

# BIOCHEMISTRY & MOLECULAR BIOLOGY TODAY



## Chair's Message

Our BMB Graduate Program Orientation event, not to mention the subsequent festive get-together, was not only successful in conveying a sense of the Program to the incoming Graduate School Class, but also provided all of us a chance to see the research efforts of our faculty, postdocs, students and staff *in toto*. I know the selection of best posters must have been difficult for the judges. The quality of the presentations was very high, and I found myself drawn to several in areas outside my own research focus that were really interesting and readily understandable to non-experts. Again the kudos for organizing and executing the event go to our Graduate Students and staff, who did an outstanding job as always. Congratulations to one and all!

While on the subject of the Graduate Program, at our last faculty meetings we addressed issues relevant to the imperative need to overhaul the funding paradigm for the Graduate Programs in general, and our own in particular. As you know, our

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faculty and students, working with our alumni, have been developing endowed funding opportunities for scholarships for our students. While we have been very successful, the need to provide competitive stipends and cover ever-increasing tuition costs outpace even these efforts. Clearly it is necessary to address the issue by working together with the School of Medicine to have a Graduate Program that can impact our educational mission and accomplish our expressed institutional goal of increasing both the excellence of our research efforts as well as the funding required to fulfill those goals. I would encourage our faculty who wish to address this issue to feel free to contact the Research Advisory Task Force (Tetsuo Ashizawa, Chair) and/or the Faculty Senate (Thomas Albrecht, Chair). Another alternative is to contact Lillian Chan and/or Wayne Bolen, who can integrate your views with those of other faculty.

Before leaving this topic, please consider making a substantial

contribution to the Mariann Blum Scholarship Fund. The Fund is growing, thanks to contributions from the family and friends of the late Mariann Blum, one of our more accomplished graduates.

We are receiving very good applications for the tenure-track faculty positions open in BMB. We are expanding the area of research emphasis to include aspects of noncoding and micro RNA synthesis, metabolism, and involvement in pathogenesis and relevant interventions in trauma and disease. If you know of likely candidates, please suggest them to Werner Braun, Chair of this year's Recruitment Committee.

Congratulations to Lillian Chan, the Director of our Graduate Program. We are very proud of her having been awarded the Mary and J. Palmer Saunders Professorship for Excellence in Teaching.

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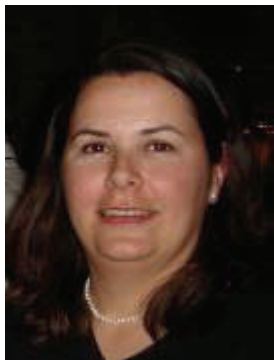
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## IN MEMORIAM - Deborah Greer



As you all know, we lost one of our excellent Research Associates, Debi Greer, in a tragic car accident. Debi came to our department a little over 5 years back. She was very helpful and friendly not only to her co-workers in the lab, but throughout the department, and she had many friends on campus. Debi's contributions to our research endeavor will always be remembered by all of us, and we will think of her fondly. Her coming to the lab dancing from the 6<sup>th</sup> floor elevator with a 5 year pin and singing "I am special.....I am special" is one special memory. We will miss her, and the lab feels empty without her. May God grant her peace in heaven.

-Dr. Satish Srivastava

## Awards and Announcements

[Dr. Kathleen O'Connor](#) was awarded the Graduate Student Organization Faculty Award for Student Advocacy. This award is presented annually to a faculty member who has repeatedly demonstrated concern for student's rights and issues and has acted on behalf of the student body.

[Dr. Lillian Chan](#) was awarded the Mary and J. Palmer Saunders Professorship for Excellence in Teaching. This award is presented to a faculty member in recognition of excellence in teaching and mentoring of students and postdoctoral fellows.

### October Seminars

October 17, **Wednesday**

**"Signaling at the Membrane: Concepts and Consequences"**

Anne Hilderliter, Ph.D.  
University of Minnesota, Duluth Campus  
Department of Chemistry and Biochemistry  
1039 University Drive  
Duluth, MN 55812-3020

October 18 , **Thursday**

**"BRAF Mutation in Papillary Thyroid Cancer: a Molecular Pathway to Clinic"**

Michael Mingzhao Xing, M.D., Ph.D.  
Associate Professor of Medicine and  
Oncology division of Endocrinology and Metabolism  
The John Hopkins University School of Medicine  
Baltimore, MD 21287



## Graduate Program News

On behalf of the BMB Program, we'd like to thank Dr. Perez-Polo for the continued and generous support of the numerous activities made possible by our Program. Our recent BMB Orientation was a tremendous success with 48 posters and a fantastic dinner served by the Bistro LeCroy. This year we were quite lucky to have David and Lisa Volk and Theron Pfeifer providing excellent music and singing. The feedback from the incoming new students has been extremely positive and our Orientation Committee, comprised of Drs. Sarita Sastry and Stan Watowich, Suzanne Tomlinson, Sergio Santa Maria, Julie Hou, Raghav Kulasegaran, Rodrigo Diaz, Anu Roychowdhury, Scott Silva, and Brian Tieu, deserves the credit for another successful event.

