INTERNATIONAL EOSINOPHIL SOCIETY, INC. WINTER 2013

EOSINOPHIL NEWS

Message from the President

Dear colleagues and friends,

After the last biennial meeting in Oxford, United Kingdom, this summer, some time has passed and we felt that a newsletter could update you with the developments in our society as well as in our field of research. For instance, this newsletter contains information regarding reagents and experimental mouse models for eosinophil research that have been particularly generated in the laboratory of Dr. James J. Lee (Scottsdale, AZ, USA). These tools will continue to greatly contribute to research in the field of eosinophils. Moreover, we list selected studies that have recently been published and hope that this service will be appreciated by our members. Please read also our information regarding the next biennial meeting in Chicago that was kindly summarized by Dr. Bruce Bochner (Chicago, IL, USA) as well as other activities.

Finally, we are sad about the death of Dr. Redwan Moqbel (Winnipeg, MB, Canada), who passed away on 9 October 2013. His death has shaken the eosinophil community, but his contribution to the field is immortal. As laymen, patients, and scientists, we thank Redwan for his outstanding contribution to science and medicine. We include an obituary that provides you with some information about this tragic loss.

Sincerely,

Hans-Uwe Simon, MD, PhD
President

8TH BIENNIAL SYMPOSIUM PHOTOS

Welcome Reception on the Liddon Quad

Group Dinner in the Dining Hall

The Availability and Utility of Eosinophil-specific Reagents and Mouse Models from Lee Laboratories

by James J. Lee, PhD, Professor, Mayo Clinic School of Medicine

When Nancy and I started to work in the area of eosinophil biology >20 years ago we were definitively outsiders. We were mouse transgenic and gene knockout aficionados who wanted to work on eosinophils (no … mental illness does not run in our families). The problem was that we did not have any background or training in granulocytes or studies in eosinophil-associated diseases. So when we arrived at Mayo Clinic, we were understandably a bit lost. However, Jerry Gleich took us under his wing and freely provided us with advice, reagents, and anything else we needed to succeed – in fact he insisted that he be allowed to help!! His kindness was truly amazing and changed our lives in many ways. We were sure that our technical skills in the mouse would move eosinophil research forward in ways that were not possible and/or had not yet been done. However, because of Jerry we also became committed to the idea of sharing anything and everything we would create. By helping everyone in this community with their science/careers we were going to repay the kindness shown to us – besides in our minds it was the right thing to do. We were also convinced that the success of Lee Laboratories and a willingness to share our reagents and mice were not mutually exclusive. Indeed, we have never wavered from this philosophy and have no regrets. Nancy and I are sure that this has been an integral component of our academic success and in the process we have been able to help out many friends and colleagues – What a deal!!

One of the advantages of being "old" (think senior) investigators is that over the years we have built-up a large repository for reagents and mouse models as we pursued our studies of all things eosinophil. As was noted at the recent IES meeting this year in Oxford, our reagents, mice, and technical insights/advice are available to everyone; we are happy to get folks started and/or move their research forward. Nancy and I do not insist on being co-authors of investigator's papers for just providing our "stuff". Instead, our goals have been far less complex: We wanted to establish meaningful collaborations with other investigators that move eosinophil research forward and lead to interesting co-authored manuscripts and grants. However, we also wanted to make it possible for investigators who did not want to collaborate or who worked in areas where there was not common interest with Lee Laboratories to easily request our reagents/mice. In these cases, we simply ask that our reagents and/or mice are acknowledged in any manuscripts/papers, abstracts, or grants as having come from the "Laboratories of Drs. Nancy and Jamie Lee". The only restrictions Mayo Clinic have put on all of our activities (i.e., the transfer and distribution of materials/mice not subject to intellectual property licenses) are the assessment of small administrative fees to partially defray the costs to Mayo for the production, maintenance, and distribution of these materials. This system has worked with amazing efficiency over the years (at testament to Mayo Clinic infrastructure) and has allowed the transfer of reagents/mice to laboratories around the world with many of these materials becoming the "gold standard" reagents/mice used in basic research and now even patient-based studies. In fact, the current tallies from our records indicate that over the last 20 years we have collaborated and/or provided Lee Laboratories materials to 1292 investigators (>64 colleagues/year) in 371 different institutions from 35 countries.

To provide everyone with a quick reference guide of the available reagents and mice from Lee Laboratories, including references related to their production, characterization, and/or use, these materials are outlined below:

