



Forum in Focus

WINTER 2015

President's Letter

Dear Forum Members,

Happy New Year! As I sit here and write this, we are all in the December madness of children's activities, shopping for all the right gifts, attempting to send out a holiday card, attending and throwing holiday parties, programs and pageants, and so much more. Although so difficult to take a moment to reflect during this busy time of year, I'd like to remind you all why we dedicate our time and talents to the Forum.

As President of the Forum, I attended the board meeting of the Texas Biomedical Research Institute. At this meeting, I was able to inform them that the approximately \$316,000 raised by the Forum in 2013-14 was awarded to scientists at Texas Biomedical to assist in developing preliminary data. This data will enable these scientists to secure future funding for projects. In all, eight different pilot studies were funded – three in the fields of the Ebola virus, three in the genetics department (relating to tropical disease and memory processes), and two in the areas of HIV-related research. We should all be very proud of being able to assist these scientists in their truly important and ground-breaking work!

There has been a lot going on at the Forum recently! In early November, **Karen Lee Zachry** graciously opened her home to host a lovely luncheon honoring the past presidents of the Forum. It was a great success! Everyone was thrilled to have so many of the past presidents attend. In addition, everyone was able to get a head-start on their holiday shopping by purchasing one of the luxurious handbags from the Barfield Collection. The Forum thanks **Lisa Kopecky** for her generosity, as she donated a portion of the proceeds back to the Forum.

The Forum is also so grateful to **Julian Gold**, and in particular **Courtney Percy**, for organizing "The Best of Fall" fashion show and luncheon on October 30th. It was



Melissa Morgan

a lovely event, and we were all able to see the new trends for Fall – always inspirational. As always, Julian Gold donated back a portion of the event's proceeds to the Forum. Remember to always shop for a cause!

Thank you to our Special Events Chairs **Julie Dorbandt**, **Jody Lutz** and **Holly Rabinowitz**, for putting on these two great events. They did a beautiful job and made it look effortless!

Coming up on the evening of February 5th, **Tammy Cochran** and **Tracee Feik** will be organizing the Roundtable Discussions at the Argyle. This is always a great event during which we can sit down with various Texas Biomedical scientists and hear from them directly about the innovative and exciting research they are doing right here in San Antonio. Remember to mark your calendars for this event!

Finally, get ready for Las Vegas! No one can forget that the event of the year, the Forum Gala, will take place on May 2, 2015! **Jordan Arriaga**, Gala Chair, **Courtney Percy**, Gala Co-Chair, and **Sara Walker**, Gala Assistant, are busy at work making sure this year's event is better than ever, and I have every confidence that will become true!

As I write this letter, all tables but one are sold out! What a tremendous accomplishment! It just goes to show the excitement for this event, year after year. There are so many people that help make this event a success every year. Remember that you too can help by attending the Gala, purchasing raffle tickets, bidding on the fabulous silent auction items and by supporting the Gala through Gala grants. Each dollar raised by the Gala directly funds Texas Biomedical scientific research pilot studies. I truly cannot think of a better cause.

So, as I wrap up, I hope you all had a wonderful holiday season with your family and friends. Let's hear it for 2015!

Sincerely,

A handwritten signature in cursive that reads "Melissa".

Melissa Morgan

The purpose of the Texas Biomedical Forum is to support the Texas Biomedical Research Institute through community relations, volunteer service and fundraising.

SUCCESSFUL FALL LECTURE LUNCHEON

On November 12, 2014, the Texas Biomedical Forum welcomed former Forum trustee Dr. Julie LaBarba as our featured lecture luncheon speaker. Dr. LaBarba discussed “Real Food for All”, a closer look at what eating local really means and why when it comes to fresh produce, we can’t let perfect be the enemy of good.



As a board certified pediatrician, health consultant and professional volunteer, Dr. LaBarba is passionate about children and nutrition. Having grown up in an Italian produce family, she learned to appreciate real food at an early age. This fostered her professional commitment to children’s nutrition and resulted in her extensive professional training and targeted advocacy for public health education and research.



Dr. LaBarba’s lecture was informative and relevant to all of those striving to maintain healthful living while being a resident of San Antonio and beyond. We enjoyed seeing more than 150 women in the audience and raised \$8,000.00 for the Texas Biomedical Forum.

