

Turning nonsense into good sense

By Nicholas Potochick and Gwendolyn Gunn

urning nonsense into good sense: a new therapy offers hope for children suffering from a heart-breaking genetic disease. A recent study by

Gunn et al. shows that a new drug restores gene function lost due to a type of "nonsense" genetic mutation responsible for the childhood disease Hurler syndrome.

Hurler syndrome is a genetic disease that affects roughly

1 in 100,000 children. The disease is characterized by shortened bones, heart and liver disease and mental retardation that begin to appear in seemingly healthy children around two years of age. Current treatments for Hurler syndrome include enzyme replacement therapy and bone marrow transplant,

both of which are expensive, painful, and have serious side effects. Most cases are caused by a "nonsense" mutation that stops production of an es-

used the new drug to treat mice with Hurler syndrome. Treatment increases enzyme levels and improves physical signs of the disease in heart, brain, and

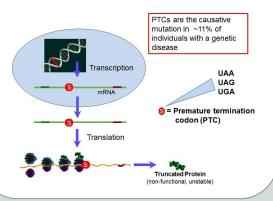
bone without any sign of toxicity, suggesting the drug may be suitable for human use.

Should the results hold up in humans, "nonsense suppression" therapy could revolutionize treatment for patients with Hurler

syndrome. And the success of this treatment strategy is guiding development of drugs for other genetic diseases, including cystic fibrosis, for which a similar drug is currently in clinical trials.

Thank you to our guest writers: Nicholas Potochick (Thompson lab) and Gwendolyn Gunn (Bedwell lab).





sential enzyme needed for recycling and disposal of cellular waste.

A new drug therapy called "nonsense suppression" restores the production of this critical enzyme. This therapy is specific to the type of genetic mutation an individual has rather than a specific disease. Gunn and colleagues

Collaborators Pursue New Treatment for Cystic Fibrosis

An ongoing collaboration between Southern Research and the University of Alabama at Birmingham through the Alabama Drug Discovery Alliance is expanding research efforts into a novel drug discovery program to find potential new treatment regimens for cystic fibrosis (patients with a nonsense mutation.

This initiative will include the use of several novel assays recently developed by microbiology professor David Bedwell, Ph.D., and others in his lab at UAB, and the screening and discovery capabilities of Southern Research. The proposed research aimed at finding a means to treat all genetic causes of cystic fibrosis.

Department Events

October 13

Seminar Series–Dr. George O'Toole, Dartmouth College–BBRB 170 (noon to 1pm)

October 20

Seminar Series—Dr. Akinyemi I. Ojesina, UAB Department of Epidemiology—"Of Bugs, Crabs and Gnomes"—BBRB 170 (noon to 1pm)

October 27

Seminar Series-Dr.Tomoaki Ogino, Case Western Reserve University-BBRB 170 (noon to 1pm)

November 3

Seminar Series-Dr. Robert W. Sobol.

University of South Alabama, Mitchell Cancer Institute—BBRB 170 (noon to 1pm)

November 10

Seminar Series—Dr. Glenn Randall, University of Chicago—BBRB 170 (noon to 1pm)

November 10

Employee of the Year Celebration BBRB Lobby (4:30 pm)

November 13-15

Microbiology Research Retreat

November 17

Seminar Series—Dr. Shannon Wallet, Department of Periodontology, UF College of Dentistry University–BBRB 170 (noon to 1pm)

December 1

Seminar Series—Dr. Avinash Bhandoola, Laboratory of Genome Integrity, NCI–BBRB 170 (noon to 1pm)

December 8

Seminar Series–Dr. Paul Kubes, University of Calgory–BBRB 170 (noon to 1pm)

December 15

Seminar Series-Rick Gourse, Ph.D., University of Wisconsin, Madison-BBRB 170 (noon-1pm)

24th Annual Microbiology Research Retreat

November 13—15, 2015
The Chattanoogan | Chattanooga, Tennessee

Abstract submission deadline
October 15







Keynote Speaker: Flavius Martin, M.D. Senior Vice President at Amgen

Dr. Martin heads the Inflammation Therapeutic Area and the Oncology and Tumor Immunotherapy research efforts at Amgen. He received his M.D. from the University of Medicine and Pharmacy in Timisoara, Romania. His postdoctoral work with John Kearney at UAB focused on fundamental aspects of B-cell biology.