Polyclonal Antisera and Monoclonal Antibodies					
Antibody Reagent	Anti-Major Basic Protein (MBP) Polyclonal Antisera	Anti-Major Basic Protein (MBP) Monoclonal Antibody	Anti-Eosinophil Associated Ribonuclease (Ear) Polyclonal Antisera	Anti-Eosinophil Associated Ribonuclease (Ear) Monoclonal Antibody	Anti-Eosinophil Peroxidase (EPX) Monoclonal Antibody
Source Antigen	Purified Mouse MBP-1	Purified Mouse MBP-1	Purified Mouse 18kDa Secondary granule proteins with ribonucleases activities	Purified Mouse 18kDa Secondary granule proteins with ribonucleases activities	Purified/Enzymatically Active Mouse Eosinophil Peroxidase
Immunized Host Animal	Rabbit	Rat	Rabbit	Rat	Mouse EPX knockout mice ($epx^{-/-}$)
Antibody Isotype	Polyclonal, IgG purified	Monoclonal, IgG2a	Polyclonal, IgG purified	Monoclonal, IgG2a	Monoclonal, IgG2a
Mouse Target Protein(s)	MBP-1 and -2 [1-4]	MBP-1 [5-9]	Ear-1,-2,-6/-7, -5/-11 [10]	Ear-1,-2,-6/-7 [11, 12]	Eosinophil peroxidase with no cross reactivity with any endogenous peroxidase including myeloperoxidase [13-15]
Species Cross Reactivity	<u>High</u>: Mouse/Rat/Hamster MBP-1 and -2 <u>Limited</u>: Guinea pig and Human	<u>High</u>: Mouse/Rat/Hamster MBP-1 and -2 with little to no cross reactivity displayed with human samples	<u>High</u>: Mouse <u>Limited</u>: Rat	<u>High</u>: Mouse with very limited cross-reactivity with Rat and absolutely no binding to human ECP/ EDN	<u>High</u>: All mammals tested, including mouse, rat, hamster, guinea pig, human, non-human primates, pig, cow <u>Limited</u>: Amphibians, reptiles, birds
Venues of Tested Utility	• Westerns • Immunoblot assessments of sample fluids • Immunohistochemistry/ Immunofluorescence staining using frozen sections and formalin-fixed, paraffin-embedded biopsies	• Westerns • Immunoblot assessments of sample fluids • Immunohistochemistry/ Immunofluorescence staining using frozen sections and formalin-fixed, paraffin-embedded biopsies	• Westerns • Immunoblot assessments of sample fluids • Immunohistochemistry/ Immunofluorescence staining using frozen sections and formalin-fixed, paraffin-embedded biopsies	• Westerns • Immunoblot assessments of sample fluids • Immunohistochemistry/ Immunofluorescence staining using frozen sections and formalin-fixed, paraffin-embedded biopsies	• Westerns • Immunoblot assessments of sample fluids • Immunohistochemistry/ Immunofluorescence staining using frozen sections and formalin-fixed, paraffin-embedded biopsies

Diagnostic Assays of Degranulation			
Secondary Granule Protein	**Major Basic Protein (MBP)-1**	**Eosinophil Associated Ribonuclease (Ear)**	**Eosinophil Peroxidase (EPX)**
Single dimensional Immunoblot Assay (i.e., unique antibody))	Rabbit Polyclonal and/or Rat Monoclonal detection support medium-based assay	Rabbit Polyclonal and/or Rat Monoclonal detection support medium-based assay	Rabbit Polyclonal and/or Rat Monoclonal detection support medium-based assay
ELISA Assays **• Sandwich ELISA (i.e., capture/ detection antibody mediated granule protein detection assay)** **• Single Antibody ELISA**	• Sandwich ELISA (i.e., rabbit polyclonal capture and rat monoclonal detection antibody assay) • Single Antibody ELISA [6]	• Sandwich ELISA (i.e., rabbit polyclonal capture and rat monoclonal detection antibody assay) • Single Antibody ELISA [6]	• Sandwich ELISA (i.e., rabbit polyclonal capture and rat monoclonal detection antibody assay) [16-18] • Single Antibody ELISA
Cross Reactivity/Species Utility	Mouse and Rat with limited utility in Guinea Pig	Mouse only	All mammals tested. Quantitative assays developed and tested for use with mouse samples [18] and for use in clinical settings with human patient samples [16, 17]

Interleukin-5 (IL-5) and Eotaxin Transgenic Models: Constitutive Ectopic Over-Expression							
Transgenic Strain	**NJ.1638** [19]	**NJ.1726** [1]	**NJ.692** [20]	**PL2-IL5** [21]	**CC-eotaxin-2** [6]	**PL2-eotaxin-2**	**NJ.1638 (X) CC-eotaxin-2** [6]
Promoter Used for Expression	CD3δ	CC10	Keratin-14	PL2	CC10	PL2	CD3δ and CC10
Target Organ/ cell type	All T cells	Lung/Clara Cells	Skin/ keratinocytes	Esophagus/ Squamous Epithelium	Lung/Clara Cells	Esophagus/ Squamous Epithelium	Lung/IL-5 (T cells) and eotaxin-2 (Clara cells)
Prominent Characteristic/ Utility	• Hypereosinophilic model • Peripheral Blood eosinophila: >200,000 eosinophils/mm^3 • Source animal to isolate and purify blood eosinophils	• Asthma model • Source animal to isolate and purify activated airway (BAL) eosinophils	• Eosinophilic fasciitis model	• Eosinophilic esophagitis model	• Asthma model • Source animal to purify eotaxin-2	• Eosinophilic esophagitis model	• Model of Severe Asthma • Model of Airway eosinophil activation and degranulation
Available Background Strains	C57BL/6J BALB/cJ	C57BL/6J BALB/cJ	C57BL/6J	C57BL/6J	C57BL/6J	C57BL/6J	C57BL/6J

