Center for Tropical & Emerging Global Diseases
UNIVERSITY OF GEORGIA

Global Health Through Research

May 2020 **Volume 5 Issue 1**

Director's Corner

The last few months have been challenging for all of us, both personally and professionally. The pandemic has caused us to shut down all but essential activities in our labs and has resulted in significant disruptions in our research activities. Like the rest of society, we all are affected by the pandemic, from those with children without school or daycare, to those at higher risk due to health conditions, to those living alone and/or secluded from family and friends. Despite the challenges, CTEGD personnel have persevered and found ways to remain productive, whether it be writing manuscripts, reviewing literature, finishing classes online or writing grants. Several of our labs have pivoted and used their expertise to address the Covid-19 pandemic; we will hear more about these efforts in future newsletters. As we go forward we expect that our "new normal" will be different than how we have operated in the past. I am confident that collectively we can overcome these hurdles and find new ways to get our research done as well as train and graduate our students.

Dan Colley, our long time Director will retire effective at the end of June after a remarkable career in tropical medicine research. He and the SCORE team have just published online a 16 article supplement to the American Journal of Tropical Medicine and Hygiene that details the effective operational research program conducted over the past decade with the goal of eliminating Schistosomiasis. Congratulations to Dan and the entire SCORE network for this monumental research effort.

Last, but not least, although our research activity has been curtailed, the parasitic diseases we work to prevent have not slowed and we expect that many parasitic diseases will increase in prevalence. The work we do has never been more necessary and the challenges for controlling and eliminating these diseases has only become more difficult. I look forward to the time, hopefully in the near future, when we can safely restart our research labs to combat these challenges.

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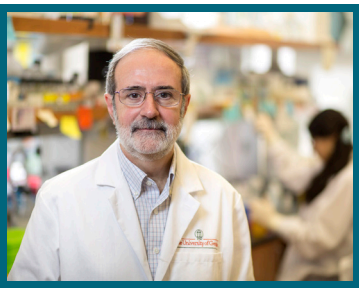
On the cover: The Arch with early morning sunlight filtering through the trees of North Campus. Credit: Peter Frey/UGA Marketing and Communications

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

Dennis Kyle elected to AAM p. 2

Trainee Spotlight p. 5



Docampo teams up with 100+ scientists to develop genetic tools p. 7

Ortega receives grant to study *Cyclospora* p. 12

In this Issue

DENNIS KYLE ELECTED TO THE AMERICAN ACADEMY OF MICROBIOLOGY

Faculty

CENTER FOR TROPICAL AND EMERGING GLOBAL DISEASES

by Donna Huber

University of Georgia researcher Dennis Kyle has been elected as a 2020 fellow by the American Academy of Microbiology. He joins a class of 68 new fellows this year.

Kyle is a GRA Eminent Scholar in antiparasitic drug discovery, with appointments in the departments of cellular biology and infectious diseases.

"Election as a Fellow of the American Academy of Microbiology is a tremendous honor and one that was achieved by the success of all the great people I've work with over the years on antiparasitic drug discovery," said Kyle, who joined UGA in 2017 as the director of the Center for Tropical and Emerging Global Diseases.

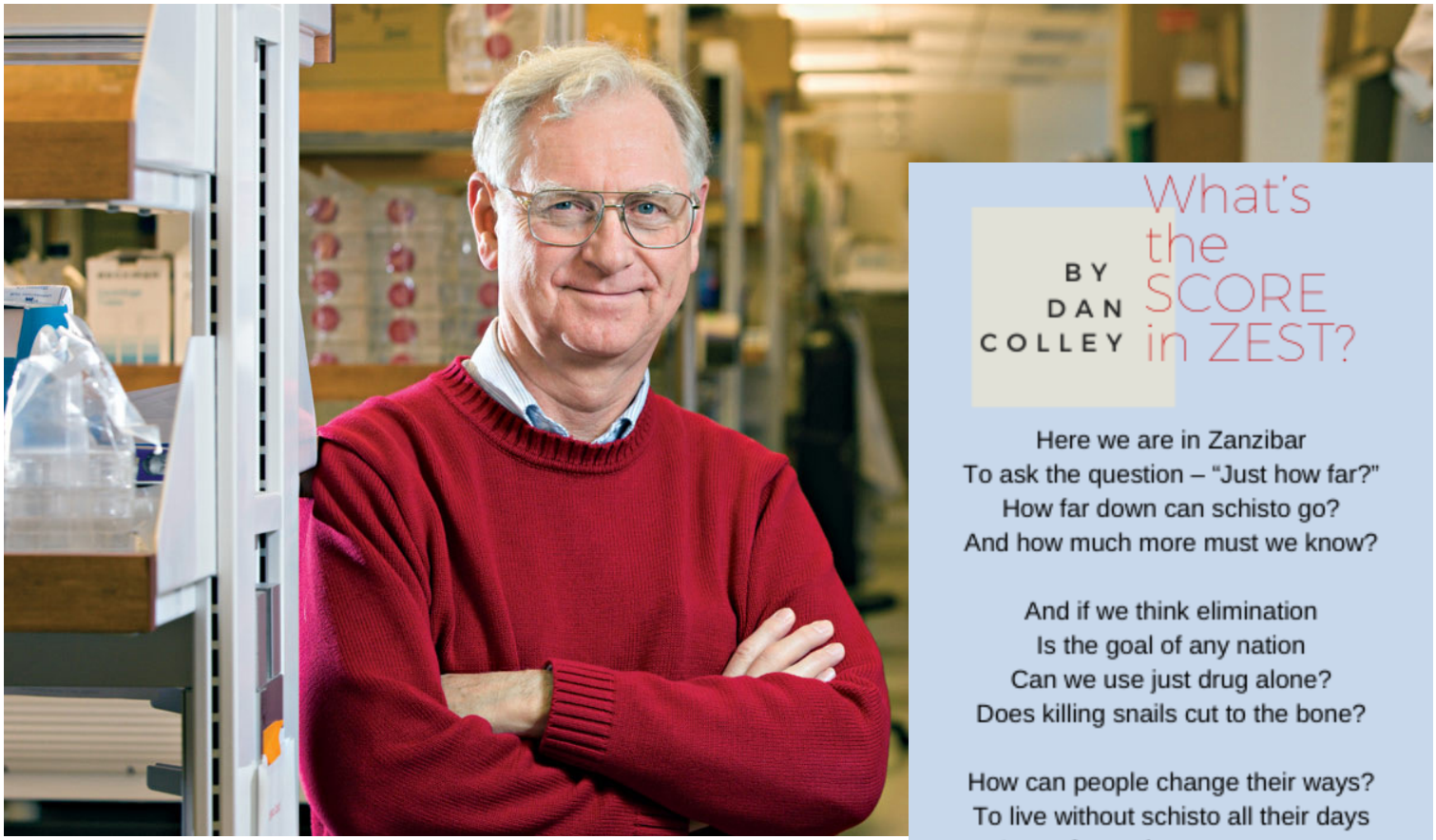
His research focuses on the discovery, development, and mechanisms of resistance to antiparasitic drugs. Currently, his laboratory is concentrating on malaria, which has become increasingly resistant to current treatments, and the brain-eating amoeba Naegleria fowleri. The Kyle laboratory has been instrumental in developing methods and tests to discover new drugs that act rapidly, effectively and can be combined with existing drugs used to treat these nearly incurable diseases.

