Breastfeeding of human infants has been shown to provide protection against many pathogenic and pathologic conditions, and much of that protection is mediated by naturally occurring glycans in milk. We have recently identified a new glycan, hyaluronan (HA), in human milk, which occurs at the highest concentration during the early stage of human lactation and decreases gradually over time. HA levels in human milk right after delivery are markedly higher than in commercial infant formulas. Importantly, we have also discovered that feeding purified HA of a specific size range to mice is protective in an epithelial damage/bacteria-induced colitis model. Additionally, our data indicate size-specific, HA fragment driven anti-microbial responses by intestinal epithelium. A special attribute of HA, different from other milk glycans, is its function as an endogenous ligand of the bacterial pattern recognition Toll-like receptors (TLRs) 4 and 2, which are known to...
be important sensors that trigger the innate host defense system. Thus HA may be a way to stimulate the unprotected infant gut to ward off pathogens. Therefore we think that HA in milk, in a size dependent manner, provides innate host protection against pathogens in the gut of immune-naive infants and children.

Preliminary studies from our lab show HA size-specific upregulation of antimicrobial responses in intestinal epithelial cells in cell cultures and mouse models. Among the virus response proteins, our data show IFIT1 is markedly induced by HA, in a size specific manner, and a combination of antibodies to TLR4 and TLR2 completely blocks this effect. Importantly, the HA we can isolate from milk also has the same stimulatory ability. The HA fragments also specifically induce human defensin 2, one member of the antimicrobial peptide family that is important in excluding pathogens and maintaining proper intestinal bacterial colonization. Again, the HA isolated from human milk has the same ability.

We envision that our proposed investigation could ultimately lead to identifying defined dietary HA supplements that would be therapeutic to infants who are formula fed and children prone to gastrointestinal infectious disease. HA would be an attractive therapeutic because it is: 1) not toxic or immunogenic due to its simple unmodified carbohydrate structure; 2) easily administered; 3) already being produced commercially on a large scale as a health food supplement as well as for medical applications. Based on our preliminary data and the previously reported biological effects of HA, we think the key to its protective potency will depend on the HA polysaccharide size(s) needed to mediate individual host responses.

Rotavirus is a debilitating intestinal infection of young children. Experiments to test whether HA fragments inhibit rotavirus infection in vitro and in vivo are being conducted in collaboration with Monica McNeal at Cincinnati Children’s Hospital. Biochemical analysis of the size and structure of HA contained in human milk is being done in collaboration with Mary Cowman of Polytechnic Institute of New York University.

We propose to develop a therapeutic strategy based on the characteristic structure of HA contained in human milk.

HA levels in human milk right after delivery are markedly higher than in commercial infant formulas.
Serpil Erzurum, MD was selected by the NHLBI and the National Advisory Council to receive the Method to Extend Research in Time (MERIT) Award. Selection for the MERIT is predicated upon consistent outstanding contributions to biomedical science. The MERIT provides long-term support for a total of ten years for her RO1-funded research studies in lung biology.

Serpil Erzurum, MD received an award for $177,761 over 1 year for “A Phase II Study in Patients with Asthma to Assess the Safety and Immunogenicity of an unadjuvanted Novartis H1N1 Influenza Vaccine Administered at Two Dose Levels” as a supplement to her current R01 grant “Redox Determinants of Severe Asthma”. Funded by the National Heart, Lung and Blood Institute of NIH.

Serpil Erzurum, MD received $415,578 over 2 years for “Imaging Inflammation in Asthma.” This award was a challenge grant issued under American Recovery and Reinvestment Act (ARRA).

Laura Nagy, PhD, was awarded $2,374,994 over 5 years for “Alcoholic Liver Disease: Biochemical, cellular and systemic responses to ethanol.” Funded by NIH National Institute on Alcohol Abuse and Alcoholism. This is a P20, Exploratory/Developmental Alcohol Research Center grant.

Carol de la Motte, PhD received an award for $2,094,113 for 5 years for “Hyaluronan regulation of microbial host defense of the intestine.” Funded by the NICHD/NIH.

Satish Kalhan, MD, was awarded $1,142,609 over 2 years for “Sulfur Amino Acid Metabolism in NAFLD”. Funded under the American Recovery and Reinvestment Act and distributed via the National Institute of Diabetes and Digestive and Kidney Diseases.

Laura Nagy, PhD

Carol de la Motte, PhD

Serpil Erzurum, MD

Satish Kalhan, MD
Awards Continued

Kay Stelmach, RN, Nurse Manager of the Clinical Research Unit (CRU) received the 2009 Maria and Sam Miller Professional Excellence Award for Cleveland Clinic RN of the Year.

In November 2009, Jessica Cohen, PhD., successfully defended her thesis entitled "Ethanol-induced liver injury: preventing apoptosis."