### The winners for the student posters were:

1<sup>st</sup> place - Debashish Sahu

Runners-up - Suzanne Tomlinson and Paul Evans

**BBSC Student Choice winner** - Diana Ferrari and Sai Gandham

### The winners for the post doc posters were:

1<sup>st</sup> place - Steven Whitten

Runners-up: Jenny Gu and Luis Holthauzen

We'd like to give a hearty congratulation to Vincent Dimayuga, of the Papaconstantinou laboratory, for being awarded a predoctoral trainee through the NIEHS Environmental Toxicology Training Program. Congratulations are also in order for Kerry Fuson and Travis Schrank for renewal of their HAMBIP fellowship awards.

We also want to recognize an outstanding Program faculty member. [Dr. Kathleen O'Connor](#) was awarded the Graduate Student Organization Faculty Award for Student Advocacy. This award is presented annually to a faculty member who has repeatedly demonstrated concern for student's rights and issues and has acted on behalf of the student body.

Also in this fall's UTMB Magazine, Drs. Deepak Srivastava, Naseem Ansari and Yogesh Awasthi have a long article entitled "Solving a medical mystery".

-Debora Botting, Graduate Program Coordinator

## BCSO News

BCSO had the annual [Summer BBQ](#) at Andy Chen's place. It was a perfect atmosphere to mingle, meet and exchange recipes with other students, post-docs and faculty. Our last student social gathering was at Molly's on September 13th 2007, on the evening of the BCSO meeting. We plan on having a similar gathering after every meeting. Talking to the energetic first year students from the BBSC and BSCB programs was refreshing and fun.



### Upcoming Events:

- ✦ The BCSO Student/Faculty Bowling Night on October 24th. So that we may have as many faculty as possible we would like to start as early as 5:30 pm. Feel free to invite a faculty member from the program to play with or against.
- ✦ The spooky Halloween Costume party at our beloved program secretary Debora Botting's ranch on the 27<sup>th</sup> of October.
- ✦ The Houston Rockets vs. Phoenix Suns at the Toyota Center on Saturday, November 17th at 7:30pm.

We would like to remind the students to start thinking about new speakers for our "Pioneering Biological Discovery" seminar series. Our last speaker, Dr. Isiah Fidler, gave an extremely entertaining and thought-provoking seminar on cancer metastasis. Our next speaker is Dr. George Somero from Stanford University and the seminar is on November 15, 2007.

If you need more details on these events or have ideas for more, do come to the [next BCSO meeting on Thursday, October 16, 2007 from 12:00-1:00pm in BSB 2.240.](#)

- Keerthi Gottipati

## RESEARCH SPOTLIGHT: SCSB Crystallization Robotics

### SCSB Crystallization Robotics: Automating the protein crystal growth process



With generous support from the Department of Biochemistry and Molecular Biology and from the Department of Neuroscience and Cell Biology, the Sealy Center for Structural Biology and Molecular Biophysics (SCSB) has recently acquired a Rigaku CrystalMation system. This is a fully integrated platform for protein crystallization, automating each step from custom screen making to crystallization trial imaging and analysis. The Robotics crystallization system consists of three independent instruments: The PHOENIX, the Alchemist II, and the Desktop MINSTRAL, integrated through the CrystalTrak crystallization database software program. This system was installed in mid August and has seen heavy use in the first months of operation.

One key advantage of this integrated automation is the ability to share data quickly and to recall information with ease at a later date. Students and researchers can easily provide data to their mentor or collaborators as a simple web URL. In addition to using standardized crystal trial screens, the system offers an extremely flexible liquid handling robot which can explore more dimensions of crystallization space than one would attempt when manually creating crystallization solutions. The software also greatly simplifies the optimization of successful experimental trials with a "one-button" optimization function. This easy optimization is only possible due to the integration offered by the CrystalTrak database software. The PHOENIX crystallization robot is a user-friendly high-speed crystal tray dispenser offering high-accuracy in small drop sizes. The ability to screen using one-tenth the amount of protein as used in a typical hand-pipetted trial not only saves protein, but also permits crystallization of proteins that are difficult to express and yield only limited amounts.