Kyle's work is largely funded by the National Institutes of Health, Medicines for Malaria Venture and a $9.4 million grant from the Bill & Melinda Gates Foundation. He has published more than 200 research papers, and his findings have been cited more than 14,000 times.

Kyle has received a number of awards over the course of his career, including the U.S. Army Achievement Medal in 1990, the U.S. Army Commendation Medal in 1988, and the U.S. Army Meritorious Service Award. He has been honored by the Southeastern Society of Parasitologists and is a fellow of the American Society for Tropical Medicine and Hygiene and the American Association for the Advancement of Science. In 2006, he was named Scientist of the Year by Malaria Foundation International.

Kyle joins more than 2,500 AAM fellows who are elected through a highly selective, peer-review process, based on their records of scientific achievement and original contributions that have advanced microbiology. Only 58 percent of this year's nominees were elected to the Class of 2020, and the newly elected fellows hail from 11 different countries.

Global Schistosomiasis Alliance pays tribute to Dan Colley on his retirement



Dr. Daniel G. Colley, Director of the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE), will be retiring from his position as Professor at the University of Georgia on June 30, 2020. He will continue as a Professor Emeritus after that time.

As a young post-doc, Dan volunteered to go to Brazil to work on schistosomiasis. With this trip, he launched a career that spanned more than half a century. "The more I learned about schisto, the more interesting it became," Dan said. By 1992, when he joined the US Centers for Disease Control, Dan had become a well-known researcher in schistosomiasis. During his nine years at CDC, he provided leadership for the US response to parasitic diseases throughout the world. Dan came to UGA in 2001 as the Director of the Center for Tropical and Emerging Global Diseases.

In 2008, Dan was asked by the Bill & Melinda Gates Foundation to lead a major operational research effort, which became the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE). In SCORE's twelve years, it has supported researchers around the world to conduct a broad range of strategic and critical studies to address gaps in knowledge needed by NTD program Managers in controlling and moving toward elimination of schistosomiasis.

Dan has been a friend and mentor to many in the schistosomiasis community. We are grateful for his research contributions and his support of the research of others during his long career.

Many in the parasitic disease research, prevention, and control community also know Dan's skills as a poet. We leave you with this ditty that Dan wrote to mark the start of the Zanzibar Elimination of Schistosomiasis Transmission.

Originally posted at
https://www.eliminateschisto.org/news/dr-daniel-g-colley-to-retire

What's the SCORE in ZEST?

BY DAN COLLEY

Here we are in Zanzibar
To ask the question – "Just how far?"
How far down can schisto go?
And how much more must we know?

And if we think elimination
Is the goal of any nation
Can we use just drug alone?
Does killing snails cut to the bone?

How can people change their ways?
To live without schisto all their days
Lots of questions we can pose
We hope the data may dispose

Still the end is not yet here
Can we predict the month and year?
No not now, but don't you see
The will is there – so who will agree?

To take it down from five to naught
More implementing should be bought
But which of the combos will work best?
That's the goal and that is our quest!

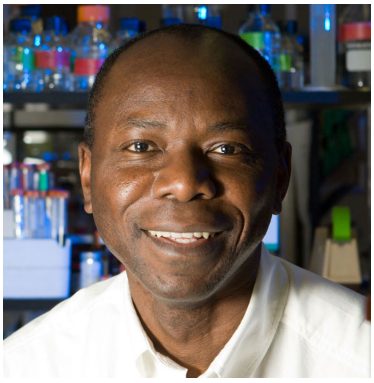
Adrian Wolstenholme retires

Adrian Wolstenholme, professor in the College of Veterinarian Medicine's department of infectious diseases, retired at the end of January.

Wolstenholme earned his Ph.D. in 1980 from the University of Cambridge. He joined the faculty of UGA in 2009 and became a member of the Center for Tropical and Emerging Global Diseases in 2013.

His major research interest was the drugs (anthelmintics) used to treat and prevent infections with parasitic roundworms (nematodes) in humans and animals. He was also very interested in the mechanisms by which the parasites become resistant to these drugs. Most anthelmintics target the nematode nervous system, causing paralysis and death, so he studied the components of the nervous system affected by anthelmintics, specifically nicotinic acetylcholine receptors and glutamate-gated chloride channels.

Kojo Mensa-Wilmot named dean at Kennesaw State University



Kojo Mensa-Wilmot has been named as dean of the College of Science and Mathematics at Kennesaw State University. He will start in his new role on August 1.

Mensa-Wilmot came to UGA in 1991 after completing his Ph.D. at Johns Hopkins University and a post-doctoral fellowship at Johns Hopkins Medical Center. Currently, he serves as department head and professor in Franklin College's department of cellular biology. He is a founding member of the Center for Tropical and Emerging Global Diseases.

Mensa-Wilmot's research has focused on Human African Trypanosomiasis, which is caused by the parsite *Trypanosoma brucei*. His laboratory is interested in first, delineating trypanosome pathways that differ significantly from host systems so that they may become the focus of efforts to discover new lead drugs. Second, they are identifying small chemical probes that may used to study trypanosome cell biology, to complement RNA interference experiments: Since there is little homology of trypanosome proteins to those in well-studied systems (e.g. vertebrates or yeasts), homology-based strategies to characterize proteins in *T. brucei* frequently yields inconclusive results.

Applications due May 25

Graduate students working in CTEGD T32 Training laboratories are invited to apply for a fellowship of the program "Training in Tropical and Emerging Global Diseases"

Potential candidates should be working in a CTEGD/T32 training laboratory and their research should focus on research areas of high interest to the CTEGD.