Please mark your calendar for the Spring lecture luncheon on March 25th at 11:30am.

PAST PRESIDENT’S LUNCHEON

On November 5, the Texas Biomedical Forum past presidents were honored at a luncheon hosted by Karen Lee Zachry, a past president herself. Guests enjoyed a lovely lunch and trunk show featuring Barfield Collection handbags. A portion of proceeds from bags sold at the event will benefit the Texas Biomedical Forum.



A special thank you to Karen Lee Zachry for opening her home and hosting the lovely event. Thanks to all who attended to honor the service of Past Presidents of the Forum.

START SPREADING THE NEWS . . .

Attention Texas Biomedical Forum Members:

Please tell your friends about The Forum and help us increase our membership! Contact Daniela Serna with potential new member information and we will gladly reach out to them and/or remind those that haven’t renewed to do so. It’s easy . . . potential members can visit www.txbiomed.org/forum/membership/initiate-renew-membership, and choose from 3 different levels of membership (\$35 Standard, \$50 Patron or \$100 Benefactor). Upon joining, new members or renewing members will start enjoying the benefits of receiving news and event information regarding our wonderful organization and its cause to support the Texas Biomedical Research Institute. Texas Biomed is such a unique place in our City of San Antonio, and we would love to spread the word about the important research it undertakes. Please help us enroll more members. Your efforts are very much appreciated!

FLY ME TO THE MOON . . . LET ME PLAY AMONG THE STARS

Join us for a dreamlike night in “Fabulous Las Vegas” at The Argyle, and enjoy the surprises in store for you! Put on your sparkles, come sip champagne or martinis and enjoy fine cuisine, all while providing funding for the pilot studies at the Texas Biomedical Research Institute!

This year’s theme was unveiled at the 2015 Gala Committee kick-off meeting on Wednesday, September 17, 2014 at The Argyle. Corbett Christie of Texas Biomedical Research Institute encouraged us to continue our Gala efforts with a reminder of how our efforts truly benefit Texas Biomed. Everyone in attendance was excited and gave great feedback to make this year’s Gala yet another success! Jordan Worth Arriaga and Courtney Percy, Gala Co-Chairs and Sara Walker, Gala Assistant, are truly grateful for all of the hard work already put into this very special event in our community. Thank you volunteers!

We are very excited to announce that we are almost sold out! All of the tables inside the Argyle have been sold, so we have opened up table seating on the patio outside the Coates Room to increase capacity. This is a lovely, paved patio with a private bar and coolers to keep your guests comfortable. Sheila Mayfield, Table Sales Chair, once again has taken her role and gone above and beyond. She is an amazing volunteer! Table sponsorship letters were promptly mailed, and the sales were quickly made. However, it’s not too late to experience Fabulous Las Vegas. The ticket sales for our well-renowned After Party are available online.

Another truly exceptional report involves the Forum Grant donations: we have received over \$29,600.00 in grants to date and are on track to achieve and surpass our \$50,000 goal. Shalimar Wallis, Grants Chair sent out timely Grants Donation letters and kicked off this effort at the November 7th Fall Lecture Luncheon. Several attendees at the luncheon, as well as the San Antonio community have generously supported the Forum Grants effort thus far.

As we get closer to the party, we want everyone to remember that our efforts to make this event successful benefit a great cause. Gala proceeds directly impact and fund the pilot studies for the great scientists at the Texas Biomed. The Institute is a unique and special place that calls San Antonio home. We hope you too will consider making a donation that directly supports the Institute’s research efforts.

For more information on the 2015 Gala, please visit www.txbiomed.org/forum.

STUDENT TOURS

Student Tours are a fantastic opportunity for area high school students, and a rewarding experience for Forum volunteers!

Each year the Forum facilitates an in depth tour of the Texas Biomedical Research Institute for several advanced placement biology and chemistry classes in San Antonio and the surrounding areas.

Student and Forum tour volunteers will be treated to lectures from scientists in the Department of Virology and Immunology and the Department of Genetics, as well as to staff guided tours of the A&T Genomics Computing Center, the suit room of the Biosafety Level 4 containment laboratory, and the Southwest National Primate Research Center.”