Please contact Dr. Mark White for further information about the robots at [white@xray.utmb.edu](mailto:white@xray.utmb.edu)

### CrystalMation™: Protein crystal growth automation process

Rigaku's CrystalMation is a fully integrated platform for protein crystallization, automating each step from custom screen making to crystallization trial imaging and analysis. Due to its modular design, CrystalMation can be configured to meet a wide range of requirements and grow with our needs. Each of the innovative workstations is available as a stand-alone instrument or in combination with one or more additional components.

CrystalMation, consisting of crystallization screen creation, plate setup, reservoir and protein dispense, plate storage and handling, image inspection and scoring, one-click optimization and software applications for experiment management, streamlines the crystallization process and offers UTMB researchers a complete solution from protein to crystal.

Automation makes sampling of larger and finer crystallization space possible. While the batch load with seamlessly integrated robots that are connected through a central database server offers a true performance of a high-throughput crystallization pipeline without user intervention, experiments can be run independently and manually on each individual robot, allowing the parameters to be finely tuned to resolve difficult cases. CrystalMation allows users the capability to design and launch experiments on the fly that are subsequently tracked by our featured crystallization database software, [CrystalTrak](#). The hits can then be identified for harvesting or follow-up.

Large scale, systematic and functional tests performed on the robotic systems indicate reproducibility and efficiency of crystal growth as well as new hit generation. In addition, liquid dispensing is consistent and reproducible, even at low volumes and a high drop-on-drop rate is consistently achieved. Inspections of all plates are completed within individually specified schedules and automatically ranked and stored in the database.

### Alchemist™ II screen making system

The Alchemist II liquid handling system provides researchers an ultimate solution to set up a wide range of coarse and fine screens for high-throughput crystallography, carrying out the repetitive and time-consuming liquid dispense task based on a given recipe.

The Alchemist II, coupled with [CrystalTrak™](#) software, enables the creation of crystallization screens simply and

## RESEARCH SPOTLIGHT: SCSB Crystallization Robotics (cont.)

easily, allowing the setup of any type of gradient and then performing all the calculations and pipetting automatically. The screen making process is simplified because the Alchemist II's unique BirdFeeder™ technology provides simple stock management and non-contact automated dispensing while eliminating the maintenance hassles associated with pumps, wash cycles and tubing. The optimized liquid classes along with the novel tapping technique enable a wide range of chemical stocks from viscous to volatile to be dispensed precisely and accurately.

The efficiency of crystallization trials is increased while allowing the screens that yield crystals to be stored and reused. An optimization screen on a 96-well-formatted deep well block in 1.5 ml can be set up in under 30 minutes. The Alchemist II deck can hold up to 74 BirdFeeders with each containing a unique chemical stock, which renders the capability of making most commonly used coarse screens. Multiple sizes of BirdFeeder and syringe render the capability of dispensing solutions in wide volume ranges from 1 µl to 10 ml with a CV of less than 2%. The barcode tracking of BirdFeeders and the Alchemist II deck position further reduce the otherwise human error on stock usage.

### Phoenix™ RE: Protein dispense system

The Phoenix RE (Rigaku Edition) liquid handling robot is a modified Art Robbins Instruments Phoenix liquid handler employed with a number of Rigaku innovations for integration with other crystallization robotics and software. The system couples a low-volume non-contact liquid dispense unit with a 96-channel dispense head to rapidly make sitting drop crystallization plates. The Phoenix RE sets up complete crystallization plates, from reservoir filling to drop setting.

The syringe head of the Phoenix RE can dispense from 100 nL to 100 µl. Each syringe uses a flexible nitinol needle that can bend without damage. The highly accurate non-contact head dispenses volumes down to 100 nL and works without system liquid, allowing complete recovery of any unused protein. Both heads will dispense their minimum volumes with less than 5% variation. The Phoenix RE excels at high-throughput, low-volume protein crystallization plate experiment production.