More info:
https://ctegd.uga.edu/opportunities/funded-training/

Trainees

Edwin Pierre Louis is a pre-doctoral trainee in the laboratory of Dr. Drew Etheridge. Originally from Haiti, he immigrated to the US to attend the University of Florida (UF), where he graduated with a Bachelor of Science in Biochem istry Molecular Biology. After earning his degree at UF, Edwin accepted a position as a biological scientist in the UF Center of Excellence for Regenerative Health Biotechnology, with a focus on gene and cell based therapeutic development, where he worked for three years. There, he first discovered his love of host-pathogen interactions as a biological scientist working under the supervision of Dr. Richard Snyder for the component Florida Biologix at this center and later merged to create Brammer Bio which was subsequently acquired by Thermo Fisher Scientific. During this time in industry, he realized that to improve his scientific capacities he would need to continue his studies by pursuing a graduate degree. As part of his prepa rations to apply to a graduate program, he joined the UGA post-baccalaureate PREP program whose mission is to prepare students interested in a graduate degree for the application process. During this time, he was granted the opportunity to join Dr. Michael Terns' laboratory for a year where he investigated the molecular mechanism of CRISPR-Cas based viral de fense in Streptococcus thermophilus as well as prime adaptation events in the type II-A CRISPR-Cas system.

Since attending UGA, Edwin has been awarded both the Gateway to Graduate School Bridge Program and the Graduate Scholars Leadership, Engagement and Development Program (GS LEAD) scholarships sponsored by the National Science Foundation (NSF).

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

Broadly, my key research interests center around how organisms like viruses and parasites manipulate their host cell in order to grow and propagate. My current project is focused on elucidating how the protozoan pathogen Toxoplasma gondii is able to use secreted protein effectors to manipulate its host cells functions.

Why did you choose UGA?

I chose to study at the University of Georgia, in part, because of my excellent post-baccalaureate experience in the PREP program. It was evident from my interactions that UGA excels at fostering a productive relationship between students and faculty. Regardless of any faculty member's relationship to the students, there was a sustained willingness for faculty to give of their time in order to see the students succeed. I also decided to pursue my PhD at UGA because of the cutting-edge research and in particular the collection of outstanding parasitologists that is uniquely found in the Center for Tropical and Emerging Global Diseases (CTEGD).

What are your future professional plans?

As I continue my graduate studies on host pathogen interaction, I plan to do some post-doctoral trainings to augment my apprenticeship and ultimately become an independent scientist to lead my own research group. I also hope to be able to give back to the local community that has contributed so much to my own personal success by donating my time and knowledge to mentor young budding scientists especially those from underprivileged homes and/or underdeveloped countries.

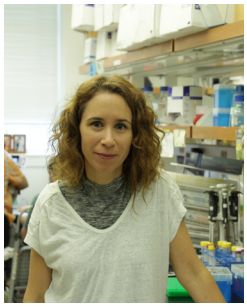
Noelia Lander receives research award

Noelia Lander, a cellular biologist and postdoctoral researcher in Roberto Docampo's laboratory, has received the 2020 Postdoctoral Award from the UGA Research Foundation.

Lander has used her research to advance understanding of a dangerous parasite affecting millions of people worldwide. She adapted the CRISPR/Cas9 genome-editing system for the study of Trypanosoma cruzi, a human parasite that causes Chagas disease. In widely cited research, she proved the usefulness of this new gene-editing system and its range of applications in T. cruzi, which historically had been difficult to manipulate. Dozens of Chagas molecular biology labs worldwide use her CRISPR/Cas9 strategy to study the parasite's proteins, characterize its metabolic pathways, understand its biology and search for new chemotherapeutic targets. More recently, she has used her system to study protein function and calcium signaling in T. cruzi. She has trained laboratory personnel and students in scientific research and is currently conducting the mentored phase of an NIH Pathway to Independence Award.

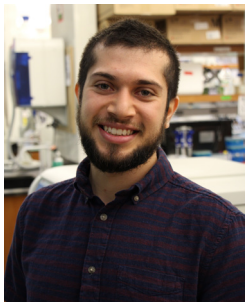
Created in 2011, Postdoctoral Research Awards recognize the remarkable contributions of postdoctoral research scholars to the UGA research enterprise. The UGA Research Foundation funds up to two awards a year to current scholars.

Lander recently accepted the postion of Assistant Professor of Biological Sciences at the University of Cincinnati.



Anat Florentin, a post-doc in Vasant Muralidharan's laboratory, has accepted a position at Hebrew University in Jerusalem.

Manuel Fierro, a Ph.D. student in Vasant Muralidharan's laboratory, successfully defended his dissertation. He will be a post-doctoral associate in the lab of Dr. Josh Beck at Iowa State University where he will be working in both the blood and liver stages of Plasmodium.



Dylon Stephens, a M.S. student in Vasant Muralidharan's laboratory, successfully defended his thesis "High-Throughput Screen to Identify Specific Inhibitors of the Plasmodium Protease, PfClpP". He will be attending the University of Texas Southwestern to pursue his Ph.D.

UGA researchers develop new genetic tools for marine organisms

Research

UGA's Roberto Docampo is part of a team of researchers developing tools to genetically manipulate marine protists, a microscopic single-cell organism that plays an important ecological role in marine ecosystems. Docampo is Barbara and Sanford Orkin/GRA Eminent Scholar in Emerging Diseases and Cellular Biology and professor in the Franklin College of Arts and Sciences. (Photo by Billy Howard)

by Donna Huber

University of Georgia researcher Roberto Docampo is part of a team developing tools to genetically manipulate marine protists, a microscopic single-cell organism that plays an important ecological role in marine ecosystems. For the first time, the researchers have developed protocols for transfection, or the introduction of foreign DNA, and gene expression in 13 species of protists.

Their results were published this month in Nature Methods. The work was funded by an $8 million grant from the Gordon and Betty Moore Foundation.

Marine protists are an untapped resource, and their study could reveal mechanisms and drug therapies to treat human and animal diseases. Protists aid in sequestering carbon dioxide, serve as a food source for many organisms (including humans), and cause the toxic red tides that have plagued Florida beaches in recent years. However, little is known about their cellular biology or evolutionary history, and no model organisms exist for this group.

Protists are a highly diverse collection of species, and the inability to genetically modify a large majority of them has been a major hurdle to their study. A few protists, such as some parasitic protists that have an impact on human or animal health, have protocols, but they are not highly representative of the broader kingdom.

Docampo and colleagues at UGA's Center for Tropical and Emerging Global Diseases joined with 53 other lab groups to build on the tools already developed for eight other species.

While they could not develop a universal protocol for genetic transfection for all protists due to their vast diversity, they were able to provide what the researchers are calling a synthetic "Transformation Roadmap."

