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EMERGING COMPANY PROFILE

BACKPACKS FOR CARS

By Michael Leviten, Senior Writer

Torque Therapeutics Inc. is making “backpacks” for immune cell therapies that release immune stimulatory molecules at particular doses and locations to boost the cells’ activity without risking systemic exposure. The technology could augment the success of CAR T’s against blood cancers and help overcome the immunosuppressive microenvironment that makes solid tumors so hard to treat.

President and co-founder Ulrik Nielsen told BioCentury that Torque’s platform — dubbed Deep-Primed — could be a gateway to the next generation of cell-based immunotherapies. “CARs are effective for limited patient populations because it’s hard to overcome immune suppression effects of tumors. Deep priming controls the T cell microenvironment and puts cells in an inflammatory microenvironment,” he said.

The technology was invented in the lab of Co-founder and Massachusetts Institute of Technology Professor Darrell Irvine, who created drug-loaded lipid nanoparticles that attach covalently to free thiol groups on cell surfaces, producing localized cell depots that slowly release the payload.

According to CEO and Co-founder Bart Henderson, Torque has expanded the technology and now has several undisclosed methods of linking backpacks to cells and controlling payload release.

Torque plans to apply the technology first to CAR T cells, and load the particles with an immunostimulatory cytokine as an alternative to systemic adjuvants.

In its Deep IL-15 program, IL-15-carrying backpacks are connected *ex vivo* via a covalent linkage to an undisclosed CAR T therapy. Once the T cells find and bind malignant cells, IL-15 is gradually released by hydrolysis, locally promoting cell proliferation and cytotoxicity to augment CAR T activity.

Henderson said high serum IL-15 levels have been associated with effectiveness of CAR Ts, but systemically delivered IL-15 has also been shown to cause an acute drop in blood

TORQUE THERAPEUTICS INC., Cambridge, Mass.

Technology: Nanoparticles that localize therapeutics to surface of cell therapies

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2015 by Ulrik Nielsen, Bart Henderson, Thomas Lars Andresen, and Darrell Irvine

University collaborators: Massachusetts Institute of Technology

Corporate partners: Not disclosed

Number of employees: 30

Funds raised: \$25 million

Investors: Flagship Pioneering

CEO: Bart Henderson

Patents: Not disclosed

lymphocytes followed by hyperproliferation of NK cells to up to 10-fold normal levels. He believes a big advantage of Torque’s technology is that it can bypass systemic exposure to the cytokine. “We see minimal expansion of bystander cells preclinically. Head-to-head with systemic IL-15 there’s a big difference and that’s really the premise of our technology,” Henderson told BioCentury.

Novartis AG and Altor BioScience Corp. each have IL-15/IL-15RA complexes — which are thought to be the active form of the cytokine — in clinical trials for cancer. Torque declined to disclose the composition of active IL-15 in Deep IL-15, but in his 2010 paper on the technology, Irvine also combined IL-15 with IL-15RA.

Torque’s next candidates are CAR Ts with IL-12 or toll-like receptor (TLR) agonists. For the latter, the company is considering using small molecule agonists, which would make it the first to engineer gradual release of a small molecule from a cell’s surface, said Henderson. “What’s unique here is we can anchor a small molecule to immune cells and nobody is doing that.”

He said the technology can be used on any cell type, and in addition to CAR Ts, Torque is prioritizing NK cells.

Torque was launched with a \$25 million Series A from Flagship Pioneering which Henderson said will take it into the clinic. The biotech is licensing its technology to a CAR T company for the first product but expects to have its own cellular therapies after that. The first clinical trial with Deep IL-15 is slated for 2018. ■

COMPANIES AND INSTITUTIONS MENTIONED

Altor BioScience Corp., Miramar, Fla.

Massachusetts Institute of Technology (MIT), Cambridge, Mass.

Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland

Torque Therapeutics Inc., Cambridge, Mass.

TARGETS

IL-12 - Interleukin-12

IL-15 - Interleukin-15

IL-15RA - Interleukin-15 receptor α chain

REFERENCES

Stephan, M., et al. "Therapeutic cell engineering with surface-conjugated synthetic nanoparticles." *Nature Medicine* (2010)

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