Eosinophil Secondary Granule Protein Encoding Gene Knockout Mice					
Knockout Strain	**MBP-1**$^{-/-}$ [12]	**MBP-2**$^{-/-}$	**EPX**$^{-/-}$ [5]	**MBP-1**$^{-/-}$ **(X) EPX**$^{-/-}$ [22]	**Ear-11**$^{-/-}$
Gene Targeted	Major Basic Protein - 1	Major Basic Protein - 2	Eosinophil Peroxidase	Double MBP-1 and EPX Knockout	Eosinophil Associated Ribonuclease -11
Prominent Characteristic/ Utility	Loss of electron dense core of eosinophil secondary granules	No Identifiable Phenotype	Loss of electron translucent matrix of eosinophil secondary granules	Collapse of eosinophilopoiesis leading to an eosinophil-deficient strain of mouse	Currently understudy in collaboration with Helene Rosenberg (NIAID, USA)
Available Background Strains	C57BL/6J BALB/cJ	C57BL/6J BALB/cJ	C57BL/6J BALB/cJ	C57BL/6J	C57BL/6J

Eosinophil-Deficient Mouse Models				
Knockout Strain	**PHIL** [23]	**MBP-1**$^{-/-}$ **(X) EPX**$^{-/-}$ [22]	**eoCRE (X) ROSA26**$^{flox\text{-}STOP\text{-}flox}$ **- DTA** [24]	**iPHIL** [25]
Mechanism of Eosinophil Ablation	Congenital eosinophil deficiency mediated EPX-promoter driven expression of Diphtheria Toxin A chain	Congenital eosinophil deficiency induced by apoptosis of eosinophil-committed progenitor cells	Eosinophil-specific expression of Cre-recombinase leading to a congenital eosinophil deficiency mediated by expression of Diphtheria Toxin A chain	Administration (i.p.) of Diphtheria Toxin
Prominent Characteristic/ Utility	Eosinophil deficiency even following allergen provocation or cross with IL-5 overexpressing strains	Eosinophil deficiency >95% following allergen provocation or cross with IL-5 overexpressing strains	Eosinophil deficiency comparable to either PHIL or ΔblGATA mice	Inducible "on-demand" eosinophil ablation in otherwise wild type mice
Available Background Strains	C57BL/6J BALB/cJ	C57BL/6J	C57BL/6J	C57BL/6J

Eosinophil-Specific Cre Expression (eoCRE) and the Targeting of Eosinophil-Specific Gene Expression								
Strain of Interest	eoCRE [24]	eoCRE (X) ROSA26$^{flox\text{-}STOP\text{-}flox}$ - GFP [24]	eoCRE (X) ROSA26$^{flox\text{-}STOP\text{-}flox}$ - DTA [24]	eoCRE (X) IL-4/-13$^{flox/flox}$	eoCRE (X) TGFβ$^{flox/flox}$	eoCRE (X) Glucocorticosteroid receptor$^{flox/flox}$	eoCRE (X) 12/15-Lipoxygenase$^{flox/flox}$	eoCRE (X) MYD88$^{flox/flox}$
Gene Targeted	Eosinophil-specific expression of Cre-recombinase through a gene knockin at the EPX locus	Eosinophil-specific expression of enhance Green Fluorescent Protein (GFP)	Eosinophil-specific expression of Diphtheria Toxin A chain (DTA)	Eosinophil-specific knockout of IL-4/-13	Eosinophil-specific knockout of TGFβ-1	Eosinophil-specific knockout of Glucocorticosteroid receptors	Eosinophil-specific knockout of 12/15-Lipoxygenase	Eosinophil-specific knockout of MYD88
Prominent Characteristic and/or Utility	100% eosinophil-specific with >98% of all eosinophils express Cre at levels sufficient to mediated loxP-loxP recombination	High-level GFP expression exclusively in eosinophils for trafficking studies	Congenital eosinophil-deficient strain of mice	Eosinophil-specific gene knockout of IL-4/-13	Eosinophil-specific gene knockout of TGFβ-1	Eosinophil-specific gene knockout of Glucocorticosteroid Receptors	Eosinophil-specific gene knockout of 12/15-Lipoxygenase	Eosinophil-specific gene knockout of MYD88 signaling
Available Background Strains	C57BL/6J BALB/cJ	C57BL/6J BALB/cJ	C57BL/6J BALB/cJ	C57BL/6J BALB/cJ	C57BL/6J	C57BL/6J	C57BL/6J	C57BL/6J