Docampo collaborated with Virginia Edgcomb and her lab at the Woods Hole Oceanographic Institute to develop genetic tools that would allow successful transfection of genes into *Bodo saltans*.

Bodo saltans is a unicellular organism found in marine and freshwater habitats. It belongs in the Discoba group which also includes the clinically significant parasitic protists *Trypanosoma cruzi*, *Trypanosoma brucei*, and *Leishmania* spp. Docampo and his team of researchers have been at the forefront of developing the genetic modification tool CRISPR-Cas9 for *Trypanosoma cruzi*, the causative agent of Chagas Disease.

"The development of tools to genetically modify [*B. saltans*] will be essential for the study of its biology and for the understanding of the evolution of the adaptions of trypanosomatids to parasitism," said Docampo, Barbara and Sanford Orkin/GRA Eminent Scholar in Emerging Diseases and Cellular Biology and professor in the Franklin College of Arts and Sciences.

B. saltans, like the other protists in this study, will serve as a model organism for related protists that may be difficult to culture in the laboratory or in which transfection protocols are unsuccessful. This study is not only a step toward closing the knowledge gap in the biology and evolution of this diverse kingdom of organisms but will also aid in the advancement of protisan biotechnology.

Environmental Predictors of Schistosomiasis Persistent Hotspots following Mass Treatment with Praziquantel

Joseph W. Walker, Nupur Kittur, Sue Binder, Jennifer D. Castleman, John M. Drake, Carl H. Campbell Jr., Charles H. King and **Daniel G. Colley.** Am J Trop Med Hyg.; 102(2), 5 Feb 2020: 328 - 338. doi: 10.4269/ajtmh.19-0658.

The frequency of PHS in individual trials ranged from 35.3% to 71.6% in study villages. Significant relationships between PHS status and MDA frequency, distance to freshwater, rainfall, baseline schistosomiasis burden, elevation, land cover type, and village remoteness were each observed in at least one trial, although the strength and direction of these relationships was not always consistent among study sites. These findings suggest that PHSs are driven in part by environmental conditions that modify the risk and frequency of reinfection.

Survey of Schistosomiasis in Saint Lucia: Evidence for Interruption of Transmission

Janice Gaspard, Madelaine M. Usey, Merlene Fredericks-James, Maria J. Sanchez, Lydia Atkins, Carl H. Campbell Jr., Paul L. A. M. Corstjens, Govert J. van Dam, **Daniel G. Colley** and William Evan Secor. Am J Trop Med Hyg.; 102(4), 1 Apr 2020: 827 - 831. doi: 10.4269/ajtmh.19-0904

To evaluate the current status of schistosomiasis in Saint Lucia, we conducted a nationally representative school-based survey of 8-11-year-old children for prevalence of Schistosoma mansoni infections using circulating antigen and specific antibody detection methods. We also conducted a questionnaire about available water sources, sanitation, and contact with fresh water.

Supplemental Articles: Operational Research on Controlling and Eliminating Schistosomiasis

SCORE. American Journal of Tropical Medicine and Hygiene. ajstmh.org/score.

These articles are available online ahead of print and summarize much of the work of the Schistosomiasis Consortium for Operational Research and Evaluation.

Optimal 10-Aminoartemisinins With Potent Transmission-Blocking Capabilities for New Artemisinin Combination Therapies–Activities Against Blood Stage *P. falciparum* Including PfKI3 C580Y Mutants and Liver Stage *P. berghei* Parasites

Ho Ning Wong, Vivian Padín-Irizarry, Mariëtte E. van der Watt, Janette Reader, Wilna Liebenberg, Lubbe Wiesner, Peter Smith, Korina Eribez, Elizabeth A. Winzeler, **Dennis E. Kyle**, Lyn-Marie Birkholtz, Dina Coertzen, and Richard K. Haynes. Front Chem. 2020 Jan 10;7:901. doi: 10.3389/fchem.2019.00901.

Early results indicate these compounds tend not to display reduced susceptibility against parasites bearing the Pf Kelch 13 propeller domain C580Y mutation characteristic of artemisinin-resistant Pf. Thus, the advent of the amino-artemisinins including artemiside and artemisone will enable the development of new combination therapies that by virtue of the amino-artemisinin component itself will possess intrinsic transmission-blocking capabilities and may be effective against artemisinin resistant falciparum malaria.

An adaptable soft-mold embossing process for fabricating optically-accessible, microfeature-based culture systems and application toward liver stage antimalarial compound testing

Steven P. Maher, Amy J. Conway, Alison Roth, Swamy R. Adapa, Phillip Cualing, Chiara Andolina, James Hsiao, Jessica Turgeon, Victor Chaumeau, Myles Johnson, Chris Palmiotti, Naresh Singh, Samantha J. Barnes, Raahil Patel, Virginia Van Grod, Robert Carter, H.-C. Steve Sun, Jetsumon Sattabongkot, Brice Campo, François Nosten, Wajeeh M. Saadi, John H. Adams, Rays H. Y. Jiang, and **Dennis E. Kyle**. Lab Chip, 2020,20, 1124-1139. doi: 10.1039/c9lc00921c

We developed a novel fabrication process in which a PDMS soft mold embosses hepatocyte-confining microfeatures into polystyrene, resulting in microfeature-based hepatocyte confinement (µHEP) slides and plates. Our process was optimized to form both microfeatures and culture wells in a single embossing step, resulting in a 100 µm-thick bottom ideal for HC/RI, and was found inexpensively amendable to microfeature design changes.

In vitro screening of the open source MMV Malaria and Pathogen Boxes to discover novel compounds with activity against Balamuthia mandrillaris

Christopher A. Rice, Luis Fernando Lares-Jiménez, Fernando Lares-Villa, **Dennis E. Kyle**. Antimicrobial Agents and Chemotherapy Apr 2020, 64 (5) e02233-19; DOI: 10.1128/AAC.02233-19

Balamuthia mandrillaris, is an under reported pathogenic free-living amoeba that causes Balamuthia amoebic encephalitis (BAE) and cutaneous skin infections. Although cutaneous infections are not typically lethal, BAE with or without cutaneous involvement usually is fatal. This is due to lack of drugs that are efficacious and that can cross the blood-brain barrier.

Plasmodium vivax Liver and Blood Stages Recruit the Druggable Host Membrane Channel Aquaporin-3

Dora Posfai, Steven P. Maher, Camille Roesch, Amélie Vantaux, Kayla Sylvester, Julie Péneau, Jean Popovici, **Dennis E. Kyle**, Benoît Witkowski, Emily R. Derbyshire. Cell Chem Biol. 2020 Mar 24. pii: S2451-9456(20)30083-0. doi: 10.1016/j.chembiol.2020.03.009.