All Forum members are encouraged to attend at least one student tour. Tours will be given Tuesdays from 9:30 to 11:30 am on the following dates:

Spring 2015

Jan. 27th – Randolph Field High School
Feb. 3rd – Homes High School
Feb. 10th – La Vernia High School
Feb. 17th – Sandra Day O’Connor High School

FOUNDER’S COUNCIL

The Forum would like to congratulate Founder’s Council on their 2014 scientific equipment grants amounting to \$68,548.83! Founder’s Council, a group of more than 300 young professionals, promotes awareness of the work going on at Texas Biomed. They host three lecture luncheons and a seated dinner for their members at The Argyle as well as other events each year.

To find out more about this organization go to www.txbiomed/joinfc.

JULIAN GOLD FALL FASHION SHOW

Julian Gold graciously hosted a Fall fashion show and luncheon in-store honoring the Forum on October 30th. The event featured DL1961 and their “perfect fitting jeans” as well as highlights from other beautiful designer collections. The event was a huge success with Julian Gold donating \$3000.00, a generous contribution from DL1961 and \$500.00 in raffle tickets sold! Thank you to Julian Gold for your contribution and your continued support to make this annual event such a success!



Roundtable Discussions

Thursday, February 5, 2015

6:00 pm to 7:30 pm

The Argyle

Please save the date for our annual Roundtable Discussions on February 5, 2015. This event is hosted by the Texas Biomedical Research Institute Forum specifically for the education of Forum members and their guests. The evening will include engaging conversations with the Institute’s top researchers along with wine and hors d’oeuvres. Please join us to learn more about what your involvement and donations are supporting at this amazing institution in our community. Invitations to follow soon for this exciting evening!

GRANTS AWARDED TO SCIENTISTS

The forum awarded nearly \$316,000 in grants to scientists at Texas Biomedical Research Institute to assist in developing preliminary data that will enable these scientists to secure future funding for projects. The following projects were funded in 2014:

Manu Anantpadma	Virology & Immunology Department	Novel macropinocytosis inhibitors as broad spectrum anti-filovirals: After screening a library of more than 350,000 molecules for inhibitors of Filovirus entry and identifying two new compounds that inhibit both Ebola virus and Marburg virus, this study aims to analyze and further understand how these compounds work.
Tim Anderson	Genetics Department	Genomic Analysis of Schistosome Hybridization: The focus of the grant is to develop and validate methodology for efficient measurement of the extent of inter-species genetic hybridization in blood flukes causing the widespread tropical disease Schistosomiasis. The parasite Schistosome haematobium is the cause of severe urogenital disease in 117 million people in Africa with about 150,000 people estimated to die each year.

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GRANTS
(Continued from Page 4)

Yasuteru Sakurai	Virology & Immunology Department	Characterization of the Role of an Endosomal Calcium Channel TPC2 in Ebolavirus Infection: Information generated from this study seeks to contribute to better understanding the overall mechanisms of Ebola virus infection and also to defining an effective target of antiviral drugs.
Andrew Hayhurst	Virology & Immunology Department	Mapping and modulating specificity of a partially cross-reactive Ebola virus nanobody: Dr. Hayhurst's team has discovered a phenomenon that has the potential to overcome the sensitivity and viral mutation issues present that have thus far prohibited the development of simple field tests for diagnosis of Ebola virus disease. By understanding and sensitizing the test, scientists will be able to develop a reliable and sensitive test capable of detecting all of the Ebola species known and potentially those yet to emerge.
Melanie Carless	Genetics Department	Development of a Rapid Screening Technology for the Identification of miRNA-mRNA Interactions: miRNAs are naturally occurring small molecules that regulate genes on a global scale. Scientists have identified several miRNAs that may be involved in memory processes that underlie many psychiatric and neurological disorders. Data generated from this experiment will be used to identify genes that may be involved in memory processes and attempt to identify biological pathways that could be important for psychiatric and neurological disorders.
Frederic Chevalier & Winka Le Clec'h	Genetics Department	The Microbiome of the Schistosome Snail Host: study aims to characterize the microbiome of several populations of Biomphalaria snails currently maintained in our laboratories and to examining the interactions between Microbiome and Schistosome parasites. Data generated will be used in future funding requests to the NIH and Bill & Melinda Gates Foundation.
Luis Giavedoni	Virology & Immunology Department	Understanding natural resistance of baboons against SIV to assist development of new anti-HIV treatments: The goal of the study is to identify gene products (proteins) in baboons that help them overcome SIV infection, which is the equivalent to HIV infection in humans. Data from the study will help researchers apply for future funding to continue and confirm the work done in nonhuman primates, a critical step in the research process.
Ruth Ruprecht	Virology & Immunology Department	Novel Molecular Strategy to Target AIDS Vaccines to Lymph Nodes Draining Mucosal Barriers: Joint study will target AIDS vaccines to lymph nodes close to mucosal sites in an effort to generate a special set of virus-specific T-killer cells that will stay in the mucosal tissues and attack virus-infected cells, eliminate them and prevent the spread of the virus. This approach has been shown effective in a small animal model and has potential to yield a safe, potent and effective vaccine that will protect against mucosal transmission of HIV.