Q: Where was miniature golf invented?

A: In Chattanooga, Tennessee, of course! Garnet Carter was the first person to patent a game of miniature golf, which he called Tom Thumb Golf, in 1927. The golf course was built on Lookout Mountain to draw traffic to the hotel that he owned.



Todd Green Promoted to Tenure Track



Todd Green, Ph.D., studied natural products as potential therapeutics against bacterial and fungal infection and various forms of cancer as

an undergraduate at the University of Alabama at Huntsville. His interest in molecular mechanisms and combatting disease at an atomic level lead him to pursue graduate training in the field xray crystallography at UAB. His graduate research focused on protein chemistry and protein structure, with an emphasis on viral protein targets. After receiving his Ph.D. in 2002, he joined the UAB Microbiology Department faculty as assistant professor.

Currently, Green's research focuses on crystallographic studies of proteins involved in polynucleotide synthesis for negative strand RNA viruses. These efforts have included: structure determination of the nucleocapsid of VSV encapsidated with various sequences of RNA, as well as complexes of the nucleocapsid with the polymerase co-factor, P. His investigation of the mechanisms of viral transcription and replication, including the involvement of cellular factors, paves the way for developing new avenues for future therapeutic design against this group of viruses.

Green's expertise in virology and xray crystallography has led to collaboration with investigators locally, nationally and internationally on viral, bacterial, human and murine targets. "I believe, as scientists, we can maximize discovery by surrounding ourselves with the right team locally and abroad," says Green.

2015 Susan Roberts Dubay Lecture



On September 1, 2015, faculty, staff, students and special guests, Dr. John Dubay and Dr. Eric Hunter, gathered at Volker Hall for the inaugural Susan Roberts Dubay Endowed Lecture.

The endowment honors the memory of Susan Dubay who worked as a research assistant in Dr. Eric Hunter's lab during the 1980s.

Susan's husband, Dr. John Dubay, said, "The fund gives us an opportunity to honor Susan's contributions but also gives me the opportunity to give something back to a department that was very good to me. My hope is that this lectureship would develop into something very notable for the department—one that would be one of a handful of Micro events that would really stand out throughout the sciences honoring Susan and giving the department another event to be proud of."

While at UAB, Susan worked for Dr. Eric Hunter who was the founding director of the UAB Center of AIDS Research. Hunter,



Dr. John Dubay

now Professor of Pathology and Laboratory Medicine at Emory University School of Medicine, gave the first Dubay lecture: "The role of viral fitness in HIV-1 transmission and disease progression."

"All in all, this was a very special day for me," said Dr. Dubay. "I'm overwhelmed with how well it went. It was great to be able to get back together with many of my old friends including Eric."

Novel Toxin (TNT) Identified



Microbiology professor Dr. Michael Niederweis and colleagues identify the first known toxin of Mycobacterium tuberculosis, a pathogen that infects 9 million people a year and kills more than 1 million.

M. tuberculosis is notable for its survival inside macrophages, the immune cells that ingest and destroy infectious bacteria. The newly identified TNT, Niederweis says, plays a key role to induce necrotic death of the infected macrophage. Thus, TNT enables the M. tuberculosis bacteria to escape from the macrophage and disseminate to other host cells in a person infected with tuberculosis, thus contributing to the survival of M. tuberculosis and spreading the disease.

Medical Students Nominate Barnum for Argus Award



Microbiology professor, Dr. Scott Barnum, is one of three outstanding professors nominated by students from the UAB School of Medicine in the category of Best Educator in Fundamentals 2 for this year's School of Medi-

cine Argus Awards.

An annual event since 1996, the Argus Awards and ceremony allows UAB medical students a tangible way to honor their mentors, professors, courses and course directors for outstanding service to medical education. Faculty members are nominated by course evaluations, and students vote to select award winners in each category.

The Argus Awards Ceremony to honor the 2015 Argus Award recipients and nominees will be held Friday, October 2, at 5:30 p.m., in Children's Harbor.