Using a recently developed P. vivax liver-stage model system we demonstrate that host aquaporin-3 (AQP3) localizes to the PVM of schizonts and hypnozoites within 5 days after invasion. This recruitment is also observed in P. vivax-infected reticulocytes.

Predaceous Toxorhynchites mosquitoes require a living gut microbiota to develop

Kerri L. Coon, Luca Valzania, **Mark R. Brown** and **Michael R. Strand**. Proc Biol Sci. 2020 Jan 29;287(1919):20192705. doi: 10.1098/rspb.2019.2705

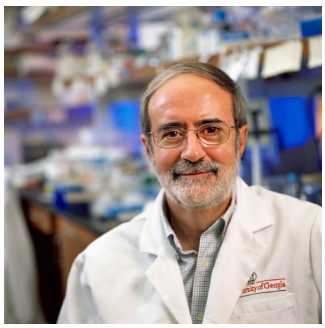
In this study, we asked whether predaceous Toxorhynchites amboinensis larvae still require living microbes in their gut in order to develop. Using the detritivorous mosquito Aedes aegypti as prey, we found that T. amboinensis larvae harbour bacterial communities that are highly similar to that of their prey.

Gene content evolution in the arthropods

Thomas GWC, Dohmen E, Hughes DST, Murali SC, Poelchau M, Glastad K, Anstead CA, Ayoub NA, Batterham P, Bellair M, Binford GJ, Chao H, Chen YH, Childers C, Dinh H, Doddapaneni HV, Duan JJ, Dugan S, Esposito LA, Friedrich M, Garb J, Gasser RB, Goodisman MAD, Gundersen-Rindal DE, Han Y, Handler AM, Hatakeyama M, Hering L, Hunter WB, Ioannidis P, Jayaseelan JC, Kalra D, Khila A, Korhonen PK Lee CE, Lee SL, Li Y, Lindsey ARI, Mayer G, McGregor AP, McKenna DD, Misof B, Munidasa M, Munoz-Torres M, Muzny DM, Niehuis O, Osuji-Lacy N, Palli SR, Panfilio KA, Pechmann M, Perry T, Peters RS, Poynton HC, Prpic NM, Qu J, Rotenberg D, Schal C, Schoville SD, Scully ED, Skinner E, Sloan DB, Stouthamer R, **Strand MR**, Szucsich NU, Wijeratne A, Young ND, Zattara EE, Benoit JB, Zdobnov EM, Pfrender ME, Hackett KJ, Werren JH, Worley KC, Gibbs RA, Chipman AD, Waterhouse RM, Bornberg-Bauer E, Hahn MW, Richards S. Genome Biol. 2020 Jan 23;21(1):15. doi: 10.1186/s13059-019-1925-7.

These analyses demonstrate how large-scale comparative genomics can provide broad new insights into the genotype to phenotype map and generate testable hypotheses about the evolution of animal diversity.

Synthesis and in vitro evaluation of new 5-substituted 6-nitroimidazooxazoles as antikinetoplastid agents



Fanny Mathias, AnitaCohen, Youssef Kabri, Núria Waddington Negrão, Maxime D.Crozet, **RobertoDocampo**, Nadine Azas, Patrice Vanelle. Eur J Med Chem. 2020 Feb 14;191:112146. doi: 10.1016/j.ejmech.2020.112146

In continuation of our pharmacomodulation work on the nitroimidazooxazole series, we report the synthesis of new 5-substituted 6-nitroimidazooxazole derivatives. Our aim was to evaluate how functionalization of the 5-position of the 6-nitroimidazooxazole scaffold affects antileishmanial and antitrypanosomal in vitro activities.

A CRISPR/Cas9-riboswitch-Based Method for Downregulation of Gene Expression in Trypanosoma cruzi

Noelia Lander, Teresa Cruz-Bustos, and **Roberto Docampo**. Front Cell Infect Microbiol. 2020 Feb 27;10:68. doi: 10.3389/fcimb.2020.00068.

In this work we used the CRISPR/Cas9 system for endogenously tagging T. cruzi glycoprotein 72 (TcGP72) and vacuolar proton pyrophosphatase (TcVP1) with the active (glmS) or inactive (M9) ribozyme. Gene tagging was confirmed by PCR and protein downregulation was verified by western blot analyses. Further phenotypic characterization was performed by immunofluorescence analysis and quantification of growth in vitro.

The Mitochondrial Calcium Uniporter Interacts with Subunit c of the ATP Synthase of Trypanosomes and Humans

Guozhong Huang, **Roberto Docampo**. mBio. 2020 Mar 17;11(2). pii: e00268-20. doi: 10.1128/mBio.00268-20

The mitochondrial calcium uniporter (MCU) is essential for the regulation of oxidative phosphorylation in mammalian cells, and we have shown that in Trypanosoma brucei, the etiologic agent of sleeping sickness, this channel is essential for its survival and infectivity. Here we reveal that that Trypanosoma brucei MCU subunits interact with subunit c of the mitochondrial ATP synthase (ATPc). Interestingly, the direct physical MCU-ATPc interaction is conserved in T. cruzi and human cells.

CRISPR/Cas9 Technology Applied to the Study of Proteins Involved in Calcium Signaling in Trypanosoma cruzi

Noelia Lander, Miguel A. Chiurillo, **Roberto Docampo**. Methods Mol Biol. 2020;2116:177-197. doi: 10.1007/978-1-0716-0294-2_13.

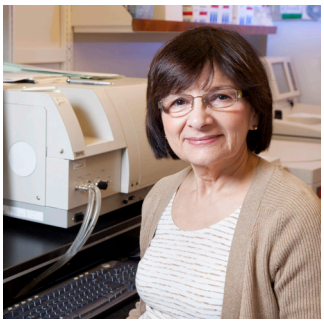
In this chapter we describe the most effective methods to achieve genome editing in T. cruzi using as example the generation of mutant cell lines to study proteins involved in calcium homeostasis.

Multi-target heteroleptic palladium bisphosphonate complexes

Micaella Cipriani, Santiago Rostán, Ignacio León, Zhu-Hong Li, Jorge S. Gancheff, Ulrike Kemmerling, Claudio Olea Azar, Susana Etcheverry, **Roberto Docampo**, Dinorah Gambino & Lucía Otero. J Biol Inorg Chem 25, 509–519 (2020). https://doi.org/10.1007/s00775-020-01779-y

In this work, we extended our studies to heteroleptic palladium–NBP complexes including DNA intercalating polypyridyl co-ligands (NN) with the aim of obtaining potential multi-target species.

