THE CURE CHRONICLES

December 2021 ISSUE

Enabling affordable and accessible advanced medicines

Hello,

In our December issue we “spotlight” the **Honorable Dr. Mark Dybul**. His work in PEPFAR has brought him global attention, but as you will see he continues to move forward in the global fight against HIV through his work at Georgetown University and Enochian BioSciences.

This has been a very news-heavy month and we will highlight the publications and advances that have grabbed the attention of the field. We also highlight the recent talks that have been posted to our site, and new Whitepapers available to our members.

News

Here’s the latest on what we are excited about:

Will CD19 CAR-T cells move to second line therapy for lymphoma? Recent results presented at the ASH (American Society of Hematology) 2021 annual meeting showed superior results for Yescarta (ZUMA-7 trial) and Breyanzi (Transform trial), while Kymriah (Belinda trial) showed equivalency to HSCT. Taken together we can assert that CAR-T cell therapy for B cell malignancy will continue to see innovation and improvements in patient outcome. Results for the ZUMA-7 trial were recently published in the New England Journal of Medicine by Locke FL, et al., December 11, 2021.

Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma

Also in the most recent *NEJM*, one of the leaders in GGTI (Global Gene Therapy Initiative), John Tisdale (Advisory Board Member), was senior author on a publication describing the biologic and clinical efficacy of LentiGlobin (bb1111; lovotibeglogene autotemcel), which is a lentiviral gene vector encoding an antisickling hemoglobin, HbA^{T87Q}. The report demonstrates impressive reduction in hemolysis and complete resolution of severe vaso-occlusive events in patients who received autologous bone marrow stem cells engineered with a lentiviral vector to express this transgene.

Biologic and Clinical Efficacy of LentiGlobin for Sickle Cell Disease

The WHO and other regulatory bodies are starting to formulate ethical guidelines around germline editing of the human genome (meaning changes that can be inherited). Vivien Marx's article in Nature Biotechnology describes the ethical uproar caused by the genome editing of three children in China. It was a clear ethical violation of existing regulations, exposed the children to an unproven and imprecise therapy that will not benefit them, and caused further distrust of cell and gene therapy in the community. A link to the article is here:

The CRISPR children

The Berlin and London patients are well-known individuals who were cured of their HIV infection in the context of receiving a bone marrow transplant (HSCT). In a recent publication in the Annals of Internal Medicine by Turk G, et al., the focus turned to "elite controllers," people living with HIV who appear to have undetectable viremia in the absence of anti-retroviral therapy (ART). However, upon more in-depth analysis of elite controllers, intact provirus can be detected. This publication presents an elite controller, where no genome-intact or replication-competent HIV could be detected even using the most sensitive techniques. This appears to be the first person cured of infection outside of receiving an HSCT, and implies sterilizing cures can be achieved by other means. Here is a link to the article:

A Possible Sterilizing Cure of HIV-1 Infection Without Stem Cell Transplantation

It has been noted by many that the first AIDS cases were reported in the US 40 years ago. In a new publication in Nature Medicine (where GGTI and Advisory Board member Dr. Steven Deeks serves as first author, and Advisory Board

member Sharon Lewin is senior author), The International AIDS Society (IAS) Global Scientific Strategy working group reviews advances in the last 5 years and looks forward to propose where research is most needed in the next 5 years. Here is a link to this excellent summary of the field, and an impactful call to research where it is most needed:

Research priorities for an HIV cure: International AIDS Society Global Scientific Strategy 2021

One of the major challenges in current approaches to CAR-T cell therapy is preventing T cell exhaustion. This is a natural metabolic process where a T cell that is continually exposed to antigen loses function. By studying this process researchers a St Jude's, led by Giedre Krenciute, found that deleting the DNMT3A gene prevents this inexorable pathway to exhaustion, and may lead to better functioning CAR-T cells. This paper highlights that exploring the epigenetic regulation of T cell exhaustion pathways is likely to reveal numerous pathways by which CAR-T cells can be engineered to better treat malignancy:

Deleting DNMT3A in CAR T cells prevents exhaustion and enhances antitumor activity

Community Advocate Spotlight

Ambassador Mark Dybul, MD

CEO Enochian BioSciences, Prof of Medicine, Georgetown University

Tell us about your background and how you came to be in your current position.

Dr. Dybul has worked on HIV and public health for more than 25 years as a clinician, scientist, teacher, and administrator. He served as the Executive Director of the Global Fund to Fight AIDS, Tuberculosis and Malaria (2013-2017) and the US Global Coordinator and Ambassador leading the President's Emergency Plan for AIDS Relief (PEPFAR). After graduating from Georgetown Medical School in Washington D.C., Dr. Dybul joined the National Institute of Allergy and Infectious Diseases, as a research fellow under director Dr. Anthony Fauci, where he conducted basic and clinical studies on HIV virology, immunology and treatment optimization, including the first randomized, controlled trial with combination antiretroviral therapy in Africa. Mark was one of the founding architects in the formation of PEPFAR. After serving as Chief Medical officer, Assistant, Deputy and Acting Director, he was appointed as its leader in 2006, becoming U.S. Global AIDS Coordinator, with the rank of

Ambassador at the level of an Assistant Secretary of State. He served until early 2009.

