Jayce Brandt
Feb. 18 - Sabatini Lab; Chris Rice, Anat Florentin
Feb. 25 - Docampo Lab; Natalie Wilson, Pei-Tsz Shin
Mar. 4 - Strand Lab; AJ Stasic
Mar. 18 - Harn Lab; Vincent Martinson
Mar. 25 - Moreno Lab; Jessica Ramadhin, Bowen Deng
Apr. 1 - West Lab; Alona Botnar, Abigail Calixto
Apr. 8 - Kyle Lab; Paul Guyett, Germain Chevignon
Apr. 15 - Kissinger Lab; Justin Wiedeman, Kerri Miazgowicz
Apr. 22 - Lammie Lab; Myriam Andrea Hortua-Triana
Apr. 29 - Champagne Lab; Msano Mandalasi

Stay Connected!

Paul D. Coverdell Center for Biomedical Research
500 D. W. Brooks Drive
Athens, GA 30602
Telephone: 706-583-0861

EMAIL: ctegd@uga.edu

WEBSITE: <http://ctegd.uga.edu>

FACEBOOK: /ctegd

TWITTER: @CTEGD

Join our CTEGD Trainees & Trainers LinkedIn Group:
<https://www.linkedin.com/groups/8155510>

Get periodic updates by email:
<http://eepurl.com/81ZAX>

CTEGD Staff

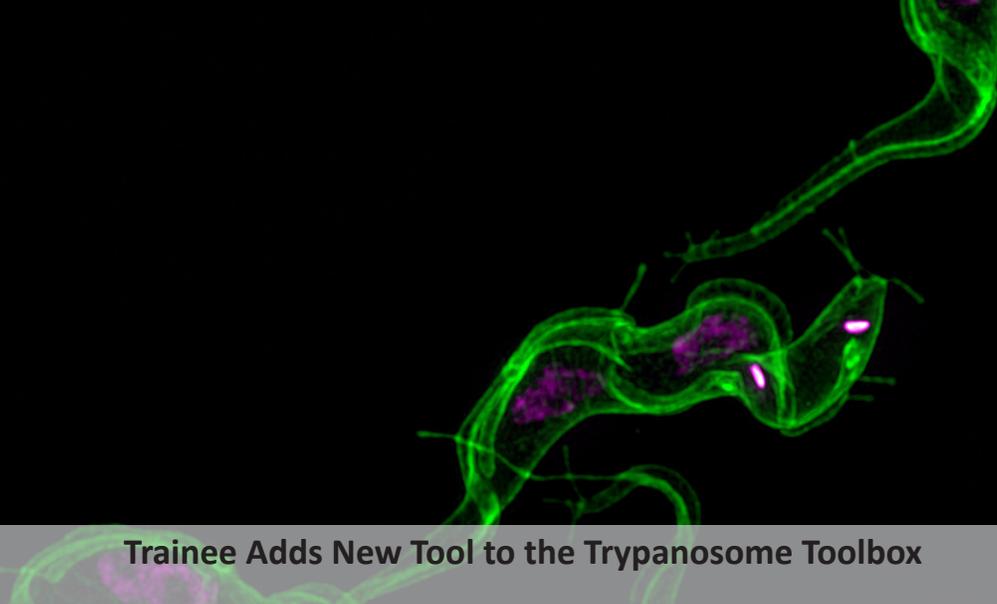
Director:	Dennis Kyle
Office Manager:	Erica Young
Accountant:	Annie Curry
Publicity Manager:	Donna Huber
IT:	David Dowless
Symposium Director:	David Peterson
Research in Progress Coordinators:	Bob Sabatini Vasant Muralidharan
T32 Director:	Silvia Moreno

Cover image description:

Dan Colley at the sand harvesters site on Lake Victoria ca. 2010. Snails infected with schistosomes could be found in the water hyacinths on the water's edge. Dan concluded his long-standing (25 years) study with his colleagues at KEMRI/CGHR in Kisumu, Kenya this past spring. He began the project while at the CDC and continued it the last 13 years at the University of Georgia with a grant from the National Institutes of Health.