Isolation and Characterization of Acidocalcisomes from Trypanosomatids



Guozhong Huang, **Silvia N. J. Moreno, Roberto Docampo**. Methods Mol Biol. 2020;2116:673-688. doi: 10.1007/978-1-0716-0294-2_40.

Here, we provide detailed subcellular fractionation protocols using iodixanol gradient centrifugations to isolate high-quality acidocalcisomes from Trypanosoma brucei, which are subsequently validated by electron microscopy, and enzymatic and immunoblot assays with organellar markers.

An Endoplasmic Reticulum CREC Family Protein Regulates the Egress Proteolytic Cascade in Malaria Parasites

Manuel A. Fierro, Beejan Asady, Carrie F. Brooks, David W. Cobb, Alejandra Villegas, **Silvia N. J. Moreno**, **Vasant Muralidharan**. mBio Feb 2020, 11 (1) e03078-19; DOI: 10.1128/mBio.03078-19

The divergent eukaryotic parasites that cause malaria grow and divide within a vacuole inside a host cell, which they have to break open once they finish cell division. The egress of daughter parasites requires the activation of a proteolytic cascade, and a subtilisin-like protease initiates a proteolytic cascade to break down the membranes blocking egress. It is assumed that the parasite endoplasmic reticulum plays a role in this process, but the proteins in this organelle required for egress remain unknown. We have identified an early ER-resident regulator essential for the maturation of the recently discovered aspartic protease in the egress proteolytic cascade, plasmepsin X, which is required for maturation of the subtilisin-like protease. Conditional loss of PfERC results in the formation of immature and inactive egress proteases that are unable to breakdown the vacuolar membrane barring release of daughter parasites.

Directing Traffic: Chaperone-mediated protein transport in malaria parasites

Anat Florentin, David W. Cobb, Heather M. Kudyba, **Vasant Muralidharan**. Cell Microbiol. 2020 May 9:e13215. doi: 10.1111/cmi.13215.

We review key pathways of protein transport originating and branching from the endoplasmic reticulum, focusing on the essential roles of chaperones in these processes. Further, we highlight key gaps in our knowledge that prevents us from building a holistic view of protein trafficking in these deadly human pathogens.

Identification of a novel base J binding protein complex involved in RNA polymerase II transcription termination in trypanosomes

Rudo Kieft, Yang Zhang, Alexandre P. Marand, Jose Dagoberto Moran, Robert Bridger, Lance Wells, Robert J. Schmitz, **Robert Sabatini.** PLoS Genet. 2020 Feb 21;16(2):e1008390. doi: 10.1371/journal.pgen.1008390.

Our results suggest a novel mechanistic link between base J and Pol II polycistronic transcription termination in kinetoplastids.

Lexis and Grammar of Mitochondrial RNA Processing in Trypanosomes

Inna Aphasizheva, Juan Alfonzo, Jason Carnes, Igor Cestari, Jorge Cruz-Reyes, H. Ulrich Göringer, **Stephen Hajduk**, Julius Lukeš, Susan Madison-Antenucci, Dmitri A. Maslov, Suzanne M. McDermott, Torsten Ochsenreiter, Laurie K. Read, Reza Salavati, Achim Schnaufer, André Schneider, Larry Simpson, Kenneth Stuart, Vyacheslav Yurchenko, Z. Hong Zhou, Alena Zíková, Liye Zhang, Sara Zimmer, Ruslan Aphasizhev. Trends Parasitol. 2020 Apr;36(4):337-355. doi: 10.1016/j.pt.2020.01.006.

Historically, RNA editing has attracted major research effort, and recently essential pre- and postediting processing events have been discovered. Here, we classify the key players that transform primary transcripts into mature molecules and regulate their function and turnover.

Identification and Localization of the First Known Proteins of the *Trypanosoma cruzi* Cytostome Cytopharynx Endocytic Complex

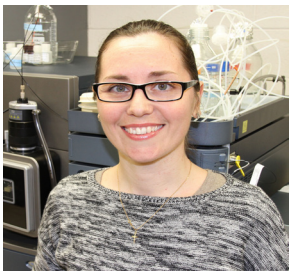
Nathan Michael Chasen, Isabelle Coppens and **Ronald Drew Etheridge**. Front Cell Infect Microbiol. 2020 Jan 17;9:445. doi: 10.3389/fcimb.2019.00445.

This work is a first glimpse into the proteome of the SPC and provides the tools for further characterization of this enigmatic endocytic organelle. A better understanding of how this deadly pathogen acquires nutrients from its host will potentially direct us toward new therapeutic targets to combat infection.

Galtonosides A-E: Antiproliferative and Antiplasmodial Cholestane Glycosides from Galtonia regalis

Yongle Du, Brooke A. Martin, Ana Lisa Valenciano, Jason A. Clement, Michael Goetz, **Maria B. Cassera**, David G. I. Kingston. J Nat Prod. 2020; 83(4):1043-1050. doi: 10.1021/acs.jnatprod.9b01064.

An extract of Galtonia regalis from the Natural Products Discovery Institute showed moderate antiplasmodial activity, with an IC50 value less than 1.25 µg/mL.



EAT-18 is an essential auxiliary protein interacting with the non-alpha nAChR subunit EAT-2 to form a functional receptor

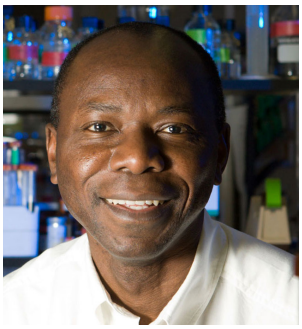
Shivani Choudhary, Samuel K. Buxton, Sreekanth Puttachary, Saurabh Verma, Gunnar R. Mair, Ciaran J. McCoy, Barbara J. Reaves, **Adrian J. Wolstenholme**, Richard J. Martin, Alan P. Robertson. 2020. PLoS Pathog 16(4): e1008396. https://doi.org/10.1371/journal.ppat.1008396

Here we describe a novel nicotinic acetylcholine receptor on the nematode pharynx that is a potential new drug target

Design, Synthesis, and Evaluation of Novel Anti-Trypanosomal Compounds

Lance T. Lepovitz, Alan R. Meis, Sarah M. Thomas, Justin Wiedeman, Alexandra Pham, Kojo Mensa-Wilmot, Stephen F. Martin. Tetrahedron. 2020 Apr 17;76(16). pii: 131086. doi: 10.1016/j.tet.2020.131086

This work underscores the importance of verifying, irrespective of close structural similarities, that new compounds designed from a lead with a known biological target engage the putative binding site.



