

A [Dinner] Meeting of the Minds

On the evening of January 14, 2017, Tsunami Owner and Chef Ben Smith and his assistant are busily prepping dinner for an intimate dinner party. The smell of sweet chili sauce and lamb fills the home of Dr. and Mrs. Steven R. Goodman. The dinner is being hosted in honor of Israeli Biochemist and Nobel Laureate Dr. Aaron Ciechanover as part of the UTHSC Vice Chancellor for Research's Distinguished Lecture Series.

Created by UTHSC Vice Chancellor for Research Steven R. Goodman, PhD, the speaker series aims to bring prestigious leaders in the field of biomedical research to the institution so they can share their knowledge and expertise with the university. Invited speakers typically spend two to three days on UTHSC's campus interacting with faculty and administration, and delivering a scientific lecture.

Aaron Ciechanover was born in Haifa, a port city in the northern part of Israel, in October 1947, one month before Israel was recognized by the United Nations as an independent state. Dr. Ciechanover majored in biology at school, and went on to receive his MSc in 1970 and his MD in 1974 from the Hadassah Medical School of the Hebrew University in Jerusalem. After three years military service as a combat physician in the Israel Defense Forces, he joined Avram Hershko's, MD, PhD, laboratory in the Faculty of Medicine at the Technion (Israel Institute of Technology) in Haifa in 1976, where he received his DSc in 1981.

In 2004, Dr. Ciechanover became one of Israel's first Nobel Prize winners in Chemistry for "the discovery of ubiquitin-mediated protein degradation." Together with Dr. Hershko and American biologist Irwin Rose, PhD, the trio was awarded for characterizing the process in our cells which allows for the degradation and recycling of proteins using ubiquitin. Their discoveries have opened up opportunities in drug discovery, and in the diagnostics and treatment for a range of disorders, from cancer to neurodegeneration.

"Since 2016, I have had the honor of welcoming over a dozen prominent investigators ranging in expertise from Sickle Cell Disease to translational genomics and cancer," Dr. Goodman said. "Dr. Ciechanover is a world leader in the field of biochemistry



From left to Right: John Bloch, Sarah Bloch, Cindy Goodman, Steve Goodman, Aaron Ciechanover, Steve Schwab, Carol Schwab, Steve Youngentob, Lisa Youngentob

and a personal friend, and I wanted UTHSC's researchers to have the ability to learn from and interact with him."

It took over eight months of planning by a committee of 20 plus leaders from various areas across UTHSC's campus, St. Jude Children's Research Hospital, the University of Memphis and the Memphis community at large to plan Dr. Ciechanover's four-day visit.

"When I asked Dr. Ciechanover to visit," Dr. Goodman said, "I understood that it would take a team to make his visit a success. I am immensely proud of all the people that dedicated their time and resources to make Dr. Ciechanover's visit happen."

The face of research at UTHSC is changing. While we take pride in being the leading State institution for research on the causes, treatment, and prevention of diseases, we strive to do better and aim to be competitive at the highest levels. Therefore, Dr. Goodman has taken on the audacious task of doubling the research portfolio at UTHSC within the next ten years. The VCR Distinguished Lecture Series demonstrates just one way Dr. Goodman shows his commitment to creating a more robust research environment for UTHSC statewide as outlined in the Operational Strategic Plan for Research. UTHSC was honored to host and learn from one of the world's leading experts in the field of biochemistry.

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A Teamwork Approach



Dr. Ciechanover touring St. Jude Children's Research Hospital
Photo by Peter Barta/St. Jude Children's Research Hospital

"Alone we can do so little; together we can do so much." - Helen Keller

In the last version of *The Research Rainmaker*, Dr. Goodman described several qualities that leaders should possess: honesty, transparency, trust, change catalyst and manager, etc. Notably, he spoke to the idea of leaders having the ability to articulate a clear and sensible vision and chart a path towards shared goals. "We have a shared vision for UTHSC Research stated in the Operational Strategic Plan for Research that is being implemented successfully with the help of faculty-driven Implementation Teams, led by the VCR's Research Cabinet," Dr. Goodman said.

It is not every day that our campus has the honor of hosting such a prestigious scientist and scholar. We wanted to illustrate for Dr. Ciechanover just why and how UTHSC is the leading State institution for research on the causes, treatment, and prevention of diseases. To plan a visit such as this took more

than just a few people in the Office of Research. We called upon leaders from across UTHSC's campus, the University of Memphis, St. Jude and the Memphis community at large. From security to fundraising and sightseeing, our team worked diligently for almost one year to ensure every detail was thoughtfully planned.