Support our mission
Give online TODAY!
<https://t.uga.edu/1GR>

Our Mission: To pursue cutting edge research on tropical and emerging diseases, train students in this field and effectively tackle global diseases of poverty.



Trainee Adds New Tool to the Trypanosome Toolbox

by Donna Huber

When Ph.D. trainee Justin Wiedeman started investigating the role of protein kinase TbCK1.2, an enzyme found near the flagellum of *Trypanosoma brucei*, he quickly ran into a problem common to parasitologists. He needed a better tool for visualizing the membranes of this parasite. Since none of the membrane probes on the market quite did the job, he looked at how he could modify one for his purpose. He found a successful candidate in Synaptic Systems' mCLING.

What is *Trypanosoma brucei*?

Trypanosoma brucei is a single cell parasite that causes Human African Trypanosomiasis (HAT), which is also known as African sleeping sickness. HAT occurs in 36 sub-Saharan countries where tsetse flies transmit the parasite to people and livestock. In cattle, the disease is known as nagana. Tsetse fly control efforts have drastically reduced the number of cases. According to the World Health Organization, in 2015, there were around 2,800 cases. However, a person can be infected for months or even years without symptoms. By the time symptoms become evident, the person is in the advanced stages of the disease and their central nervous system is impaired.

New tools are needed to study trypanosomes

There is still much to be learned about the parasite that could lead to better detection and more effective treatment. A major obstacle to the study of this tiny organism is the lack of tools and technology. Kojo Mensa-Wilmot's research group in the Center for Tropical and Emerging Global Diseases at The University of Georgia has been instrumental in developing techniques and tools to increase the research community's understanding of *T. brucei*. Now, Wiedeman has added a new tool to the trypanosome biology toolbox – a general method of outlining trypanosomes in fluorescence microscopy experiments.

"We are the first group to solve this general problem in super-resolution microscopy of *T. brucei*," said Wiedeman. "mCLING is a highly versatile tool for studying trypanosome biology – it can be used with live or fixed trypanosomes."

Fluorescent microscopy has been a leading method of studying *T. brucei*; however, there are limitations to this technology. Super-resolution microscopy offers great advantages over standard fluorescence microscopy. By employing several tech-

niques to increase resolution, it allows for the observation of objects smaller than what can be seen with visible light. Yet, it is not without its own limitations, most notably the inability to determine the periphery of cells. Without knowing the outer edges of the parasite, orientation of organelles and other structures within the cell is difficult.

"For *Trypanosoma brucei*, most of the membrane probes available do not work well in fixed trypanosomes," said Wiedeman. "Researchers have been forced to use crude methods to outline trypanosomes in fluorescence microscopy."

These "crude methods" include superimposing a transmitted light image or hand-drawing the outline. However, this workaround only allows for a two-dimensional study of the cell. Therefore, Wiedeman turned to a dye called mCLING that has been developed to track the membranes of neurons using super-resolution microscopy to see if he could adapt the technology to *T. brucei* membranes.

mCLING allows for the visualization of *T. brucei* membranes

"mCLING labels the flagellum and plasma membrane vividly, sometimes providing details of cell structure that rivals images obtained with scanning electron microscopy," said Wiedeman.

continued on next page

Newly Funded Projects:

Rick Tarleton received a grant from Janssen Research Foundation to screen compound libraries for reversal/prevention of dormancy and/or amastigote to trypomastigote stage conversion in Chagas disease.

Roberto Docampo received an NIH grant for drug target validation in *Trypanosoma cruzi*.

Anat Florentin received an American Heart Association Fellowship to study the function of the bacterial Clp complex in the apicoplast of malaria parasites.

Adrian Wolstenholme received an NIH grant to screen *C. elegans* mutant strains for new clues about ivermectin and its mode of action.