Mymetics' promising HIV vaccine candidate obtains funding to begin study at Texas Biomedical Research Institute

Epalinges, Switzerland, 29 September 2014 – Mymetics Corporation (OTCQB: MYMX), a pioneer in the research and development of virosome-based vaccines to prevent transmission of human infectious diseases across mucosal membranes, announced today that its innovative HIV vaccine candidate will enter a new preclinical trial to confirm excellent results obtained in a previous trial.

Research to be funded by the Bill & Melinda Gates Foundation

The study will be led by Dr. Ruth Ruprecht, Scientist & Director of the Texas Biomed AIDS Research Program.

This new study follows a successfully completed smaller study at the Institute of Laboratory Animal Science (ILAS) in Beijing, China in which a two-component vaccine protected all monkeys against repeated AIDS virus exposures from persistent infection – an unprecedented result.¹ One of the vaccine components further showed a strong safety and tolerance profile in a Phase I clinical trial in human volunteers.²



Dr. Ruth Ruprecht

Dr. Ruth Ruprecht said, “Mymetics’ HIV vaccine candidate is unique in its design. First, it uses building blocks from a special part of the HIV envelope protein, called gp41, and second, it was engineered to stop HIV from crossing the mucosal barriers – with promising initial results. We are extremely proud that this study is to be funded by the Bill & Melinda Gates Foundation. We hope to confirm the previous findings and learn more about this vaccine’s mechanism of action in providing mucosal protection.”

Ronald Kempers, CEO of Mymetics, commented, “We are very honored and pleased about our collaboration with Dr. Ruth Ruprecht, a leading expert in the HIV field. This collaboration and funding represents an important milestone and recognition of the work performed by the Mymetics team and partners over the last years and

provides a basis to further develop our HIV vaccine candidate.”

He added: “After the signing of the license and collaboration agreement earlier this year for our Respiratory Syncytial Virus vaccine candidate which is funded by Astellas Pharma, this new funding and collaboration for our HIV vaccine candidate is another confirmation that we are on the right track and are building a strong foundation for success with the right partners.”

New trial to begin October 2014

With its HIV-1 (human immunodeficiency virus type 1) vaccine candidate, produced through its proprietary virosome technology and judicious antigen design, Mymetics aims to provide both a first line of defense through mucosal protection as well as a second line of defense against infection through the generation of blood antibodies. The new trial, to begin in October 2014, will involve 36 rhesus monkeys (n=12 per group) and compare two antigen vaccination regimens with placebo, followed by intra-vaginal challenges with live virus that carries an envelope that differs from the one in the vaccine preparation. Results are expected at the end of 2015.

About HIV and the Mymetics vaccine approach

2.3 million new people were infected by HIV in 2012 while an estimated 1.6 million people died of AIDS in that year (source: WHO). HIV-related illness remains one of the leading global causes of death and is projected to

¹ Immunity, Feb 2011 Bomsel et al.

² PLOS ONE Feb 2013, Leroux-Roels et al.

remain so in the coming decades. There is as yet no vaccine available against HIV. However, results of a large Phase III clinical study in Thailand showed a modest protective effect of 31%, providing encouraging support for the feasibility of an effective HIV vaccine. The Thai study tested unrelated HIV vaccine candidates and was reported in September 2009 in the *New England Journal of Medicine*.