During Dr. Ciechanover's visit, he met with university leadership, faculty, staff and students from UTHSC, the University of Memphis and St. Jude. Over 30 faculty researchers, students and postdocs braved the winter weather during Dr. Ciechanover's visit to meet with the Nobel Laureate. He also spent several hours on St. Jude's campus touring the hospital, meeting representatives from their administration and learning from faculty and students about the work they do in the fight against childhood cancer and other life-threatening diseases. It is thanks to the help from key players at St. Jude that this part of Dr. Ciechanover's visit took place.



Photo by Peter Barta/St. Jude Children's Research Hospital

Subscribe to the UTHSC Researchers Listserv!

The Office of Research recently established a new e-mailing list specifically geared toward all research Faculty, Post Docs, and Graduate Students at UTHSC. We plan to use this new method of communication to let the UTHSC research community know of important events, workshops, opportunities, news, etc. that specifically pertains to them.

To subscribe to the Researchers e-mailing list, please visit <http://listserv.uthsc.edu/mailman/listinfo/researchers> and follow the subscription instructions.



Incorporated into Dr. Ciechanover's schedule was a time for him to share his knowledge and expertise through intimate interactions with the local Memphis community. Entitled, "An Intimate Evening with Dr. Aaron Ciechanover" and mirroring Israel's 70 years of existence, the Nobel Laureate hosted a community conversation and open dialogue discussing his life experiences and coming of age alongside the state of Israel while also sharing the challenges and opportunities for growth in the Holy Land. The town hall took place on January 15, 2018 in the Social Hall of the Memphis Jewish Community Center and had over 40 people in attendance. It took a subcommittee of eight people from UTH-SC and across the Memphis community to market and execute this community conversation.

"It was such an honor to be able to listen and learn from Dr. Ciechanover," said Elyan Shor, a PhD student at the University of Memphis. "Hearing personal recounts of his life experiences as a young, Israeli researcher and Jew was fascinating. He was entertaining, engaging and thought-provoking. I am grateful to have had the opportunity to attend this wonderful event."

Using the words of Dr. Ciechanover himself, "no words to thank you for a truly royal, but mostly heart-warming, friendly hospitality. It was just perfect, and the snow made it even better. I enjoyed every moment, and being a vet of hundreds of visits, this one was truly an exception. Please thank on my behalf to all your wonderful people who worked so hard – including our two security guys – to make it such a successful one."

Have a story we should include?

Submissions and ideas can be sent to Sarah Bloch at sabloch@uthsc.edu

Photos Clockwise from Top Left: Dr. Ciechanover at "An Intimate Evening with Dr. Aaron Ciechanover." Top Right: Dr. Ciechanover and Dr. Randy Buddington, Middle Right: Guests at "An Intimate Evening with Dr. Aaron Ciechanover." Bottom Right: Drs. Steve Goodman, Aaron Ciechanover and Lee Schwartzberg

Photos by Joseph Martin/Joseph Martin Photography



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Discovering the Ubiquitin Proteolytic System:

"Biochemistry is the science of life. All our life processes - walking, talking, moving, feeding - are essentially chemical reactions. So biochemistry is actually the chemistry of life, and it's supremely interesting." -Dr. Aaron Ciechanover

At a time when the biomedical world was racing to uncover the secrets surrounding the translation of the information coded by DNA to RNA and proteins, a young Aaron Ciechanover was "falling in love with biology."

Born to Polish immigrants, Aaron and his elder brother Joseph were encouraged to study from an early age, and it was Joseph who bought Aaron his first microscope at the age of 11.

"From early days, I remember my strong inclination towards biology, though it has taken different directions at different times," Dr. Ciechanover said. "I remember collecting flowers on Mount Carmel and drying them in the heavy Babylonian Talmud of my brother. Then came the turtles and the lizards,



Photos by Joseph Martin/Joseph Martin Photography

and extracting chlorophyll from leaves with alcohol. I had a deep feeling that the future somehow resided in biology, in deciphering basic mechanisms, as so little was then known."

Upon graduating high school, Aaron had to make a choice: join the Israeli Defense Force or postpone his service and obtain a university education, particularly in areas that are relevant to the military, such as medicine and different disciplines in engineering



and sciences. He chose medicine in the hopes of one day becoming a practicing physician. However, after a few years of study, Dr. Ciechanover began to question his choice. After switching courses to pursue biochemistry and enrolling the help of a young Dr. Avram Hershko, who had just himself completed his post-doctoral training with Gordon Tomkins at the University of California in San Francisco (UCSF) and was recruited to establish a Unit of Biochemistry at the Technion in Haifa, Dr. Ciechanover immersed himself in the lab. It would not be until November of 1976 when Dr. Ciechanover would officially start his graduate studies with Dr. Hershko.