REFERENCES

1. Lee JJ, McGarry MP, Farmer SC, Denzler KL, Larson KA, Carrigan PE, Brenneise IE, Horton MA, Haczku A, Gelfand EW, Leikauf GD, Lee NA. Interleukin-5 expression in the lung epithelium of transgenic mice leads to pulmonary changes pathognomonic of asthma. J Exp Med. 1997;185(12):2143-56.
2. Macias MP, Welch KC, Denzler KL, Larson KA, Lee NA, Lee JJ. The Identification of a New Murine Eosinophil Major Basic Protein (mMBP) Gene: Cloning and Characterization of mMBP-2. J Leukoc Biol. 2000;67:567-76.
3. Shen HH, Ochkur SI, McGarry MP, Crosby JR, Hines EM, Borchers MT, Wang H, Biechele TL, O'Neill KR, Ansay TL, Colbert DC, Cormier SA, Justice JP, Lee NA, Lee JJ. A causative relationship exists between eosinophils and the development of allergic pulmonary pathologies in the mouse. J Immunol. 2003;170:3296-305.
4. Takeda K, Haczku A, Lee JJ, Irvin CG, Gelfand EW. Strain dependence of airway hyperresponsiveness reflects differences in eosinophil localization in the lung. American Journal of Physiology and Cell Molecular Physiology. 2001;281(2):L394-402.
5. Denzler KL, Borchers MT, Crosby JR, Cieslewicz G, Hines EM, Justice JP, Cormier SA, Lindenberger KA, Song W, Wu W, Hazen SL, Gleich GJ, Lee JJ, Lee NA. Extensive eosinophil degranulation and peroxidase-mediated oxidation of airway proteins do not occur in a mouse ovalbumin-challenge model of pulmonary inflammation. J Immunol. 2001;167(3):1672-82.
6. Ochkur SI, Jacobsen EA, Protheroe CA, Biechele TL, Pero RS, McGarry MP, Wang H, O'Neill KR, Colbert DC, Colby TV, Shen H, Blackburn MR, Irvin CC, Lee JJ, Lee NA. Co-Expression of IL-5 and Eotaxin-2 in Mice Creates an Eosinophil-Dependent Model of Respiratory Inflammation with Characteristics of Severe Asthma. J Immunol. 2007;178(12):7879-89.
7. Jacobsen EA, Ochkur SI, Pero RS, Taranova AG, Protheroe CA, Colbert DC, Lee NA, Lee JJ. Allergic Pulmonary Inflammation in Mice is Dependent on Eosinophil-induced Recruitment of Effector T Cells. J Exp Med. 2008;205(3):699-710. PMCID: 2275390.
8. Lee JJ, Jacobsen EA, McGarry MP, Schleimer RP, Lee NA. Eosinophils in Health and Disease: The *LIAR* Hypothesis. Clin Exp Allergy. 2010;40(4):563 - 75. PMCID: 2951476.
9. Masterson JC, McNamee EN, Jedlicka P, Fillon S, Ruybal J, Hosford L, Rivera-Nieves J, Lee JJ, Furuta GT. CCR3 Blockade Attenuates Eosinophilic Ileitis and Associated Remodeling. The American journal of pathology. 2011;179(5):2302-14. PMCID: 3204091.
10. Cormier SA, Yuan S, Crosby JR, Protheroe CA, Dimina DM, Hines EM, Lee NA, Lee JJ. T(H)2-mediated pulmonary inflammation leads to the differential expression of ribonuclease genes by alveolar macrophages. Am J Respir Cell Mol Biol. 2002;27(6):678-87.
11. Cormier SA, Taranova AG, Bedient C, Nguyen T, Protheroe C, Pero R, Dimina D, Ochkur SI, O'Neill K, Colbert D, Lombari TR, Constant S, McGarry MP, Lee JJ, Lee NA. Pivotal Advance: Eosinophil Infiltration of Solid Tumors Is an Early and Persistent Inflammatory Host Response. J Leukoc Biol. 2006;79(6):1131-9. PMCID: NIHMISD 56203.
12. Denzler KL, Farmer SC, Crosby JR, Borchers MT, Cieslewicz G, Larson KA, Cormier-Regard S, Lee NA, Lee JJ. Eosinophil major basic protein-1 does not contribute to allergen-induced airway pathologies in mouse models of asthma. J Immunol. 2000;165(10):5509-17.
13. Nair P, Ochkur SI, Protheroe C, Simms E, Lee NA, Lee JJ. The identification of eosinophilic gastroenteritis in prednisone-dependent eosinophilic bronchitis and asthma. Allergy Asthma Clin Immunol. 2011;7(1):4. PMCID: 3060837.