Using a combination of standard-resolution and super-resolution fluorescence microscopy, he was able to confirm mCLING labels the plasma and flagellar membranes of *T. brucei*. Furthermore, using the Zeiss ELYRA S1 super-resolution microscopy in the Biomedical Microscopy Core, mCLING allowed for a 3D reconstruction of the parasite. This is the first time such an image has been reported. Finally, using the new ImageStream X Mark II in the CTEGD Cytometry Shared Resource Laboratory, he discovered mCLING could be used to track endocytosis (the process of importing molecules into the cell) in real time.

Recognizing mCLING's potential to inform other studies of trypanosome biology, Weideman optimized protocols for using it with immunofluorescence assays and thus making possible what had been impossible with the overlay technique – visualizing the location of organelles in the vertical dimension relative to the cell body.

“It is especially well-suited for studying flagellar membrane biogenesis as well as kinetically tracking uptake of the plasma membrane into vesicles inside trypanosomes,” said Wiedeman. Other laboratories have already implemented these protocols in their own research. Steve Hajduk's group, also in the Center for Tropical and Emerging Global Diseases, is using mCLING to study nanotubes in *T. brucei*.

This tool will allow for the study of trypanosomes in finer detail than ever before and the Mensa-Wilmot Research Group anticipates unlocking previously unseen secrets in *T. brucei*.

The full published study is available online: Wiedeman J, Mensa-Wilmot K (2018). A fixable probe for visualizing flagella and plasma membranes of the African trypanosome. *PLoS One* 13(5):e0197541. <https://doi.org/10.1371/journal.pone.0197541>

Other published articles

Mark Brown and collaborators at the University of Nevada and Indian Institute of Chemical Technology published “Insulin receptor knockdown blocks filarial parasite development and alters egg production in the southern house mosquito, *Culex quinquefasciatus*” in [PLoS Neglected Tropical Diseases](#).

Pat Lammie and collaborators also published in [PLoS Neglected Tropical Diseases](#) their studies on the impact of school water, sanitation, and hygiene improvements on infectious disease using serum antibody detection. He also published with other collaborators on the use of bead-based serologic assay to evaluate Chikungunya virus epidemic, Haiti in [Emerging Infectious Diseases](#). In the same journal, he and collaborators published “[Integrated Serologic Surveillance of Population Immunity and Disease Transmission](#)”.

Michael Cipriano and **Stephen Hajduk** had the review article “Drivers of persistent infection: pathogen-induced extracellular vesicles” published in [Essays in Biochemistry](#).

Silvia Moreno and her laboratory had their study, “Tagging of weakly expressed *Toxoplasma gondii* calcium-related genes with high-affinity tags”, published in [The Journal of Eukaryotic Microbiology](#).

Dan Colley and his collaborators at the CDC and in Kenya reported on functional studies of T regulatory lymphocytes in human schistosomiasis in Western Kenya in [The American Journal of Tropical Medicine and Hygiene](#). They also published on the impact of mother's schistosomiasis status during gestation on children's IgG antibody responses to routine vaccines 2 years later and anti-schistosome and anti-malarial responses by neonates in Western Kenya in [Frontiers in Immunology](#).

Adrian Wolstenholme and his collaborators published “Deciphering the molecular determinants of cholinergic anthelmintic sensitivity in nematodes: When novel functional validation approaches highlight major differences between the model *Caenorhabditis elegans* and parasitic species” in [PLoS Pathogens](#).

Belen Cassera and her collaborators reported on antiplasmodial diterpenoids and a benzotropolone from *Petradoris pumila* in the [Journal of Natural Products](#). She and other collaborators also published “Antimalarial activity of the isolates from the marine sponge *Hyrtios erectus* against the chloroquine-resistant Dd2 strain of *Plasmodium falciparum*” in [Zeitschrift für Naturforschung C](#).

Dennis Kyle and his collaborators published in [Nature Communications](#) “A comprehensive model for assessment of liver stage therapies targeting *Plasmodium vivax* and *Plasmodium falciparum*”. He and other collaborators also published “Reversal of chloroquine resistance of *Plasmodium vivax* in Aotus monkeys: in [Antimicrobial Agents and Chemotherapy](#).”