Useful Links

Annual Retreat
Employee Site
Faculty Directory
Microbiology Newsfeed
Giving Opportunities

Conference Rooms Schedule Trainee Career Opportunities Microbiology Seminar Series Department Calendar

Congratulations to the August 2015 Hiramoto Travel Awards Recipients







- ◆ Xiaojiao Xue, North American Cystic Fibrosis Conference in Phoenix, AZ
- Beth A Walters, EMBO Conference: Protein Synthesis and Translational Control
- Danielle A Chisolm, Molecular Mechanisms of Immune Cell Development and Function, Big Sky, MT

All Microbiology graduate students (Ph.D. students with a primary Microbiology faculty member as a dissertation mentor) in good standing are eligible to apply for a Hiramoto Travel Award. Information about applying for the award is available at Raymond N. Hariamoto Endowment.

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Our Twitter account is an easy way for faculty, trainees, and staff to keep up with department activities. If you have information to share via Twitter, send it to erobnson@uab.edu.

Max D. Cooper Travel Award for UAB Medical or Graduate Students

By Ella Robinson



Max D. Cooper, Ph.D., is said to be one of the most influential scientists in the field of immunology. While at UAB, he became UAB's—and Alabama's—first Howard Hughes Medical Institute Investigator and, in 1989, Alabama's first scientist to be elected to the National Academy of Sciences. In 2010, he received the prestigious Robert Koch Award. Cooper, who is now professor of pathology and laboratory medicine at Emory University, is credited with a series of landmark discoveries that provide a framework for understanding the role that white blood cells play in fighting infections and even in the development of leukemia, lymphomas and autoimmune diseases.

The Max D. Cooper Travel Award conveys Cooper's lifelong love for journey and adventure. He and his family have traveled throughout the United States and the world in the pursuit of academic training and discovery. The annual award assists with the travel cost of attending a meeting, workshop or advanced courses offered by scientific societies for UAB medical or graduate stu-

dents with academic pursuits in the field of immunology.

This award is made possible through an endowment fund established by Cooper's family to recognize his extraordinary accomplishments as professor of medicine, pediatrics, microbiology, and pathology and as Director of the Division of Developmental and Clinical Immunology at UAB. Information about applying for the award is available at Max D. Cooper Endowed Immunology Travel Award.

Patel Receives Cooper Travel Award



Preeyam Patel (Kearney lab) is the win-August 2016.

Patel says she is very excited to re- of allergic disease." ceive the Cooper award and be able to travel to Mel-

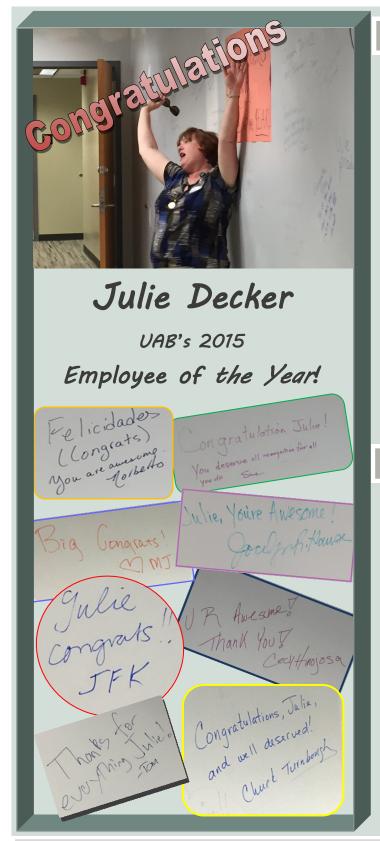
bourne next August. "While at ICI, I will present my work from Dr. John Kearney's lab demonstrating that phosphorylcholine-specific receptors CD36 and platelet actiner of the 2015 Max D. Cooper Travel vating factor receptor (PAFR) are necessary for the or-Award. She will use this award to help chestration of house dust mite-induced allergic disease," defray the cost of travel to attend the says Patel. "My studies further show that administration International Congress of Immunology of antibodies to phosphorylcholine decrease the en-(ICI) meeting in Melbourne, Australia, in gagement of house dust mite allergen with these PCspecific receptors and result in dampened development

What truly Southern sweet treat was invented in Chattanooga, Tennessee?