14. Nunez-Nateras R, Protheroe CA, Stanton ML, Ochkur SI, Jacobsen EA, Hou Y-X, Ferrigni E, Andrews PE, Colby TV, Lee NA, Castle EP, Lee JJ. Predicting Response to Bacillus Calmette-Guérin (BCG) in Patients with Carcinoma in Situ of the Bladder. Urologic Oncology 2013:In press.
15. Protheroe CA, Woodruff SA, DePetris G, Mukkada V, Ochkur SI, Janarthanan S, Lewis JC, Pasha S, Lunsford T, Harris L, Sharma VK, McGarry MP, Lee NA, Furuta GT, Lee JJ. A novel histological scoring system to evaluate mucosal biopsies from patients with eosinophilic esophagitis. Clinical Gastroenterology and Hepatology. 2009;7(7):749 - 55 e11. PMCID: 2706311.
16. Nair P, Ochkur SI, Protheroe CA, Radford K, Efthimiadis A, Lee NA, Lee JJ. Eosinophil Peroxidase in Sputum Represents a Unique Biomarker of Airway Eosinophilia. Allergy. 2013:In press. PMCID: NIHMS 481669.
17. Ochkur SI, Kim JD, Protheroe CA, Colber D, Condjella RM, Bersoux S, Moqbel R, Lacy P, Kelly EA, Jarjour NN, Schleimer RP, Furuta G, Nair P, Lee JJ, Lee NA. A Sensitive High Throughput ELISA for Human Eosinophil Peroxidase: A Specific Assay to Quantify Degranulation from Patient-derived Sources. Journal of Immunological Methods. 2012;384(1-2):10–20. PMCID: 3432656.
18. Ochkur SI, Kim JD, Protheroe CA, Colbert D, Moqbel R, Lacy P, Lee JJ, Lee NA. The Development of a Sensitive and Specific ELISA for Mouse Eosinophil Peroxidase: Assessment of Eosinophil Degranulation Ex Vivo and in Models of Human Disease. Journal of Immunological Methods. 2012;375(1-2):138-47. PMCID: 3375321.
19. Lee NA, McGarry MP, Larson KA, Horton MA, Kristensen AB, Lee JJ. Expression of IL-5 in thymocytes/T cells leads to the development of a massive eosinophilia, extramedullary eosinophilopoiesis, and unique histopathologies. J Immunol. 1997;158(3):1332-44.
20. Foster EL, Simpson EL, Fredrikson LJ, Lee JJ, Lee NA, Fryer AD, Jacoby DB. Eosinophils increase neuron branching in human and murine skin and in vitro. PLoS One. 2011;6(7):e22029. PMCID: PMC3140999.
21. Masterson JC, McNamee EN, Hosford L, Capocelli KE, Ruybal J, Fillon SA, Doyle AD, Eltzschig HK, Rustgi AK, Protheroe CA, Lee NA, Lee JJ, Furuta GT. Local hypersensitivity reaction in transgenic mice with squamous epithelial IL-5 overexpression provides a novel model of eosinophilic esophagitis. Gut. 2012:e-pub Nov 2012.
22. Doyle AD, Jacobsen EA, Ochkur SI, McGarry MP, Shim KG, Nguyen DTC, Protheroe C, Colbert D, Kloeber J, Neely J, Shim KP, Dyer KD, Rosenberg HF, Lee JJ, Lee NA. Expression of the Secondary Granule Proteins Major Basic Protein (MBP)-1 and Eosinophil Peroxidase (EPX) is Required for Eosinophilopoiesis in Mice. Blood. 2013;122(4):781-90. PMCID: NIHMSID #495374.
23. Lee JJ, Dimina D, Macias MP, Ochkur SI, McGarry MP, O'Neill KR, Protheroe C, Pero R, Nguyen T, Cormier SA, Lenkiewicz E, Colbert D, Rinaldi L, Ackerman SJ, Irvin CG, Lee NA. Defining a link with asthma in mice congenitally deficient in eosinophils. Science. 2004;305(5691):1773-6.
24. Doyle AD, Jacobsen EA, Ochkur SI, Willets L, Shim K, Neely J, Kloeber J, Lesuer WE, Pero RS, Lacy P, Moqbel R, Lee NA, Lee JJ. Homologous recombination into the eosinophil peroxidase locus generates a strain of mice expressing Cre recombinase exclusively in eosinophils. J Leukoc Biol. 2013;pre-print:doi jlb.0213089 [pii] 0.1189/jlb. PMCID: publisher provided directly to PMC.
25. Jacobsen EA, LeSuer WE, Willetts L, Zellner KR, Mazzolini K, Antonios N, Beck B, Protheroe C, Ochkur SI, Colbert D, Lacy P, Moqbel R, Appleton J, Lee NA, Lee JJ. Eosinophil Activities Modulate the Immune/Inflammatory Character of Allergic Respiratory Responses in Mice. Allergy. 2013:In press.

By Bruce Bochner, MD, 2015 IES Scientific Program Director

On behalf of the leadership at IES, I am excited to provide a brief update on plans for our next meeting, to be held in Chicago, Illinois, USA from 14-18 July 2015. On the heels of our outstanding meeting this past summer in Oxford, I am delighted as a native Chicagoan to serve as the meeting organizer for 2015. We have already evaluated several locations in the downtown area, and have chosen the Holiday Inn Mart Plaza (www.martplaza.com) to host the meeting. Its central location, ready access to public transportation (e.g., you can get there by public train directly from the O'Hare International Airport for just a few dollars), well-equipped meeting rooms, great views of the city, comfortable accommodations and reasonable rates are just a few of the benefits of this venue. We have also learned that through its visitors' bureau, the city of Chicago will also be able to provide us with additional services to make this an even more enjoyable event. We are at the very early stages with respect to programming and social events, but already appreciate that several of our members have expressed interest in helping to organize the meeting. For now, I hope you can join us, and please put a "save the date" on your calendars.

In Memorium

With grieved hearts we announce the passing of our dearly loved Redwan (Ridvan) Moqbel on 9 October in Winnipeg after a protracted battle with cancer.

Born in a border town on the Iraq/Iran border (14 August 1947), Redwan's family history is linked with the earliest days of the Baha'i Faith. Redwan served the Baha'i community in the UK and Canada in volunteer capacities, including as a member of the national governing council of the Baha'i community of the United Kingdom for 13 years.

Redwan was a speaker of rare eloquence, clarity and depth whose spiritual beliefs were firmly anchored in Baha'u'llah's writings and whose abundant humour was never at the expense of others. His life-long focus was on creating unity. He loved everyone but particularly youth whom he mentored on three continents. In confirmation of his efforts, Redwan received the Lieutenant Governor of Manitoba's Award for the Advancement of Interreligous Understanding in January 2013.