### Desktop Minstrel™: Crystal imaging for protein crystallography

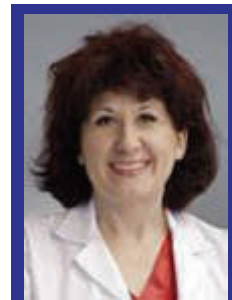
Designed to fit on a lab bench the Desktop Minstrel system automatically images crystallization experiments and links images with crystallization conditions. The data is captured in [CrystalTrak™](#), a complete virtual crystallization laboratory, which provides a chemical and crystallization database, data analysis tools, and methods for easily designing optimization and initial crystallization screens. CrystalTrak provides a simple, yet powerful interface, for viewing images and conditions for evaluation and scoring. Additionally, CrystalTrak Web uses web browser technologies to provide remote viewing over the web or across other platforms used by SCSB members such as LINUX, Mac/OS, or even Windows.

Using a high-resolution imaging system that can visualize hanging drop, sitting drop, microbatch, and free interface diffusion experiments across most commercially available plate types, the Desktop Minstrel combined with the CrystalTrack database facilitates scoring and reporting, as well as experimental design and project management.

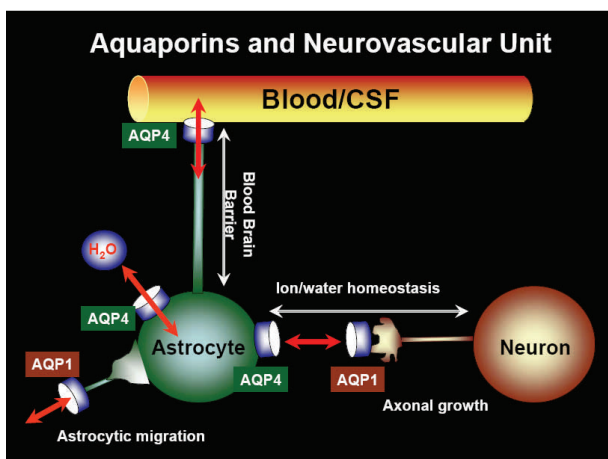


## Faculty Focus: Olivera Nestic-Taylor, Ph.D., Assistant Professor, BMB

*A graduate of the University of Belgrade, Yugoslavia, Dr. Nestic studied in Canada and Germany before coming to UTMB in 1999. She has participated in numerous studies with Dr. Regino Perez-Polo and other neurotrauma researchers at UTMB and abroad. She was appointed to the position of Assistant Professor, Biochemistry and Molecular Biology in September 2007.*



My long-term goal is to study the interaction between neurons, glial cells, blood and cerebrospinal fluid (CSF) within a so-called “neurovascular unit” in the injured, diseased or aged central nervous system (CNS). The term “neurovascular unit” has only recently been coined and reflects the growing recognition that only an integrative approach will result in clinically relevant insights into different conditions of diseased or injured brain or spinal cord. The consequences of neurodegeneration due to CNS injury, disease or aging are devastating, but the few currently available treatments are only partially effective. Therefore a tremendous need exists for identifying new treatments, which will be discovered only through an integrative approach to investigate novel aspects of these pathologies .



One aspect of those interactions that has been largely neglected, in spite of its obvious scientific and clinical significance, is a possible disturbance of osmolite/water homeostasis in diseased, aged or injured brain and spinal cord. Any significant aberration in ion/water homeostasis within CNS usually results in serious, untreatable conditions. The most obvious include brain edema, the main cause of morbidity in brain injury or stroke, and the formation of fluid-filled cysts (syringomyelia), which is the most serious complication in spinal cord injury patients and

responds poorly to currently available treatments. Our data, however, suggest that impaired ion/water homeostasis may contribute to other devastating consequences of brain or spinal cord injury, such as chronic, untreatable pain, a novel finding.

My current research focuses on the role of water channels, or **aquaporins** (AQP), in regulating ion/water homeostasis in normal and injured spinal cords and in normal and injured neonatal brains. Two out of the thirteen identified mammalian aquaporins, AQP-1 and AQP-4, are expressed in different cells in the CNS, but their roles in neuropathological conditions are poorly understood. Our studies implicate astrocytic AQP-4 as the key AQP in the regulation of isotonicity and maintenance of ion/water homeostasis in spinal cords, and we have shown that some pathological conditions after SCI results from dysfunctional AQP-4. However, recent data from our and other labs suggest that **aquaporins are more than just water channels**. For example, our recent findings suggest that AQP-1-mediated water transport may have a novel

role - in axonal growth. AQP-1 may therefore have an important function in excessive axonal sprouting after SCI and so cause underlying development of pain or autonomic dysreflexia - two devastating and as yet untreatable complications after SCI. We are currently following three lines of research: (1) dissecting the intracellular pathways involved in mediating the role of AQP-1 in axonal growth; (2) characterizing crosstalk between AQP-4 and AQP-1; and (3) identifying interventions targeting AQP-1 and AQP-4 in spinal cord or brain injury.