The MoonPie! The Chattanooga Bakery was founded in the early 1900s as a subsidiary of the Mountain City Flour Mill in Chattanooga, Tennessee. The bakery's original purpose was to use the excess flour produced by the mill. In 1917, a Kentucky coal miner asked the bakery's traveling salesman, Earl Mitchell, for a snack "as big as the moon." And, that's how the bakery developed a product which is still known as the MoonPie.

How much did the first MoonPies cost? Find the answer at — moonpie.com/about.



Welcome

Carlos Orihuela - Associate Professor

Cecy Hinojosa - Research Associate (Orihuela Lab)

Kelley Bradley - Research Assistant (Orihuela Lab)

Norberto Juarbe-Gonzalez - Postdoc (Orihuela Lab)

Anukul Shenoy - Graduate Student (Orihuela Lab)

Sara Notararigo - Postdoc (Leon-Ruiz Lab)

Harriett Williams - Volunteer (Briles Lab)

Reshmi Mukerji - Research Assistant (Briles Lab)

Ruth McDowell - Postdoc (Tse Lab)

Manyu Li - Visiting Scientist (Luo Lab)

Luhua Qiao - Visiting Scientist (Luo Lab)

Anthony Sellers - Student Assistant (Zajac Lab)

Wei Yang - Volunteer (Hu Lab)

Tiger Wang - Postdoc (Hu Lab)

Chunyan Ling - Visiting Scientist (Novak Lab)

Farewell

Alexia Carrillo - Postdoc (Justement Lab)

Fareena Bilwani - Postdoc (Klug Lab)

Shaonli Das - Research Associate (Tse Lab)

Brian Anderson - Research Technician (Tse Lab)

Pat Coan - Research Assistant (Briles Lab)

Xuerui Luo—Visiting Scientist (Hu Lab)

Save the Date

March 15, 2016

<u>Bertram M. Marx Lecture</u>

Speaker: Roy Curtiss, III, Ph.D.

*Submit information for the newsletter via email to Ella Robinson at erobnson@uab.edu.



Publications | July I - September 30, 2015

Agamasu C, Ghanam RH, Saad JS. Structural and Biophysical Characterization of the Interactions Between Calmodulin and the Pleckstrin Homology Domain of Akt. J Biol Chem. 2015 Sep 21. pii: jbc.M115.673939. [Epub ahead of print] PMID: 26391397

Blacher E, **Dadali T**, Bespalko A, Haupenthal VJ, Grimm MO, Hartmann T, **Lund FE**, Stein R, Levy A. Alzheimer's disease pathology is attenuated in a CD38-deficient mouse model. Ann Neurol. 2015 Jul;78(1):88-103. PMID: 25893674

Black LL, Srivastava R, Schoeb TR, Moore RD, Barnes S, **Kabarowski JH**. Cholesterol independent suppression of lymphocyte activation, autoimmunity and glomerulonephritis by Apolipoprotein A-I in normocholesterolemic Lupus-prone mice. J Immunol. 2015 Sep.

Chena A, Mannb B, Gao G, Heath R, King J, Maissoneauve J, Alderson M, Tate A, Hollingshead SK, Tweten RK, **Briles DE**, Tuomanen El, Paton JC. <u>Multivalent Pneumococcal Protein Vaccines Comprising Pneumolysoid with Epitopes/Fragments of CbpA and/or PspA Elicit Strong and Broad Protection. Clin Vaccine Immunol.</u> 2015 Aug 5. [Epub ahead of print] PMID: 26245351

Chisolm DA, Weinmann AS. <u>TCR-signaling events in cellular metabolism and specialization</u>. Front Immunolo.2015 Jun. 8;6:292 <u>6</u>: 292. PMID: 26106392.

Justice JL, Verhalen B, Kumar R, Lefkowitz EJ, Imperiale MJ, Jiang M. Quantitative Proteomic Analysis of Enriched Nuclear Fractions from BK Polyomavirus-infected Primary Renal Proximal Tubule Epithelial Cells. J Proteome Res. 2015 Sep 9. [Epub ahead of print] PMID: 26354146

We're on the web:

http://www.uab.edu/microbiology

Li H, Fu YX, Wu Q, Zhou Y, Crossman DK, Yang P, Li J, Luo B, Morel LM, **Kabarowski JH**, Yagita H, Ware CF, Hsu HC, Mountz JD. <u>Interferon-induced mechanosensing defects impede apoptotic cell clearance in lupus.</u> J Clin Invest. 2015 Jul 1;125(7):2877-90. PMID: 26098211