Mark has written extensively in scientific and policy literature, he is a member of the National Academy of Medicine and has received several Honorary Degrees and awards, including a Doctor of Science, *Honoris Causa*, from Georgetown University.

Tell us what the focus of your efforts is at the present time and what motivates you.

- Potential cures/effective treatments for HIV, HBV, solid tumors and effective treatment and prophylaxis for pan SARS-coronaviruses and influenza viruses
- Access for all, including investment in innovations in delivery mechanisms, e.g. closed systems, that are less expensive and easier to use for greater access. Part of that access should be decentralized/local production and research capacity to maximize ideas and innovations from all over the world not just from high-income countries.
- Greater understanding of cross section between root causes of environmental destruction and health, e.g. pollution, smoking, eating/agriculture and animal health, urbanization, poverty, inequality in education and opportunity. And from that understanding, more investment in innovations that cross health and environment with heavy emphasis on decentralized/local innovation linked to a global network to scale best ideas.

What is your vision for the future and how would you overcome any challenges?

A world where most diseases can be effectively prevented, treated or cured at low cost and will enable access for all.

To overcome, we need greater investment and institutions focused on innovation in new tech to prevent and fight diseases but also on low-cost production and research infrastructure for global network of innovation.

Creating a “global mindset” so that every problem and solution is considered from a local to global linkage vision.

If there is one thing that would make a difference to your efforts, what would it be?

Revolutionary change in how we envision and invest in science and innovation to see everything as interconnected and create a global mindset

What is a fun fact about yourself that you would like to share?

I am a foodie but wish I had the fortitude to become a vegetarian (in another life perhaps)

Whitepapers

Interested in learning more? Read our latest whitepapers on the Caring Cross website. Click below to access them.

➡️ **Centralized vs Decentralized Manufacturing of Personalized Cell Therapies: Overview and Logistics**

➡️ **Introduction to Chimeric Antigen Receptor (CAR) engineered immune cells**

Upcoming Events

Next month's **education tutorial** will be the fourth in a series of 8 presented by Rimas Orentas, PhD -

CAR target antigen binding moieties (series 4/8).

In this educational webinar we will continue to look at specific aspects of what make a good chimeric antigen receptor (CAR), focusing on different ways that the

CAR can bind to its target.

➡️ **Register for the event**

Date: **January 07, 2022**
Time: **3:00pm EST / 12:00pm PST**
Location: **Zoom** (link provided upon registration)

This event will last approximately 30-40 minutes and will consist of a presentation and Q&A session following.

Next month's **seminar** will be presented by Nirali N. Shah, MD, MHSc, from the NIH Pediatric Oncology Branch, a global leader in CAR-T cell therapy.

Current Challenges in CD19 CAR T-cells for Pediatric ALL: Implications for the Global Community.

➡️ **Register for the event**

Date: **January 21, 2022**
Time: **3:00pm EST / 12:00pm PST**
Location: **Zoom** (link provided upon registration)

This event will last approximately 30-40 minutes and will consist of a presentation and Q&A session following.

All our events are on Fridays at 3pm EST, and require registration to access the live webinar. A recorded replay will be available to Caring Cross Community members only **(Membership is free).**

Recent Events

If you missed these recent events, click on the links below to view them.

One Center's Experience Manufacturing & Analyzing CAR T Cells

CAR-T cell target identification (series 3/8)

A phase I/II clinical trial using locally manufactured CAR-T cells for the treatment of pediatric acute lymphocytic leukemia in Moscow, Russia.

From T Cells to Engineered Effectors: CAR-T cell background (series 2/8)

If you are not a member, you can become a member and view all our past events.

Caring Cross Community

One of our high-impact community advocates is Moses Supercharger. Based in Uganda, Moses has created a new YouTube channel called "Stigmaless Television." Here, Moses has posted songs that encourage all us to strive for the 95/95/95 goal, and to live out positively. Do yourself a favor, listen, and enjoy, perhaps starting with the song "Optimistic," (supported by UNAids):

➡ **OPTIMISTIC**

We created this membership community to connect healthcare professionals, scientists and engineers, community advocates and business leaders that are on a mission to develop new advanced medicinal cures - and help make them affordable to all who need them.

Join us inside to collaborate in a group, learn from seminars and training, and gain access to job opportunities or internships.

➡ **Become a member**

What else would you like to hear about in this newsletter?
Reply to let us know.

Thank you for being here, and please look out for another update next month!

- Caring Cross

P.S. Are you following along with us on LinkedIn? Be the first to know about our progress and share in the conversation!
>> Join us on LinkedIn

Caring Cross Inc.
708 Quince Orchard Road
Suite 250-D
Gaithersburg, Maryland 20878