Selected articles (2005-2007):

1. **Nesic-Taylor, O.**, Cittelley D., Ye Z., Xu G-Y., Unabia G., Lee J.C., Svrakic N.M., Liu X-H., Youle R.J., Wood T.G., McAdoo D., Westlund K.N., Hulsebosch C.E., & Perez-Polo J.R. Exogenous Bcl-x<sub>L</sub> fusion protein spares neurons after spinal cord injury. *J. Neurosci. Res.*, 79(5):628-37, 2005.
2. Hu X, **Nesic-Taylor O**, Qiu J, Rea, HC, Fabian R, Rassin DK, Perez-Polo JR. Activation of Nuclear Factor-kB signaling pathway by Interleukin-1 after hypoxia/ischemia in neonatal rat hippocampus and cortex. *J. Neurochem.* 93:26-27, 2005.
3. **Nesic O.**, Lee, J, Johnson KM Ye Z., Xu G-Y, Unabia GC, Wood TG, McAdoo, DJ, Westlund KN, Hulsebosch CE & Perez-Polo JR. Transcriptional profiling of spinal cord injury-induced central neuropathic pain. *J. Neurochem.*, 95 (4):998-1014, 2005.
4. **Nesic O.**, et al. Acute and chronic changes in aquaporin 4 expression after spinal cord injury. *Neuroscience.* 2006 Dec 13;143(3):779-92.2006.
5. Cittelley, D., **Nesic, O.** and Perez-Polo, J.R. Phosphorylation of Bcl-x<sub>L</sub> after spinal cord injury. *J. Neurosci. Res.* Accepted for publication. 2007.
6. Cittelley, D., **Nesic, O.** and Perez-Polo, J.R. Detrimental effects of anti-apoptotic treatments in spinal cord injury. *Exp. Neurology.* Accepted for publication. 2007.
7. **Nesic et al.**, Novel AQP-1 roles in Spinal Cord Injury. *J. Neurotrauma.* Submitted.

## Publications & Grant Awards

Zhang B, Luo S, Dong XP, Zhang X, **Liu C**, Luo Z, Xiong WC and Mei L. Beta-catenin regulates AChR clustering in muscle cells through interaction with rapsyn. *Journal of Neuroscience* 27: 3968-3973, 2007

Evans PM, Zhang W, Chen X, Yang J, Bhakat K and **Liu C**. Krüppel-like factor 4 is acetylated by p300 and regulates gene transcription via modulation of histone acetylation. *J Biol Chem* [Epub ahead of print].

Das S, Chattopadhyay R, **Bhakat KK**, Boldogh I, Kohno K, Prasad R, Wilson SH, **Hazra TK**. 2007. Stimulation of NEIL2-mediated oxidized base excision repair via YB-1 interaction during oxidative stress. *J. Biol. Chem.* **282**: 28474-84

### Grants:

**Dr. G.A. Shakeel Ansari**, Ph.D. received an NIH grant titled "Hepatic Steatosis and the Lipid Metabolome". Budget period 09/30/07-8/31/12. Total direct cost \$1,125,000.

**Dr. David Gorenstein** has been awarded an R01 multi-investigator grant, in the Bioengineering Research Partnership format, by the National Cancer Institute along with co-PIs Prof. Fredika Robertson of MD Anderson and Mauro Ferrari, Ph.D. of the University of Texas Health Science Center at Houston. The title is "Nanovectors for the characterization and destruction of breast cancer vasculature".

*To have your publication or award included in the monthly newsletter, please send the information directly to Lisa Pipper (lpipper@utmb.edu) by the 1st of each month.*

## Administrator's Notes

### Upcoming Fire Safety Inspection by the State

A team of state fire inspectors is coming to UTMB and will be focusing on research buildings. This effort was instituted as a result of a serious lab fire that occurred in the Chemistry Building at UT Austin. Environmental Health and Safety will be providing faculty and lab personnel with instructions for making sure that labs meet fire safety standards. If serious violations are found, the inspectors can order the building to be shut down, so we ask everyone to review lab conditions carefully and address any issues as soon as possible. **There will be no advance notice of the dates of the inspectors' visit.**

### New Rates for Reimbursement of Travel Expenses

New rates became effective on October 1. The mileage reimbursement rate is now 48.5 cents a mile (with certain restrictions.) The new rates are on the [travel website](#).