Maillard N, Wyatt RJ, Julian BA, Kiryluk K, Gharavi A, Fremeaux-Bacchi V, **Novak J**. <u>Current Understanding of the Role of Complement in IgA Nephropathy.</u> J Am Soc Nephrol. 2015 Jul;26(7):1503-12. PMID: 25694468

Padgett LE, Anderson B, Liu C, Ganini D, Mason RP, Piganelli JD, Mathews CE, Tse HM. Loss of NOX-derived superoxide exacerbates diabetogenic CD4 T cell effector responses in Type 1 Diabetes. Diabetes. 2015 Aug 12. [Epub ahead of print] PMID: 26269022

Opata MM, Hollifield ML, **Lund FE**, Randall TD, Dunn R, Garvy BA, Feola DJ. <u>B Lymphocytes Are Required during the Early Priming of CD4+ T Cells for Clearance of Pneumocystis Infection in Mice. J Immunol. 2015 Jul 15;195(2):611-20. PMID: 26041535</u>

Ray A, Basu S, Gharaibeh RZ, Cook LC, **Kumar R**, **Lefkowitz EJ**, Walker CR, Morrow CD, Franklin CL, Geiger TL, Salzman NH, Fodor A, Dittel BN. <u>Gut Microbial Dysbiosis Due to Helicobacter Drives an Increase in Marginal Zone B Cells in the Absence of IL-10 Signaling in Macrophages. J Immunol. 2015 Aug 31. PMID: 26324769</u>

Rodenburg CM, McPherson SA, Turnbough CL Jr., Dokland T. <u>Structure and Assembly of the Bacillus</u> <u>anthracis Exosporium</u>. Microsc. Microanal. 2015 Sept 23. [Epub ahead of print]

Stripling J, Kumar R, Baddley JW, Nellore A, Dixon P, Howard D, Ptacek T, Lefkowitz EJ, Tallaj JA, Benjamin WH Jr, Morrow CD, Rodriguez JM. Loss of Vancomycin-Resistant Enterococcus Fecal Dominance in an Organ Transplant Patient with Clostridium difficile Colitis After Fecal Microbiota Transplant. Open Forum Infect Dis. 2015 Jun 3;2(2):ofv078. PMID: 26180828

Publications continued from page 7

Sun J, Siroy A, Lokareddy RK, Speer A, **Doornbos KS**, Cingolani G, **Niederweis M**. The tuberculosis necrotizing toxin kills macrophages by hydrolyzing NAD. Nat Struct Mol Biol. 2015 Aug 3. [Epub ahead of print] PMID: 26237511

Tao J, Kang KD, Hall SD, Laube AH, Liu J, Renfrow MB, Novak J, Luo G. The Serum Very-Low-Density Lipoprotein Serves as a Restriction Factor against Hepatitis C Virus Infection. J Virol. 2015 Jul;89(13):6782-91. PMID: 25903344

Tse HM, Kozlovskaya V, Kharlampieva E, Hunter CS. Minireviw: Directed differentiation and encapsulation of islet β-cells: recent advances and futureconsiderations. Mol Endocrinol. 2015 Sep:me20151085. [Epub ahead of print]

Turkeshi E, Zelenukha D, Vaes B, Andreeva E, **Frolova** E, Degryse JM. Predictors of poor-quality spirometry in two cohorts of older adults in Russia and Belgium: a cross-sectional study. NPJ Prim Care Respir Med. 2015 Jul 23;25:15048. PMID: 26201999

Xiao L, **Ptacek T**, **Osborne JD**, Crabb DM, Simmons WL, **Lefkowitz EJ**, Waites KB, Atkinson TP, **Dybvig K**. <u>Comparative genome analysis of Mycoplasma pneumoniae</u>. BMC Genomics. 2015 Aug 16;16(1):610. PMID: 26275904

Sarvagna Velidandla Scores Big in International Chess Tournament

Daughter of Uma Mudunura (research assistant for the Lund-Randall lab), Sarvagna Velidandla, represented Alabama in the 2015 Susan Polgar Foundation Girls' Invitational Chess Tournament in St Louis, Missouri, in July. She tied for ninth place in the overall 61-player event representing the US, Canada, Brazil, Costa Rica and Guatemala. She was also awarded second place in her age group, tenth place in Blitz chess and Best Sportsmanship.