In 1976, Redwan obtained his PhD at the University of London, UK (LSH & TM). He became a faculty member there at the National Heart and Lung Institute in 1980. He was among the first to identify the immunological cell types that regulate asthma and allergy.

Recruited to the Department of Medicine, University of Alberta as a Professor in 1995, he served as the Director of the Pulmonary Research Group. There he received such prestigious awards as Alberta Heritage Medical Senior Scholar, Heritage Scientist and Heritage Senior Investigator.

In 2008, Redwan became Professor and Head of the Department of Immunology at the University of Manitoba, and Professor Emeritus at the University of Alberta. He was well recognized for his mentorship of young biomedical scientists, whom he encouraged to adopt "a noble goal."

An international authority on the immuno-molecular basis of asthmatic inflammation, in particular the role of eosinophils, Redwan's research garnered him numerous distinctions and awards. The International Eosinophil Society, of which he was a founding member, awarded him their highest honour, The Paul Ehrlich Award, named a mentoring award after him, and further honoured him with the prestigious Service Award in recognition of his "cardinal leadership" and innovative research.

A recent example of his work as a champion reconciler was his role in organizing a scientific conference in which protagonists in the controversy over Lyme Disease came together in an atmosphere of mutual respect.

Aggressive treatment for sinus cancer in 2006 resulted in a cure for Redwan, but from 2009 he suffered recurrences with metastatic lung and chest wall cancer. He accepted his ordeals with gratitude, grace and fortitude.

Left to cherish his memory are his wife, Shar Mitchell, Redwan's son, Sam Moqbel, (Amy and grandsons, Thomas and Evan), Redwan's daughter, Marianne Greenhowe, (Gordon and grandson, Oliver), Shar's father, Jack Mitchell, Shar's children, Gabriel Lenz, (Erica Carlisle), Colby Lenz, Asher Lenz, (Emily Dragoman), Redwan's brother, Sarmad, his sister, Sharaf, their families in Iraq, and hundreds of friends worldwide.

"O my God, Thy Trust hath been returned unto Thee." - Baha'u'llah

In lieu of flowers, contributions can be made to:
The Canadian Lyme Disease Foundation
www.canlyme.com
9131 – 118th St., Edmonton, AB T6G 1T6

CancerCare Manitoba Foundation
www.cancercarefdn.mb.ca
1160-675 McDermot Ave., Winnipeg, MB R3E 0V9

Riverview Health Centre Foundation (3E) Palliative Unit
http://www.riverviewhealthcentre.com
1 Morley Avenue, Winnipeg, MB R3L 2P4

If you will be sending a donation, please mention your affiliation with the International Eosinophil Society, Inc.

Eosinophils in the News

GRANTS RECEIVED

Mike Wechsler, Professor of Medicine and Director of the Asthma Program at National Jewish Health in Denver, recently received NIAID U-01 funding to do a clinical trial examining the effects of anti-IL5 in patients with eosinophilic Granulomatosis with Polyangiitis (also known as Churg-Strauss syndrome). Collaborating with Dr. Wechsler in this multi centered study are **Gerald Gleich** (U Utah, Salt Lake City), **Amy Klion** and **Paneez Khoury** (NIH), **Peter Weller** and **Praveen Akuthota** (Beth Israel Deaconess Medical Center, Boston), Ulrich Specks (Mayo Clinic, Rochester), Benjamin Raby (Brigham & Women's Hospital, Boston) and **Bruce Bochner** (Northwestern University, Chicago), as well as several European investigators including **Florence Roufosse** (Belgium).

The development and clinical applications of 111-Indium-labelled eosinophil scanning. Medical Research Council (UK) April 2012-2015. Professor Edwin Chilvers (Principal Investigator) with **Neda Farahi** (Co-Investigator).

The National Heart, Lung and Blood Institute awarded the University of Wisconsin School of Medicine and Public Health a Program Project Grant (2013 – 2018). Nizar Jarjour, MD, is the overall PPG Principal Investigator and leader of a project on "The Role of Eosinophils in Airway Inflammation and Remodeling". Deane Mosher, MD, leads a project on "Cell Movement through a TH2-conditioned Extracellular Matrix", and James Malter, MD (University of Texas Southwestern) leads a project on "The Role of Pin1 in Airway Remodeling". **Sameer Mathur, MD, PhD** and Loren Denlinger MD, PhD are leaders of a laboratory and clinical Core, respectively. Co-investigators include IES members **Elizabeth (Becky) Kelly, PhD; Stephane Esnault, PhD**; and **Mats Johansson PhD**. This PPG provides an integrated approach to investigate novel aspects of asthma pathobiology focusing on how the eosinophil can contribute to disease severity, progression, exacerbation, and resistance to therapy, with implications for other illnesses where eosinophils are known to be an important participant.

AWARDS

Sarah Bettigole, Best Oral Presentation, The transcription faxtor XBP-1 is a critical regulator of eosinophil development, IES 8th Biennial Symposium.

Neda Farahi, Best Oral Presentation, Use of III-Indium labeled autologous eosinophils to establish in vivo kinetics of human eosinophils, IES 8th Biennial Symposium.

