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Young & Partners Pharmaceutical Executive Summit 2024: Brave New World – Where Are We Heading?

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By Don Tracy, Associate Editor

Peter Marks, director, Center for Biologics Evaluation and Research, FDA, presented the keynote presentation on the future of gene therapy as part of the 20th Annual Young & Partners Pharmaceutical Executive Summit held at the Yale Club of New York.

Peter Marks. Image Credit: Don Tracy

Starting off this year's Young & Partners Pharmaceutical Executive Summit, Peter Marks, director, Center for Biologics Evaluation and Research, FDA, delivered a keynote speech entitled "Brave New World – Where Are We Heading?" In this keynote speech, Marks offered a preview of ways that gene therapies will improve moving forward.

"It's in an interesting place right now," stated Marks. "There was a lot of investment in 2018 but began cooling off as the pandemic continued, with a number of companies falling out. There was also an interest in genome editing and in vivo genome editing, but some of that has cooled off as well."

Marks first spoke of two major styles of gene therapy; either through ex vivo taking cells from somebody; or in vivo; modifying the cells with a gene therapy. In the first generation, genetically modified hematopoietic stem cells had been made, or it was given locally such as into the eye or systemically.

"The major ways that these have been done for these two different applications; outside of the body versus directly administering generally have had separate sets of vectors," he explained. "Modifications in in vitro are done with lentiviral or retroviral vectors, namely with associated viral vectors and associated viruses. It's a virus that does not generally cause disease in people, it can lose part of its genome, and although it's small, it can't carry very large pieces of DNA, but it can deal with any number of genetic diseases."

The speech then shifted to where gene therapy could go moving forward. Marks explained the history behind CAR-T therapy and how as a type of ex vivo gene therapy, it has been a game changer for treating particular blood cancers.

“CAR-T cell development was something that was developed over the past 15 years, a lot of it coming out of University of Pennsylvania, but also out of Memorial Sloan Kettering,” stated Marks. “The current paradigm for autologous chimeric antigen receptor T-cells is that you generally harvest white blood cells from a person who has the malignancy that you want to treat, you then purify the T-cells, activate those T-cells, transfuse them with the construct that recognizes the cell type you want to kill, and then formulate them and give them back to a person, usually after another round of chemotherapy.”

Marks also discussed how gene therapies can be used to potentially correct genetic defects responsible for diseases like cystic fibrosis, sickle cell anemia, and muscular dystrophy. Further, they are being explored for potential use in vaccines against infectious diseases and genetic disorders that disrupt metabolic processes.

Despite the promise that gene therapy has demonstrated, Marks explained that there are a key number of challenges regarding future directions, including:

- **Delivery efficiency:** Making sure that therapeutic genes are delivered to the correct cells in the body.
- **Safety:** At times, viral vectors can trigger immune responses or insert genes into unintended locations, leading to adverse events.
- **Manufacturing:** Production of gene therapy can potentially be expensive and challenging at the same time.
- **Regulatory:** Approval of a finished product can be a lengthy process, with a number of additional challenges.

Despite the number of challenges, Marks believes that ongoing research and technological advancements are addressing these issues, demonstrating potential to transform the treatment of many diseases and cement itself as a groundbreaking approach to treating diseases at the genetic level.