Jessie Kissinger and her collaborators had “EuPathDB: The Eukaryotic Pathogen Genomics Database Resource” published in [Eukaryotic Genomic Databases](#), which is part of the Methods in Molecular Biology book series.

Michael Strand and his collaborators published “Parasitic insect-derived miRNAs modulate host development” in [Nature Communications](#). He and collaborators published in [G3, Genome Report: Whole genome sequence of the parasitoid wasp *Microplitis demolitor* that harbors an endogenous virus mutualist](#).

Don Champagne and his collaborators published a study on marine leech anticoagulant diversity and evolution in [Journal of Parasitology](#).

Srinivasan Ramakrishnan and **Roberto Docampo** published “Membrane proteins in trypanosomatids involved in Ca²⁺ homeostasis and signaling” in [Genes](#).

Courtney Murdock and her collaborators published on the carry-over effects of urban larval environments on the transmission potential of dengue-2 virus in [Parasites & Vectors](#).

Belen Cassera and her collaborators had their article “Metabolomic profiling reveals a finely tuned, starvation induced metabolic switch in *Trypanosoma cruzi* epimastigotes”, selected to appear in a special virtual issue of ASBMB journal content on “Omics of lipids, glycans and polar metabolites,” hosted at JBC.



Silvia Moreno Honored

Silvia J. Moreno has been named a Distinguished Research Professor by The University of Georgia. The title is awarded to faculty who are internationally recognized for their original contributions to knowledge and whose work promises to foster continued creativity in their discipline.

Dr. Moreno, a professor in the cellular biology department and director for the NIH Training Grant in Tropical and Emerging Global Diseases, is recognized for her studies on calcium signaling in parasitic protozoa.

Her work defined the link between calcium signaling and pathogenesis of infectious organisms. Her research focuses on *Toxoplasma gondii*, a pathogen that infects one-third of the world population. She and her team discovered mechanisms of calcium signaling in parasites and novel compartments that store calcium that are different from those present in mammalian cells. Her laboratory developed new genetic tools to study calcium that could be used for high-throughput assays to find new pharmacological agents for the potential treatment of parasitic diseases.

Based on another fundamental discovery from her lab, that *Toxoplasma* takes specific nutrients from its host, she proposed the development of therapeutics that combine

host-encoded and parasite-encoded functions as a novel approach for chemotherapy.

Silvia Moreno was recently named Corresponding Member of the Latin American Academy of Sciences. She is a distinguished research professor in the department of cellular biology and also serves as director of CTEGD's NIH-funded Training Grant in Interdisciplinary Parasitology, Vector Biology, Emerging Diseases. Her research team works with *Toxoplasma gondii*, an apicomplexan parasite that infects almost one-third of the world population.

The Academia de Ciencias de América Latina, created in 1982 under the sponsorship of the Pontifical Academy of Sciences, promotes and contributes to the advancement of mathematical, physical, chemical, earth, and life sciences, and to their application to the development and integration of Latin America and the Caribbean. The Academy promotes cooperation among scientific institutions and the exchange of persons and scientific knowledge for the integration of Latin American and the Caribbean; studies of sciences policy that contribute to the stable and continuous development of the countries of Latin American and the Caribbean; science at different educational levels and among the entire population.

Trainees Honored

Katherine Wakely, a graduate student in Ynes Ortega's laboratory, received first place for the Dr. Jim Ayres Young Investigator Award from the Georgia Association for Food Protection.

Anat Florentin, a postdoctoral researcher in Vasant Muralidharan laboratory received the 2018 Postdoctoral Research Award. Created in 2011, the Postdoctoral Research Award recognizes the remarkable contributions of postdoctoral research scholars to the UGA research enterprise. The UGA Research funds up to two awards per year to current scholars.

Ciro Cordeiro, a postdoctoral researcher in Roberto's Laboratory, was invited to talk at the joint meeting of the Phyco-logical Society of America & International Society of Protistologists in Vancouver, Canada on how inositol phosphates regulate phosphate homeostasis in unicellular eukaryotes.