Stephen Matthews, Best Poster Presentation, Eosinophil granule stability and viability are critically dependent on cystatin F, IES 8th Biennial Symposium.

Kalmia Buels, Best Poster Presentation, Mouse intestinal eosinophils have an antigen presenting cell phenotype and acquire luminal antigen, IES 8th Biennial Symposium.

Elizabeth Jacobsen, Best Poster Presentation, Eosinophils influence the inflammatory phenotype of asthma in an inducible knock-in eosinophil deficient mouse model of asthma, IES 8th Biennial Symposium.

HOT OFF THE PRESS*

Netali Ben Baruch-Morgenstern, Dana Shik, Itay Moshkovits, Michal Itan, Danielle Karo-Atar, Carine Bouffi, Patricia C Fulkerson, Diana Rashkovan, Steffen Jung, Marc E Rothenberg, Ariel Munitz. Paired immunoglobulin-like receptor A is an intrinsic, self-limiting suppressor of IL-5–induced eosinophil development. *Nat Immunol* (2013) Published online: 10 November 2013 doi:10.1038/ni.2757

Ha SG, Ge XN, Bahaie NS, Kang BN, Rao A, Rao SP, Sriramarao P. ORMDL3 promotes eosinophil trafficking and activation via regulation of integrins and CD48. *Nat Commun*. 2013;4:2479. doi: 10.1038/ncomms3479.

Farahi N, Loutsios C, Peters AM, Condliffe AM, Chilvers ER. Use of Technetium-99m-labeled Eosinophils to Detect Active Eosinophilic Inflammation in Humans. *Am J Respir Crit Care Med*. 2013 Oct 1;188(7):880-2.

Esnault S, Kelly EA, Johansson MW, Liu LY, Han S-T, Akhtara M, Sandbo N, Mosher DF, Denlinger LC, Mathur SK, Malter JS, Jarjour NN. Semaphorin 7A is expressed on airway eosinophils and upregulated by IL-5 family cytokines. *Clin Immunol*. In press Nov 2013

Han ST, Mosher DF. IL-5 induces suspended eosinophils to undergo unique global organization associated with priming. *Am J Respir Cell Mol Biol*. 2013 Oct 24. [Epub ahead of print]

Burnham ME, Koziol-White CJ, Esnault S, Bates ME, Evans MD, Bertics PJ, Denlinger LC. Human airway eosinophils exhibit preferential reduction in STAT signaling capacity and increased CISH expression. *J Immunol*. 2013. 191(6):2900-6.

Nussbaum JC, Van Dyken SJ, von Moltke J, Cheng LE, Mohapatra A, Molofsky AB, Thornton EE, Krummel MF, Chawla A, Liang HE, Locksley RM. Type 2 innate lymphoid cells control eosinophil homeostasis. *Nature*. 2013. Oct 10;502:245-8.

Bouffi C, Rochman M, Zust CB, Stucke EM, Kartashov A, Fulkerson PC, Barski A, Rothenberg ME. IL-33 markedly activates murine eosinophils by an NF-κB-dependent mechanism differentially dependent upon an IL-4 driven autoinflammatory loop. *J Immunol*. 2013. Oct 15;191:4317-25.

Nair P, Ochkur SI, Protheroe C, Radford K, Efthimiadis A, Lee NA, Lee JJ. Eosinophil peroxidase in sputum represents a unique biomarker of airway eosinophilia. *Allergy*. 2013. Sept;68:1177-84.

Laviolette M, Gossage DL, Gauvreau G, Leigh R, Olivenstein R, Katial R, Busse WW, Wenzel S, Wu Y, Datta V, Kolbeck R, Molfino NA. Effects of benralizumab on airway eosinophils in asthmatic patients with sputum eosinophilia. *J Allergy Clin Immunol*. 2013. Nov;132:1086-96.

Stoeckle C, Simon HU. CD8+ T cells producing IL-3 and IL-5 in non-IgE-mediated eosinophilic diseases. *Allergy*. 2013. Dec;68:1622-5.

Geering B, Stoeckle C, Rozman S, Oberson K, Benarafa C, Simon HU. DAPK2 positively regulates motility of neutrophils and eosinophils in response to intermediary chemoattractants. *J Leukoc Biol*. 2013. Oct 25. [Epub ahead of print]

** articles published after September 2013*

EOSINOPHIL RESOURCES

Please visit www.eosinophil-society.org/eosinophil-resources/website-and-listservs for a link to these resources:

- American Partnership for Eosinophilic Disorders (APFED)
- Children's Hospital of Philadelphia - Center for Pediatric Eosinophilic Disorders
- Churg Strauss Syndrome Association (CSSA)
- Cincinnati Center for Eosinophilic Disorders
- Diagnostics Development
- HES Listserv
- NJ/PA Eosinophilic Support Group
- Office of Rare Diseases
- TIGER

Job Mart

Postdoctoral Fellow

CINCINNATI CHILDREN'S HOSPITAL MEDICAL CENTER

The Division of Allergy and Immunology at Cincinnati Children's Hospital Medical Center has an opening for a Postdoctoral Fellow. The goal of the research is to identify novel pharmaceutical targets for the treatment of patients with eosinophilic diseases including eosinophilic gastrointestinal disorders, hypereosinophilic syndromes, asthma and food allergies.