Traditional approaches to creating a vaccine against HIV have aimed to elicit specific blood antibodies or CTLs (cytotoxic T cells). Both approaches have been largely unsuccessful to date, and importantly, no or very little protection has been seen with heterologous challenges, in which the virus strain differs from the original vaccine. A CTL response has the further drawback of requiring infection to have already occurred. Despite their importance as protection mechanisms, neither approach is suitable for protecting against initial mucosal transmission of HIV.

A vaccine that blocks HIV transmission across mucosal membranes represents a highly promising approach to preventing HIV infection; however, few studies have focused on this approach, until now. It builds however on the findings that certain people are not infected with HIV, even though they are exposed to it very frequently. Women and men who produce IgA antibodies against the HIV gp41 protein in their mucosal secretions have been found to display resistance to HIV transmission and infection. Mymetics has used its technology and expertise to design a vaccine candidate specifically intended to induce a mucosal antibody response against HIV while also inducing blood antibodies.

Ebola Virus and Texas Biomed In the News

Ebola virus continues to dominate headlines, and the virology and immunology team at Texas Biomed have been highly sought after to provide insight into the current outbreak and updates on the progress of scientific research. The team has given interviews with media outlets worldwide from the Rio Grande Valley to France. In addition to media interviews, team members are being asked to participate in more public presentations.

Dr. Ricardo Carrion, pictured in the news story here, also participated in a local, San Antonio panel discussion on Ebola virus for the University of the Incarnate Word. The story was streamed by KSAT-12 and can also be found online on the KSAT 12 website.

About Mymetics

Mymetics Corporation (OTCQB: MYMX) is a Swiss-based biotechnology company registered in the US and trades on the OTCQB venture stage marketplace for early stage and developing U.S. and international companies. Companies are current in their reporting and undergo an annual verification and management certification process.

Mymetics develops next-generation preventative vaccines for infectious diseases. Mymetics' core technology and expertise are in the use of virosomes, lipid-based carriers containing functional fusion viral proteins and natural membrane proteins, in combination with rationally designed antigens. The company's vaccines are designed to induce protection against early transmission and infection, focusing on the mucosal immune response as a first-line defense, which, for some pathogens, may be essential for the development of an effective prophylactic vaccine.

Mymetics currently has 5 vaccines in its pipeline: HIV-1/AIDS, intranasal Influenza, Malaria, Herpes Simplex Virus and the RSV vaccine (out licensed to ClearPath – Astellas). The company's intranasal Influenza vaccine and the HIV-1 vaccine have successfully completed Phase I clinical trials in healthy human volunteers. A Phase 1b clinical trial for its Malaria vaccine on children in Tanzania has been completed, while the HSV vaccine candidate is in the preclinical phase. For further information in Tanzania has been completed, while the HSV vaccine candidate is in the preclinical phase. For further information, please visit mymetics.com.

Dr. Anthony Griffiths participated in a Harvard Alumni meeting in Dallas in mid-October, thanks to the coordination of Craig and Elise Boyen. He returned to Dallas one week later to participate in a panel discussion on the Ebola virus



Dr. Ricardo Carrion

disease and the Dallas response to the virus. This public discussion resulted in several print and online stories in the *Dallas Morning News* that can still be viewed online. Dr. Griffiths also participated in a mid-November "Think Science" talk for Texas Public Radio pictured here. Dr. Griffiths presented on Ebola virus disease, while Dr. Karl Klose of UT Health Science Center San Antonio discussed antibiotic resistance.

Innovative method for studying malaria parasites receives 4-year NIH grant of up to \$1.8 million

Malaria researchers use new genomic tools to individualize parasite analysis

The National Institutes of Health (NIH) awarded Texas Biomedical Research Institute staff scientist Ian Cheeseman, Ph.D. over \$450,000 in first-year funding and is expected to receive up to \$1.8 million over four years to continue research into a new method for sequencing the genomes of individual malaria parasites, which he and colleagues at Texas Biomed developed and announced earlier this year in the journal *Genome Research*.

This research will allow scientists to improve their ability to characterize malaria parasites infecting patients. Each malaria infection can contain multiple genetically distinct strains of malaria parasites, each of which may affect disease progression differently. Until now, scientists lacked the tools to characterize the genomes of these individual malaria parasites.

“We think about these infections as containing the sort of diversity you would see in a human village,” Cheeseman said. “We could previously only look at the village as a whole, but new technology developed here at Texas Biomed now allows us to identify everyone in the village directly.”