UGA Flow Day 2018

The CTEGD Cytometry Shared Resource Laboratory hosted a UGA Flow Day on June 26, 2018. The day was spent educating UGA scientists on the application of flow cytometry and how it can be used to facilitate their research. More than 100 people registered and 70 attended. The response was very encouraging for the future of our shared resource laboratory and the use of our instruments in research on campus. The response was so positive that we are tentatively scheduling follow-up educational events for the Fall and Winter.

Don Harn, Lisa Shollenberger, and Yvonne Paterson received a patent for the use of *Listeria* vaccine vectors to reverse vaccine unresponsiveness in parasitically infected individuals.



Trainee Spotlight: Anat Florentin

Anat Florentin, a post-doctoral associate in Vasant Muralidharan's laboratory, is originally from Israel. She received her BSc degree from Tel-Aviv University and MSc from the Weizmann Institute of Science. She obtained her Ph.D. also from the Weizmann Institute where she studied programmed cell death mechanisms using the fruit fly as a model organism. Dr. Florentin moved to the United States 4 years ago when she joined the Muralidharan Research Group. During her time at UGA, she has received a number of awards in recognition of her research:

American Heart Association Postdoctoral Fellowship (2018-2020)

Postdoctoral Research Award, UGA Office of Research (2018)
Foreign travel award, UGA Office of Research (2018)

Best Poster Presentation award at the UGA GSPS Research Day (2016)

Best Postdoctoral Poster award at the 2015 UGA Conference on Drug Discovery (2015)

Why did you choose UGA?

Since my background is in basic cell biology and genetics, I knew very little of the biology of parasites but was determined to study malaria. While I was looking into different places in Europe and the US, I met with another Israeli, Lilach Sheiner who, at the time, was doing her postdoctoral training with Dr. Boris Striepen at UGA. She told me very good things of CTEGD and of a great newly recruited faculty who studies malaria. I came for a visit, and was impressed by the engaging scientific community, the super friendly atmosphere and the variety of different parasites and approaches to study tropical neglected diseases. I am so glad I made this decision!

What is your research focus/project and why are you interested in the topic?

The goal of my research is to understand the unique cell biology of malaria parasites and to identify potential drug targets. In order to do that I develop and apply genetic and molecular tools that are used to manipulate the genome of the parasite. During my years in the lab I was involved in several projects; One of them studies mechanisms by which the parasite transports proteins into the host red blood cell. Another interesting project focuses on a conserved complex from bacterial origin that resides within a unique parasite

organelle called the apicoplast. Lastly, I am looking for genes that might be involved in programmed cell death processes in the parasites.

What are your future professional plans?

I want to establish my own research lab, conduct independent research and train the next generation of future scientists.

Have you done any field work or is there a collaborator/field site that you would like to visit in order to enhance your training?

Although we use field samples in our studies, I have never been to any field site, and would absolutely love to visit one. I am positive it will enhance my training and will add another layer to the work that I am doing. I am sure that visiting any field site in a malaria endemic area, such as Africa or Southeast Asia would be an enriching experience that would underline the significance of our work.

What is your favorite thing about UGA and Athens, GA?

Many things... At CTEGD I cherish the collaborative atmosphere, the variety of parasitism-related topics, the strong basic science that goes together with field studies and translational research. I am highly appreciative of the fact that I have access to a huge amount of knowledge by working side by side with top experts in these fields.

Athens is also great. Moving here in 2014 with a family of 2 young kids couldn't go smoother! We found here a great community of friends, great public schools, and amazing nature. I love the mountains, the trees and the wildlife around us!

Any advice for students interested in this field?

There is still so much to do and learn in the field of parasitology and every discovery that you make may impact the life of the millions that suffer from these diseases. Don't hesitate if you don't know much about parasites. No matter what your background is, you can use the tools and knowledge that you acquired and apply them to this challenging but rewarding research!