Details about project areas can be found at: www.cincinnatichildrens.org/research/divisions/a/allergy-immunology/default/

The Division is a high-energy, dynamic, and interactive environment that is interested in recruiting self-motivated individuals with the drive to succeed and the desire to be competitive at the international level. Candidates with a strong background in immunology, molecular biology, informatics, genomics, cellular biology and signal transduction are encouraged to apply.

For consideration, please send CV, a brief statement of scientific/research interests, and contact information for three references to:

Marc Rothenberg, MD, PhD
Cincinnati Children's Hospital Medical Center
Division of Allergy and Immunology
3333 Burnet Avenue
Cincinnati, OH 45229
Email: marc.rothenberg@cchmc.org

Cincinnati Children's Hospital Medical Center is an Affirmative Action/Equal Opportunity Institution. Women and Minorities are encouraged to apply.

CALENDAR OF EOSINOPHILIC EVENTS

American Academy of Allergy, Asthma & Immunology Annual Meeting
28 February-4 March 2014
San Diego, CA

British Society for Haematology
28-30 April 2014
Birmingham, United Kingdom

American Thoracic Society
16-21 May 2014
San Diego, CA

European Hematology Association
12-15 June 2014
Milan, Italy

European Academy of Allergy and Clinical Immunology
7-11 June 2014
Copenhagen, Denmark

2014 EosConnection - 12th Annual Patient Education Conference (APFED)
12 July 2014
Denver, Colorado

American College of Allergy, Asthma and Immunology
6-10 November 2014
Atlanta, GA

World Allergy Organization International Scientific Conference 2014 (WISC 2014)
6-9 December 2014
Rio de Janeiro, Brazil

9th Biennial Symposium of the International Eosinophil Society, Inc.
14-18 July 2015
Chicago, IL

THE EOSINOPHIL NEWS IS SEEKING CONTRIBUTORS — NEXT ISSUE SPRING 2014!
Whether you are interested in writing a recurring column or a one-time piece, have an idea for new content, or information about a newsworthy item, we would like to hear from you. Pictures are always appreciated. Contact Hans-Uwe Simon at president@eosinophil-society.org. To place an ad in the newsletter, contact Kate Filipiak at kfilipiak@eosinophil-society.org.

Trainee Update

by Neda Farahi, BSc PhD
IES Trainee Member
University of Cambridge, UK

Whilst the 'dreaming spires' of Oxford may seem like a distant memory, the enthusiasm and interest generated at the IES Symposium still remains at the forefront of our minds. From a trainee perspective, the meeting was a success. Fellow trainees I spoke with valued the close level of interaction with senior investigators this meeting created. The new session on eosinophil methodology was also well received, particularly by those new to the field. Last, but not least, the 18 IES travel awards were very much appreciated, particularly in these times of economic austerity.

Since October 2013, I have been elected as a trainee member of the IES Board of Directors. This is a new role and one that was initiated to ensure that the trainee members (which includes both graduate students and postdoctoral researchers), have their voices heard and their needs met. The hope is to bring trainee members closer to the IES and to enhance interactions such as networking opportunities. We would like to incorporate a trainee-focused session at the next IES symposium and, with the newly updated website, aim to encourage communications and exchanges all year round.

If you are a trainee member and want to get more actively involved in the IES affairs, please feel free to contact me by email with any thoughts and suggestions you might have. nf231@cam.ac.uk

I look forward to hearing from you!

IES, Inc. Board of Directors

CONTACT INFORMATION FOR MEMBERSHIP, MEETING, WORKSHOP

Kate Filipiak
Executive Director
International Eosinophil Society, Inc.
555 East Wells Street
Suite 1100
Milwaukee, WI 53202
Tel: (414) 276-6445
Fax: (414) 276-3349
kfilipiak@eosinophil-society.org

Website Committee Update

by Ariel Munitz, PhD, Website Committee Co-Chair

One of the decisions, made at the past IES meeting in July in Oxford, United Kingdom 2013 was to re-evaluate the IES website and identify strategies to increase visibility to members and/or the general public. In order to accomplish this task, a Website Committee was organized consisting of:

Sameer K. Mathur, MD, PhD
Ariel Munitz, PhD
Amali E. Samarasinghe, PhD
Christina Stoeckle, PhD
Neda Farahi BSc, PhD

Following various conference calls, the Committee has decided to construct the IES website as an interactive tool for eosinophil researchers worldwide. In order to achieve this long-term goal a few short-term goals were set. First, the website requires a facelift to update the current design. Second, information regarding IES members and their research skills and overall interest is lacking and requires periodical updates.

Therefore, the committee has decided to announce a "photo contest" (with prizes!) where eosinophil-related graphics will be submitted, displayed and IES members will select the winning graphic. The winning graphic will be used as a rotating photo gallery in the renewed website and will let everyone (including the public) enjoy the beautiful figures from our research laboratories.

In addition, each IES member will receive an e-mail requesting him/her to update their scientific interests and hallmark publications. This may assist in facilitating collaborative efforts in the future between IES members.

We look forward for your cooperation and are always open for new suggestions!

If you are interested in joining the Website Committee, please contact IES at info@eosinophil-society.org.