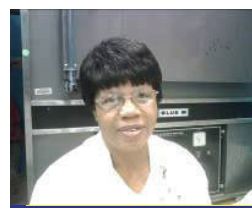
### Unused and Under-utilized Computers

Now that the Department is responsible for acquiring, assigning, and maintaining supported computers, the IT Task Force is developing recommendations for appropriate and cost-effective ways of managing computers the Department pays for. To allow existing resources to be utilized as efficiently as possible, the Task Force is asking faculty and staff to assess existing equipment and identify any computers that are not being used and could be "re-deployed" to fill a current need. In addition, the Task Force asks Department members to consider whether any high-capacity computers are currently dedicated to tasks requiring minimal capability – for example, running a single instrument. These might be "swapped-out" for computers that are less advanced but still entirely capable of meeting the operating requirements, allowing the higher-capacity computers to be used in areas with more complex computing needs. Information about computers that could be used in other areas can be provided to Lisa Pippier. Lisa can also help with assessment of current computing needs if there is uncertainty about specific requirements.

- Marianne

## Congratulations and Best Wishes to Martha Harris and Betty Johnson

**Martha Harris**, Lab Tech Assistant I, is retiring from UTMB on October 31, 2007. In her 23 years here, Martha has assisted many research groups with cleaning of glassware and sterilization of the groups' "dishes", and she's seen several autoclaves come and go. She has been an important part of the support services that contribute to the fulfillment of the Department's research mission. We wish her the best as she turns her attention to being with her family and visiting her former home of Shreveport, LA.



**Betty Johnson** has embarked upon Retirement: Round 2. Betty's official retirement from UTMB was marked on February 28, 2001. But after having a month off for good behavior, Betty continued working three days a week in the critical role of Lab Supervisor for the Thompson group. She has worked on countless grant proposals and has helped a long line of graduate students and post-docs achieve success in their research projects. Betty has decided that she now wants to shift her focus to travel and other interests. The 5<sup>th</sup> Floor of MRB is not the same without her, and the Department salutes her for all her efforts during 33 years of dedicated and highly professional service.





**Featured Abstract by BMB Faculty****Aldose reductase inhibition prevents endotoxin-induced uveitis in rats.**

[Yadav UC](#), [Srivastava SK](#), [Ramana KV](#).

Department of Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, Texas.

**PURPOSE:** The purpose of the present study was to elucidate the role of the polyol pathway enzyme aldose reductase (AR) in the mediation of ocular inflammation in a rat model of endotoxin-induced uveitis (EIU). **METHODS:** EIU was induced by a subcutaneous injection of 200 mug lipopolysaccharide (LPS) in male Lewis rats treated with the AR inhibitor, zopolrestat (25 mg/kg body weight, intraperitoneally) or its carrier. The rats were killed 24 hours after LPS injection, the eyes were enucleated immediately, and aqueous humor (AqH) was collected. The number of infiltrating cells, protein concentration, and levels of nitric oxide (NO), tumor necrosis factor (TNF)-alpha, and prostaglandin E(2) (PGE(2)) in the AqH were determined. Immunohistochemical analysis was performed in paraformaldehyde-fixed eye sections by staining with antibodies against iNOS, COX-2, TNF-alpha, NF-kappaB, and AR. The levels of reactive oxygen species (ROS) in rat eye sections were determined by dihydroethidium (hydroethidine) fluorescence staining. **RESULTS:** In the EIU rat eye AqH, both the number of infiltrating cells and protein concentrations of the inflammatory markers, TNF-alpha, NO, and PGE(2) were significantly higher than in the control rats, and inhibition of AR by zopolrestat suppressed the LPS-induced increases. The LPS-induced increased expression of AR, TNF-alpha, iNOS, and COX-2 proteins in the ciliary body, corneal epithelium, and retinal wall was also significantly inhibited by zopolrestat. Furthermore, AR inhibition prevented the LPS-induced increased levels of ROS and activation of NF-kappaB in the ciliary body, corneal epithelium, and retinal wall of the rat eye. AR inhibition also prevented the LPS-induced activation of NF-kappaB and expression of COX-2 and iNOS in the human monocyte cell line U-937. **CONCLUSIONS:** The results indicate that AR inhibition suppresses the inflammation in EIU by blocking the expression and release of inflammatory markers in ocular tissues, along with the attenuation of NF-kappaB activation. This finding suggests that AR inhibition could be a novel therapeutic target for the treatment of uveitis and associated ocular inflammation.

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Research Coordinator's Corner  
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