Molecular Therapy
Editorial

ASGCT Meeting Showcases Fast-Paced Development of Gene and Cell Therapy Technologies

Genetic and cellular engineering has always been a cornerstone of the American Society of Gene and Cell Therapy (ASGCT). This year's meeting took technology development to yet an even higher level. Appropriately, the meeting was held entirely in a virtual fashion, enabled by today's information technology. This actually allowed attendees to easily switch between sessions and listen to presentations, which is often not possible in conventional in-person meetings, requiring long walks between meeting rooms that may even be too crowded to enter. Questions were posted to presenters in the style of online chats, and poster and exhibit halls were virtually accessible. Through the virtual format, the meeting reached attendees around the globe.

Given the rapid pace of commercial development of gene therapy drugs, it may not be surprising that a considerable number of presentations were from members of biotechnology and pharmaceutical industries. These covered topics such as viral vector manufacturing, characterization of vector preps, even to the level of single vector genome analysis, and various aspects of assay development. Engineering of lymphocytes, gene editing technologies, nanoparticle technologies, and viral vector development are now increasingly merging. An example is the history of the CAR-T cell technology in cancer immunotherapy. As Carl June, a pioneer of chimeric antigen receptor (CAR)-T cell therapy for blood cancers, explained in his George Stamatoyannopoulos Memorial Lecture, the CAR sequences are traditionally delivered to primary T cells using lentiviral vectors. However, gene editing can now be used to specifically insert the receptor construct into desired places in the cellular genome. Similarly, gene editing can be used to delete endogenous T cell receptors to aid in the redirection of antigen specificity. CARs are now also being utilized to develop regulatory T cells (Tregs) to suppress unwanted immune responses to vectors and transgene products in gene therapy. For instance, one presentation found that a CAR-Treg specific for the capsid of adeno-associated virus (AAV) could suppress immune responses not only to AAV but also to its therapeutic gene product. Another study presented during the presidential symposium showed how gene editing through homology-directed repair (HDR) can be used to enforce expression of the transcription factor FoxP3, thereby turning $CD4^+$ T cells into stable Tregs. In parallel, gene editing was employed to introduce a T cell receptor specific for a pancreatic islet antigen. These engineered Tregs can now be used to treat the autoimmune disease type 1 diabetes. The DNA template for HDR is typically delivered by an AAV vector, while CRISPR/Cas or other nucleases carry out the sequence-specific DNA cut. For *in vivo* applications, this may be accomplished by co-delivery of a second AAV vector that encodes the nuclease (and in the case of CRISPR, also the guide RNA). Alternatively, nanoparticles may be used for this purpose, thus representing a combination of viral and non-viral technologies.

In other exciting developments, Feng Zhang, a pioneer of the CRISPR/Cas system, showcased as part of his Presidential Symposium Lecture how gene editing has now entered use in diagnostics. For example, among many other seminal contributions, his research resulted in a portable test system called SHERLOCK (specific high sensitivity enzymatic reporter unlocking), which utilizes an enzyme complex that can cleave RNA with specificity. This sensitive test has recently been adapted to detect coronavirus in human samples. With regard to infectious diseases, the meeting also covered recent advances in genetic vaccines and mRNA-based approaches, which are rationally designed and avoid the use of inactivated pathogens. This topic is not only timely because of the COVID-19 pandemic, where early phase I clinical trials results from an mRNA vaccine have now been made public, but also because of its wider promise for protection from a number of viral and bacterial pathogens. Giving the virtual meeting a personal and unusual touch, we were able to marvel about these advances in our living rooms while watching lectures recorded in the presenter's living room.

This was also true for the *Molecular Therapy* family of journals' annual editorial board meeting, a joint meeting of the editorial teams of each member of our journal family. Historically, we have tried many different time slots for this meeting, from morning to evening, eventually settling these past few years on a lunchtime meeting which has boosted attendance greatly. We retained the lunchtime meeting this year but of course it was held virtually, which had the added value of allowing members of our editorial teams worldwide to "attend," thereby further boosting attendance to levels we have not seen before. At the meeting, we presented the latest journal stats, which showed continued unprecedented growth of all the journals and rises in impact factor well beyond our early hopes and expectations, boding well for the next year and beyond. Of course, we look forward to seeing as many of you as possible in person at ASGCT 2021. New technology is not only driving gene and cell therapy research, but also the way we share and communicate that research.

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