Update on Cryptosporidium spp.: highlights from the Seventh International Giardia and Cryptosporidium Conference

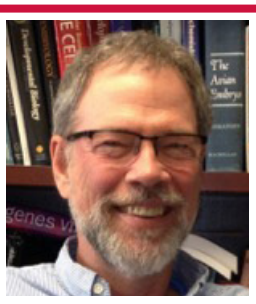
Giovanni Widmer, David Carmena, Martin Kváč, Rachel M. Chalmers, **Jessica C. Kissinger**, Lihua Xiao, Adam Sateriale, Boris Striepen, Fabrice Laurent, Sonia Lacroix-Lamandé, Gilles Gargala and Loïc Favennec. Parasite 27, 14 (2020). doi: 10.1051/parasite/2020011.

High quality presentations discussed at the conference reflected decisive progress and identified new opportunities that will engage investigators and funding agencies to spur future research in a “one health” approach to improve basic knowledge and the clinical and public health management of zoonotic cryptosporidiosis.

A terminal α3-galactose modification regulates an E3 ubiquitin ligase subunit in Toxoplasma gondii

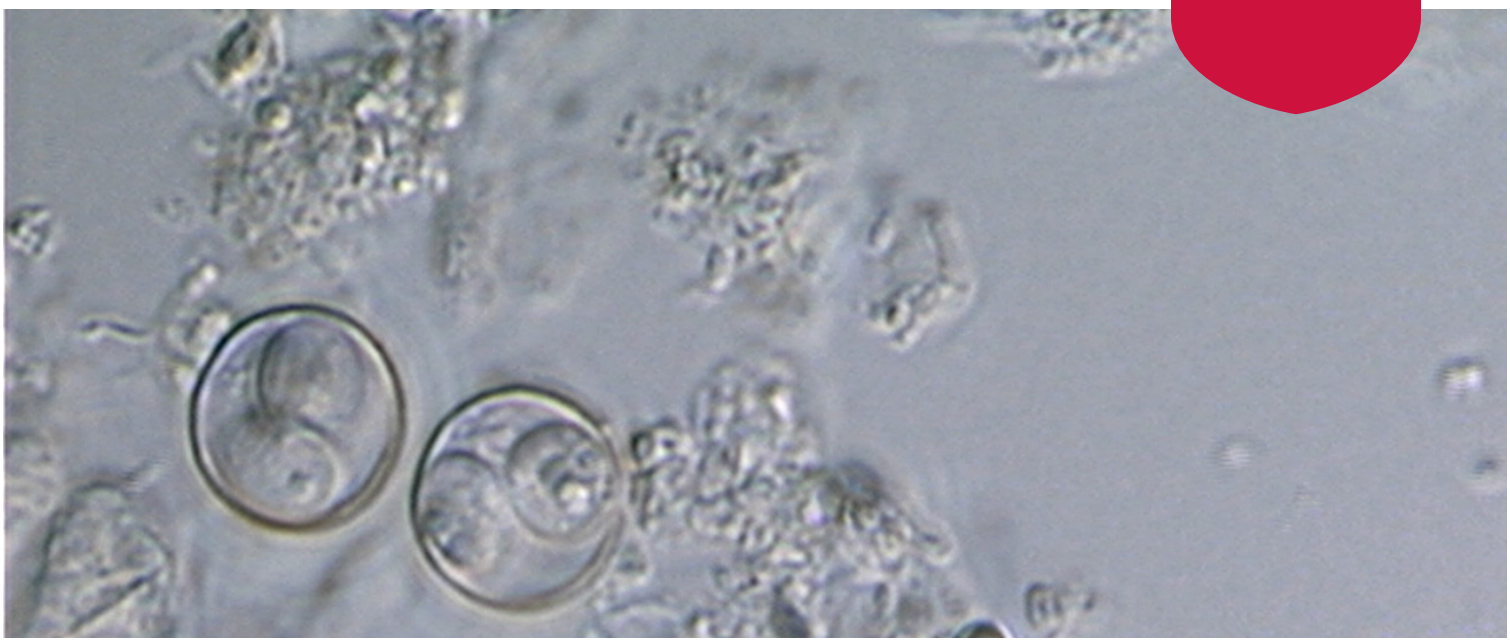
Msano Mandalasi, Hyun W. Kim, David Thieker, M. Osman Sheikh, Elisabet Gas-Pascual, Kazi Rahman, Peng Zhao, Nitin G. Daniel, Hanke van der Wel, H. Travis Ichikawa, John N. Glushka, Lance Wells, Robert J. Woods, Zachary A. Wood, and **Christopher M. West**. J Biol Chem. 2020 May 15. pii: jbc.RA120.013792. doi: 10.1074/jbc.RA120.013792.

To define the final sugar and its linkage, here we identified the glycosyltransferase that completes the glycan and found that it is closely related to glycogenin, an enzyme that may prime glycogen synthesis in yeast and animals.



Ynes Ortega receives grant to study Cyclospora presence in the U.S.

Grants



by Donna Huber

Historically, *Cyclospora* infection in the United States has been associated with imported fresh produce. However, in 2018, the U.S. saw two significant outbreaks associated with vegetables grown in the United States.

"We had more than 2,000 non-travel associates cyclosporiasis cases," said Ynes Ortega, member of the Center for Tropical and Emerging Global Diseases and associate professor in the Department of Food Science and Technology's Center for Food Safety.

Fresh produce vegetable trays containing broccoli, cauliflower, carrots, and dill dip, which are not often associated with Cyclospora outbreaks, were implicated in the first outbreak affecting 250 people and lettuce from a salad mix used by a fast food chain was the source of the second outbreak with 511 cases.

"*Cyclospora* has previously been detected in salad greens produced in the US and lettuce implicated in the second outbreak was produced in the U.S.," said Ortega. "Clearly, we need to determine if *Cyclospora* is not only a parasite present in other countries but also in the U.S."

Cyclospora cayetanensis, the single-cell parasite that causes cyclosporiasis, was first described by Ortega in the 1990s. A person becomes infected with the parasite by consuming contaminated food, mostly fresh fruits and vegetables, and water. Infection results in gastrointestinal illness characterized primarily by diarrhea. Cyclosporiasis is treated with sulfa drugs, fluids, and rest. If left untreated, the symptoms can persist for up to a month and can be recurring. Prevention of infection is accomplished by frequent hand washing by those who process fruits and vegetables, thoroughly rinsing fruits and vegetables with water prior to consumption, and avoiding potentially contaminated water while traveling in countries where *C. cayetanensis* is endemic.