Pathobiology Department Board: September, 2009

Discovery. It's a big word. In Pathobiology, it means researchers dedicated to the solution of problems in human health. As we develop strategies for preventing, detecting, and controlling disease, we are looking to what is NEXT. We are committed to investigating inflammation and repair—the common denominator of human disease. Our collaborations with scientists, physician-scientists, and clinicians are advancing the future of healthcare. A rapid translation of our findings in the lab to the patient allows us to bridge the gap between laboratory and clinical research. We work in an environment of discovery. Walk and see what's NEXT.
New Publications-Editor

Achkar, JP

Comhair, Suzy


Culver, Daniel

de la Motte, Carol

Dweik, Raed

Erzurum, Serpil


Fiocchi, Claudio

Kalhan, Satish


Kirwan, John


McCullough, Arthur


McCurry, Kenneth


Nagy, Laura


Olman, Mitchell


Stuehr, Dennis
Mitchell Olman, MD has been appointed 2008 - 2009 Chair of the Scientific Program Committee of the Allergy, Immunology and Inflammation Assembly of the American Thoracic Society.

Raed Dweik, MD, director of the Pulmonary Hypertension Summit on November 20-21, 2009 at the InterContinental Hotel & Bank of America Conference Center in Cleveland, Ohio.

Loyola University Chicago, IL for the 29th Midwest Enzyme Chemistry Conference, Invited Speaker, October 2009.


On October 3rd, Team “Becky’s Babes” participated in the American Diabetes Association’s signature fundraising walk, Step Out: Walk to Fight Diabetes. Becky Sebastian, a Lead Research Technologist was recently diagnosed with Type I Diabetes and in support of her, her coworkers (Jessica Cohen, Megan McMullen, Michele Pritchard and Pamela Soda) created a team to raise funds and walk to raise awareness. As word of the team spread, Becky’s Babes gained two additional members, Elizabeth Sabens (Case Western Reserve University) and Dan Sebastian (Becky’s husband). In six months, the team, with the help of friends, family, and coworkers (including many members of Pathobiology) raised $2133! This impressive total ranked Becky’s Babes the 4th highest corporate team and 6th highest team overall for fundraising.

On the day of the walk, participants were greeted with a fun and lively kick-off breakfast. There was music and raffles which made the event fun for people of all ages. All of the Cleveland Clinic teams had their pictures taken and were given commemorative t-shirts from both the American Diabetes Association and the Cleveland Clinic. The actual walk was a challenging four miles, but volunteers lined the streets, cheering the walkers along the way and providing rest stops with refreshments. At the finish line participants received a bag filled with prizes and a prepared lunch.

Every step that was taken and every dollar the team raised helped combat a disease that is so prevalent among our friends and family. Diabetes is a disease in which the body does not produce or properly use insulin. The cause of diabetes continues to be a mystery, although both genetics and environmental factors appear to play roles. Diabetes has deadly serious consequences, for which there is no cure. There are 23.6 million Americans living with diabetes, a disease whose incidence is outpacing heart disease, cancer and AIDS. Donations raised for Step Out: Walk to Fight Diabetes help the Association to provide community-based education programs, protect the rights of people with diabetes and fund critical research for a cure.

Thank you and congratulations to Team Becky’s Babes for their dedication and commitment to such a noble cause.
New Employees

John Barta
Research Student
Administration Office

Amy Castilano, B.S.
Research Student
Olman Lab

David Coe, Ph.D.
Postdoctoral Fellow
Stuehr Lab

Lisa Dominak, Ph.D.
Postdoctoral Fellow
Olman Lab

Cindy Kangas
Research Technologist
Aronica Lab

Jennifer Leising
Research Technologist
Olman Lab

Jennifer Hillian, Ph.D.
Postdoctoral Fellow
Nagy Lab

Nichole Nageotte
Animal Husbandry Technician
Nagy Lab

Eunsuk Oh (Adele), M.D.
Visiting Scientist
Kirwan Lab

Kelly Paschke, B.S.
Research Technician
Dweik Lab

Mircea Pavkov, Ph.D.
Postdoctoral Fellow
Olman Lab

Suphagaphan Ratana-
maneechat (Tarn), M.D.
Research Scholar
Erzurum Lab

Benjamin Savasky, B.S.
Research Technician
Erzurum Lab

Xiaoying Tang, M.S.
Senior Research Technologist
McCurry Lab

Jia Yu
Graduate Student
Erzurum Lab

Zhihao Yu, Ph.D.
Postdoctoral Fellow
Stuehr Lab

Not pictured:
Susan Abouhassan, M.D.
Rotating Clinical Fellow
Hsieh Lab

Luciana Hannibal, Ph.D.
Postdoctoral Fellow
Stuehr Lab

Amrita Kabi, Ph.D.
Postdoctoral Fellow
McDonald Lab

Brian Schroer, M.D.
Rotating Clinical Fellow
Hsieh Lab
Department Party
The Pathobiology department comes together to celebrate the holidays in 2009.
Adopt a Family:

Pathobiology “adopted” a family in need for the Holiday Season. A single mother and her five children were grateful when the presents were delivered to their home two days before Christmas. Our department was able to give the children all the items on the wish list and more due to monetary and gift donations. Thank you to everyone who donated their time, money and gifts, the family was truly thankful.

Question!!!

How many people can you find from pathobiology department in this photo?

Send us your answer for a surprise gift.

fenneln@ccf.org

Contact information

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To learn more, visit our department on the web:
http://www.lerner.ccf.org/pathobio