"At that time, his group focused mostly on studying intracellular proteolysis, and I learnt from him that he had given up on trying to identify the mediator(s) and mechanism(s) involved in serum-induced 'pleiotropic response'. The model system that was chosen to study proteolysis was degradation of abnormal hemoglobin in the reticulocyte which is the terminally differentiating red blood cell. We were looking for a non-lysosomal and energy requiring proteolytic system and the reticulocyte no longer contains lysosomes which are removed during the final stages of its maturation before its release into the circulation."

The researchers assumed that the same mechanism involved in differentiation and maturation of the reticulocyte is also involved in the removal of "naturally occurring" mutant abnormal hemoglobins that are synthesized in different hemoglobinopathies, such as thalassemia and sickle cell anemia, and also in the destruction of the amino acid analogs containing abnormal hemoglobins.

"We wanted to believe and hoped that this mech-

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-anism would turn out to be ‘universal’, and involved in degradation of normal proteins in all cells. Years later this assumption turned out to be correct.”

Ciechanover spent an important part of his graduate studies in the laboratory of Dr. Irwin A. Rose (Ernie), an American biochemist and collaborator of Dr. Hershko’s. In 1975, ubiquitin was discovered but no one knew what the protein did. The collaborative trio decided to uncover the mystery.

“In a breakthrough discovery, we found that the target substrate is covalently modified by multiple moieties of APF-1, a reversible modification that renders the protein substrate susceptible to degradation. This was a novel type of post-translational modification and clearly a new biological paradigm, that the elucidation of which required - as I feel today in retrospect - a different type of knowledge in biology and enzymology, and an original experimental approach. Elucidation of this modification would not have been possible without Ernie’s advice that was based on his immense knowledge in enzymology and protein chemistry, accompanied by his unbiased original thinking and approach to problem resolving. This discovery, along with the discovery in 1980 that APF-1 is ubiquitin, made Ernie and his fellows critically important partners in the historical trail of the discovery of the ubiquitin system.”

The discovery revealed that ubiquitin functions almost like a quality assurance manager. When it is time for a protein to be broken down, a ubiquitin molecule attaches itself to the protein. The tagged protein is then taken to one of many barrel-shaped chambers called proteasomes, a protein complex that digests the protein into smaller pieces. The protein fragments can be recycled and used in the construction of other substances in the cell. An understanding of this process helped researchers understand diseases, like cystic fibrosis, Parkinson’s and many types of cancer, that occur when the process goes awry.

With two fellowships (from the Leukemia Society of America and the Israel Cancer Research Fund), Dr. Ciechanover went on to carry out postgraduate studies under the supervision of Harvey Lodish at MIT. After three years, he returned to Israel to join the faculty of medicine at the Technion where he continued his research with many students, fellows and physicians, and where he is currently a Distinguished Research Professor in the Center for Vascular and Cancer Biology in the Rappaport Faculty of Medicine and Research Institute.

“I was happy to return to Israel, to my family and

friends, to a place I felt I belong. I established my own independent research group and laboratory, obtained extramural competitive funding, and continued my research on the ubiquitin system. I have been lucky to have, along the years, a group of extremely talented graduate students and post-doctoral fellows.”

In 2000, he received the Albert Lasker Award for Basic Medical Research and in 2003 the Israel Prize for Biological Research.

On January 16, 2018 Memphians woke up to a blanket of snow and ice. Even with almost a year of planning under our belts, it’s impossible to plan for everything that can go awry. As mentioned in another article, we had incorporated a visit to St. Jude Children’s Research Hospital into Dr. Ciechanover’s schedule. When we found out UTHSC was under



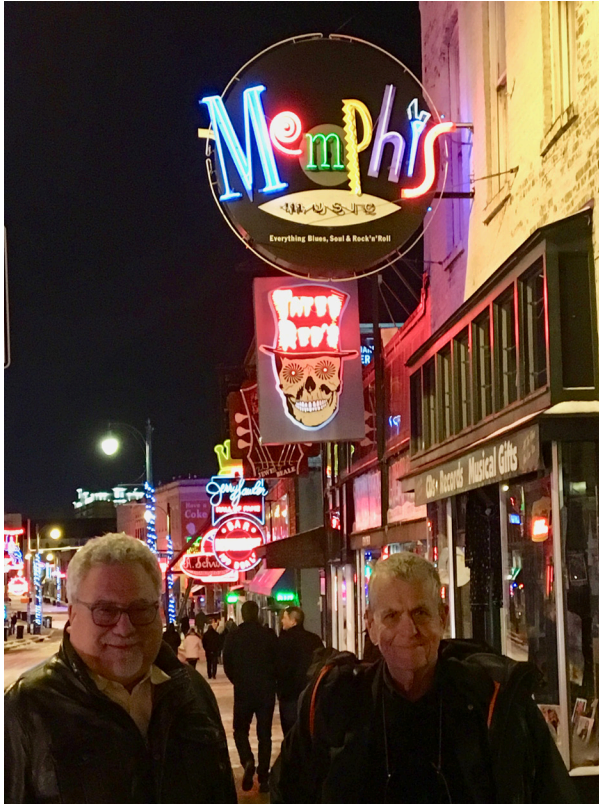
an Administrative Closing we called on St. Jude to be our savior for Dr. Ciechanover’s scientific lecture. They, thanks to a wonderful partnership between our institutions, welcomed us with open arms.