Ortega has been awarded a 2-year grant from the Center for Produce Safety, a non-profit organization committed to addressing issues faced by the produce industry, to investigate *C. cayetanensis* presence in the United States.

"We will be testing surface water for the presence of *Cyclospora cayetanensis*, improving sample collection methods, and genotyping of the parasite," said Ortega.

Up until 2018, it was believed that Cyclospora was not present in the United States. Therefore, one of the main goals of this grant is to determine how widely distributed this parasite is within the United States. To aid in this determination, a simpler and more sensitive method of detection is needed which Ortega's laboratory is already working on.

"These two objectives are critical to implement monitoring and intervention strategies not only in the U.S. but also in endemic locations, with the ultimate goal of reducing the number of domestic cases of cyclosporiasis," said Ortega.

DETAILED ANALYSIS OF CRYPTOSPORIDIUM NON-CODING GENE EXPRESSION

National Institues of Health, **Jessica Kissinger**

The second leading cause of diarrhea in infants globally is Cryptosporidium and it can be life threatening in the immunocompromised. Cryptosporidium is a parasite that is spread via a fecal oral route, primarily by the ingestion of unfiltered water (chlorine does not kill it). This project proposes to use genome studies to characterize RNA molecules that the parasite may use to manipulate the human host cells it infects. Candidates will be experimentally tested.

UNDERSTANDING THE HIGHLY DIVERGENT MITOCHONDRIAL ATP SYNTHASE IN T. GONDII

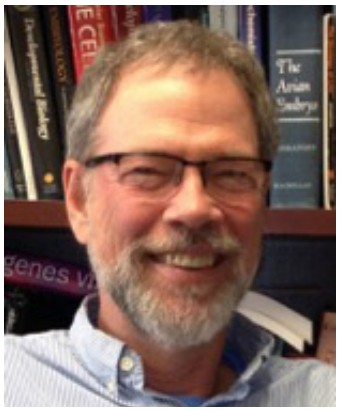
National Institutes of Health, **Diego Huet**

Toxoplasma gondii is a protozoan parasite that can cause fetal abnormalities and poses a severe risk to immunocompromised individuals, such as HIV patients and organ transplant recipients. No known vaccines or drugs can eradicate persistent T. gondii infections in humans and the parasite is a leading cause of death attributed to foodborne illness in the United States. This research seeks to characterize the parasite's unusual mitochondrial ATP synthase to understand its highly divergent metabolism and identify new targets for the development of anti-parasitic compounds.

TRYPANOSOMA CRUZI DORMANCY AND ITS IMPLICATIONS FOR THERAPEUTIC TREATMENT

National Institues of Health, **Rick Tarleton**

We have recently discovered that a subpopulation of Trypanosoma cruzi parasites (the cause of Chagas disease) is able to enter a metabolically inactive state that makes them resistant to anti-parasitic drugs. The goal of this project is to understand how this state of dormancy is generated and how existing drugs can be delivered, and new drugs discovered, so as to eventually clear these otherwise drug resistant forms from hosts.



IDENTIFICATION OF F-BOX PROTEINS IN TOXOPLASMA

Research Foundation of New York/NIH, **Chris West**

Regulated protein degradation is an important way that cells regulate their functions. But how this occurs in human parasites is largely unknown. This work seeks to identify the factors that determine which proteins will be degraded as a parasite grows.

REPURPOSING DRUGS FOR TREATMENT OF PRIMARY AMOEBIC MENINGOENCEPHALITIS

National Institues of Health, **Dennis Kyle**

This proposal is to repurpose drugs to treat the "brain eating" amoeba parasite, Naegleria fowleri, that kills otherwise-healthy young people because current treatments are not effective. We will use rate-of-kill assays we developed to assess phenotypic screen hits from a 15K library and also determine if the drugs are effective against different strains of the amoebae. By using a target product profile for primary amoebic meningoencephalitis (PAM) treatment drugs, we will downselect the best candidates and assess their efficacy in the mouse model of disease to identify new drugs that could be used immediately for treatment of PAM.

CTEGD Names Travel Fund for Daniel G. Colley

Giving

One day Daniel Colley raised his hand to volunteer, setting in motion five decades of scientific adventures. It was 1969, and Colley's postdoctoral adviser, ByronWaksman, a renowned immunologist at Yale University School of Medicine, had stepped into the laboratory and asked if anyone wanted to go to Brazil. Colley, today a UGA immunologist and Fellow of the American Association for the Advancement of Science, became fascinated by schistosomiasis, a parasitic worm infection plaguing poverty-stricken communities in sub-Saharan Africa and around the world.

After his Brazil sojourn, Colley arrived at Vanderbilt University in 1971 to begin setting up a lab and a career-long effort to understand the immunological paradox of schistosomiasis. In 1992, he joined the Centers for Disease Control and Prevention (CDC) and a year later was promoted to director of the Division of Parasitic Diseases. After retiring from the CDC, he arrived at UGA in 2001 as professor of microbiology and director of the Center for Tropical and Emerging Global Diseases. During the past decade, Colley has been director of UGA's Schistosomiasis Consortium for Operational Research and Evaluation (SCORE). In June 2020, Colley retired from the University of Georgia. He has been named Professor Emeritus.

That trip to Brazil was instrumental in shaping Colley's career. As a mentor, he is passionate about providing the same opportunity to new scientists. Early in his career at UGA, he established the Training Innovations in Parasitological Studies (TIPS) fellowship through funding from the Ellison Medical Foundation, funding that has since ended. In honor of Daniel Colley's commitment to understanding diseases of poverty and training the next generation of scientists, the Center for Tropical and Emerging Global Diseases is establishing the Daniel G. Colley Training in Parasitology Fund to continue his legacy.

Financial gifts may be made online at https://gail.uga.edu/giving/as/daniel-colley-fund

Support CTEGD

Financial contributions from alumni and friends are vital to accomplishing CTEGD's mission to pursue cutting edge research in emerging global diseases and to train students in this field.

To truly impact global health through research, support from a variety of sources is required and donations from individuals, foundation, and corporations play a significant role.

Regardless of size, your gift can have an impact.

The CTEGD Fund is an unrestricted fund that allows us to support various initiatives of the students and faculty, such as those featured in this issue. A portion of this fund goes to the annual Molecular Parasitiology & Vector Biology Symposium, an annual regional scientific meeting that has free registration.

Also, your tax-deductible gift provides travel opportunities to trainees. Such opportunities include attending national and international conferences to present their research as well as travel to international research sites. These international research opportunities are life-changing experiences for our graduate students and postdoctoral trainees.

Learn more about how you can support our research and training efforts: https://ctegd.uga.edu/give/