Grants and Contracts July I - September 30, 2015

Bedwell, David M

Southern Research Institute

The Identification of New Treatments for Cystic Fibrosis Caused by Premature Termination Codons-Bedwell Subcontract

Hu, Hui

Alliance for Cancer Gene Therapy
A Novel T-Cell Quiescence Mechanism in Anti-Ovarian
Tumor Responses

Jiang, Mengxi

American Heart Association

Mechanisms of BK Polyomavirus Interaction with the DNA Damage Response

Kearney, John F

National Institute of Allergy and Infectious Diseases/ NIH/DHHS

Commensal-Dependent Maturation of the Natural IgM Repertoire

Klug, Christopher A

National Institute of Diabetes and Digestive and Kidney Diseases/NIH/DHHS

Defining Pathways Promoting HSC Self-Renewal by Mesenchymal Stem/Stromal Cells

Novak, Jan

National Institute of Diabetes and Digestive and Kidney Diseases/NIH/DHHS

Abnormal STAT3 Singnaling and Aberrant O-Glycosylation of IgA1 in IgA Nephropathy

Saad, Jamil S.

National Institute of General Medical Sciences/NIH/DHHS

Structural Basis for HIV-1 Gag Interactions with Cellular Constituents

Thompson, Sunnie R.

DOD - Army Medical Research Acquisition Activity The Role of the Cellular Stress Program for Prostate Cancer Cells to Grow in the Bone Microenviroment



Around Campus and About Town



UAB Women's Soccer vs Marshall

October 9, 2015—7:00 pm UAB West Campus Field

Admission: adults \$5.00, ages 6-17

\$3.00

Barktoberfest

October 9, 2015—6:00—10:00 pm Avondale Brewing Company

Admission: \$20

Drink awesome beer, eat delicious food, listen to classic polka music, and help raise money for your favorite local charity, Hand in Paw! A \$20 ticket gets you: one beer ticket - one food ticket (beer braised brat and a huge soft pretzel from Klingler's!) - entry into the pet costume contest - entry into the stein hoist contest - one raffle ticket - one novelty keepsake - various prizes awarded during the night.









24th Annual Tannehill Halloween Fairyland

October 31, 2015—1:00 –9:00 pm

Tannehill Ironworks Historical State Park

Admission: adults \$4.00, seniors \$3.00, ages 6-11 \$2.00

Enjoy a non-scary Halloween party at the state fairgrounds. Activities include moonwalks, face painting, balloon animals, a bungee jump, along with a train rides for a small additional charge. In the evening, children can "trick or treat" at more than 200 campsites.

Chris Thile

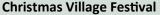
November 2, 2015—7:00 pm

<u>Alys Robinson Stephens Performing Arts</u>

<u>Center</u>

Admission: \$54.50; \$46.50; \$33.50

American virtuoso mandolinist Chris Thile performs a solo evening of flawless musicianship and mind-blowing exploration – from bluegrass to Bach and back again.



November 4-November 8, 2015

Birmingham Jefferson Convention Complex (BJCC) Exhibition Halls

Admission: adults \$12:00, ages 6-12 \$5.00

Kick off your Christmas shopping with a day at Christmas Village. An amazing variety of gift ideas will provide you with creative gift solutions for everyone.

Holiday Spectacular

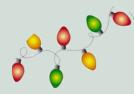
December 3—December 20, 2015—check show times on

Red Mountain Theatre Company

Admission: \$30

HolidaySpectacular

Celebrate the holidays with a spectacular display of all your favorite music of the season! RMTC Conservatory students perform alongside professional actors to warm your heart and set the stage for a magical holiday season! Rated G



ASO Holiday Family Concert

December 20, 2015—3:00 pm Alys Robinson Stephens Performing Arts Center

Admission charged

Celebrate the Holidays with your Alabama Symphony. Resident Conductor Chris Confessore conducts a joyous family friendly Holiday program filled with your favorite holiday music as well as an audience sing-along. There may be a special guest from the North Pole, as well.



University of Alabama at Birmingham Department of Microbiology

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