At 3:30pm in the Marlo Thomas Center at St. Jude Dr. Ciechanover delivered a VCR Distinguished Lecture. Entitled, “The Ubiquitin Proteolytic System: From Basic Mechanisms Thru Human Diseases and on to Drug Targeting,” over 150 researchers congregated to hear from the Nobel Laureate. Dr Ciechanover’s address highlighted the timeline of discovery for the ubiquitin pathway, what we knew decades ago about the pathway to where it’s been and where we think it is going.

For those whom could not attend Dr. Ciechanover’s scientific lecture, you can watch a recording here: <https://www.uthsc.edu/research/about/events/distinguished-lecture-series/recorded-lectures.php>. When prompted, please log in using your UT Net-ID and password to view the recording. If you have question, please contact Sarah Bloch at sabloch@uthsc.edu for assistance.

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Home of the Blues, Birthplace of Rock and Roll:
Dr. Ciechanover Explores The Bluff City



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<--- SCAN ME --->

The Snow Days Miracle of Winter 2018 AKA “With a Lot of Help from My Friends” A Message from the Vice Chancellor for Research

A Pictorial Story

A blanket of snow in Memphis closed down UTH-SC January 15th to the 17th. The challenge faced by the Office of Research was that this coincided precisely with our visit from Nobel Laureate and Professor Dr. Aaron Ciechanover. How did wonderful teamwork and dedication turn this challenge into a memorable experience for all involved? I will tell that story with pictures.

Dinner at the Goodman’s on the 14th, included Chancellor Schwab. Aaron receives his tie-dyed Aaron Ciechanover t-shirt. He loved the shirt and his “Blue-Suede Shoes” book given to him by VCR Goodman. Aaron is a big Elvis fan.



Dr. Ciechanover and Chancellor Schwab at Dr. Goodman’s home



Some of the Office of Research Staff, a.k.a. the “No Quit” team



The Graceland tour group including Office of Research Staff, UT Foundation Staff, and UTHSC Faculty

The 15th spent at St. Jude, Graceland and the Memphis Jewish Community Center where Aaron spoke on his life in Israel since the creation of the country.

On the 15th, Steve Goodman called Sarah Bloch with the idea of holding the VCR Distinguished Lecture at an alternative site, should UTHSC again be closed on September 16th. Sarah called Dr. Ryan Potts and the team at St. Jude. By the morning of the 16th when UTHSC had a snow day, St. Jude offered us the Marlo Thomas Auditorium for the VCR Distinguished Lecture. Despite the snow, over 150 researcher were in attendance.



Drs. Ciechanover and Goodman at Graceland

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Dr. Ari VanderWalde who was instrumental in putting together the Graceland tour as well as “An Intimate Evening with Dr. Aaron Ciechanover”

Photo by Joseph Martin/Joseph Martin Photography



Dr. Steve Youngentob, Sr. Associate VC for Research, Mrs. Cindy Goodman behind, and Dr. Lee Schwartzberg to her left at “An Intimate Evening with Dr. Aaron Ciechanover”. All played key roles in putting Dr. Ciechanover’s visit together

Photo by Joseph Martin/Joseph Martin Photography



(Pictured Left to Right): Drs. Junmin Peng, Aaron Ciechanover and Ryan Potts after Dr. Ciechanover’s VCR Distinguished Lecture on Jan. 16th



(Pictured Left to Right): Officer Bobby Bramlett, Dr. Aaron Ciechanover, and Lieutenant Charles Gutelius, a.k.a. the “two security guys,” who assisted us throughout Dr. Ciechanover’s visit



Dr. Aaron Ciechanover delivering his VCR Distinguished Lecture at St. Jude on Jan. 16th to over 150 researchers

“My dear friend Steve,
No words to thank you for a truly royal, but mostly heart-warming, friendly hospitality. It was just perfect and the snow made it even better, I enjoyed every moment, and being a vet of hundreds of visits, this one was truly an exception, much thanks to you, of course.

Say warm hello to Cindy and please thank on my behalf to all your wonderful people who worked so hard – including our two security guys – to make it such a successful one.

Be well, and take a rest today. Enjoy the NBA game. As ever,
Aaron”

-Steven R. Goodman, PhD
Vice Chancellor for Research