Single cell genomics was pioneered in cancer research to identify how tumors evolve during the progression of a disease, but it has been difficult to adapt them to other organisms, according to Cheeseman.

“One of the major surprises we found when we started looking at individual parasites instead of whole infections was the level of variation in drug resistance genes,” said Shalini Nair, a colleague of Cheeseman’s in the Department of Genetics at Texas Biomed. “The patterns we saw suggested that different parasites within a single malaria infection would react very differently to drug treatment.”

According to the World Health Organization, malaria remains the world’s deadliest parasitic disease, killing 627,000 people in 2012, many of whom were children younger than five.

“We’re now able to look at malaria infections with incredible detail,” Cheeseman added. “This will help us understand how to best design drugs and vaccines to tackle this major global killer.”

At 31, Cheeseman is one of the youngest recipients of such an award in the country. In 2010 only 17 of 26,183 NIH R01 funded scientists were aged 31 and under, according to an NIH report on the age of RO1 principal investigators from 1980 to 2010 (<http://report.nih.gov>).

“To be able to embark on such a well-supported research project so early in my career is a phenomenal boost,” remarked Cheeseman, whose early research was supported by Texas Biomedical Forum funding.

This research is being supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number R01AI110941.



Ian Cheeseman, Ph.D.



Research Milestone in CCHF Virus Could Help Identify New Treatments

New research into the Crimean-Congo hemorrhagic fever virus (CCHFV), a tick-borne virus which causes a severe hemorrhagic disease in humans similar to that caused by Ebola virus, has identified new cellular factors essential for CCHFV infection. This discovery has the potential to lead to novel targets for therapeutic interventions against the pathogen. New research into the Crimean-Congo hemorrhagic fever virus (CCHFV), a tick-borne virus which causes a severe hemorrhagic disease in humans similar to that caused by Ebola virus, has identified new cellular factors essential for CCHFV infection. This discovery has the potential to lead to novel targets for therapeutic interventions against the pathogen.

The research, reported in a paper published today in the journal PLoS Pathogens and conducted by scientists at the Texas Biomedical Research Institute and their colleagues, represents a milestone in efforts to develop a treatment for CCHFV, which has a fatality rate approaching 30%.

“This new research is the first to indicate where the virus penetrates into the cell to infect it, revealing the site at which a drug therapy would need to act,” said Robert Davey, Ph.D., of the Texas Biomed Department of Virology and Immunology, who led the research.

The virus is endemic to much of Eastern Europe, the Middle East, Asia and Africa, and recent studies have detected CCHFV in ticks collected in Spain, indicating that the virus continues to spread. CCHFV killed a US Army serviceman stationed in Afghanistan in 2009, and was initially mistaken for Ebola virus.

CCHFV is primarily transmitted to people from ticks and from infected livestock during the slaughtering process, although human-to-human transmission can occur from close contact with blood or other fluids from infected persons. There are no widely accepted therapies available to prevent or treat the disease.

Virus entry into the cell is the first and critical step in the virus replication cycle. To better understand the pathway for infection, researchers sought to identify cell proteins controlling CCHFV transport through the cell. Dr. Olena Shtanko, a postdoctoral scientist in the lab, demonstrated that after passing through

early endosomes, membrane-bound vesicles within cells, the virus is delivered to multivesicular bodies which are made from large collections of these vesicles. Findings suggested that these multivesicular bodies are critical for infection by CCHFV, being the sites where the virus first penetrates into the cytoplasm to start replicating and taking over the cell.

“The next step in the process is to now identify drugs that can prevent interaction of the virus with the multivesicular bodies” Davey said. Several new drug candidates are presently being tested by Shtanko with promising results.

Several other important viruses, like Influenza virus (cause of the flu) and Lassa fever virus also use multivesicular bodies to infect cells. The identified drugs have the potential to be developed into broad spectrum antiviral treatments.

The research was funded by the Ewing Halsell Foundation, Douglass Foundation and the U. S. Defense Threat Reduction Agency (DTRA). In addition to Davey and Shtanko, co-authors of the PLoS Pathogens article included Raisa Nikitina and Alexander Chepurnov of the Institute for Clinical Immunology in Novosibirsk, Russian Federation, and Cengiz Altuntas of the Texas Institute of Biotechnology Education and Research at the North American University in Houston.





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