

BioCentury

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EMERGING COMPANY PROFILE

MEDITOPE: KEYHOLE CONJUGATION

BY STEPHEN HANSEN, SENIOR WRITER

Meditope Biosciences Inc.'s meditope-enabled linker technology could improve upon first-generation antibody-drug conjugates by producing ADCs that are more stable and homogeneous.

First-generation ADC technologies typically link cytotoxic agents to naturally occurring amino acids on mAbs, such as cysteine or lysine. Because any given mAb contains numerous cysteine and lysine sequences, conjugating the payload to a naturally occurring amino acid can result in a heterogeneous drug mixture. Some mAbs may have no cytotoxic drugs attached, while others in the same product may have six or more linked payloads.

The cytotoxic agent also can link to different sites on the mAb, affecting the stability or functionality of the molecule. For instance, a cytotoxic compound conjugated near the mAb's binding site can affect its ability to bind an antigen.

Meditope is among several next-generation ADC companies seeking to create homogeneous products by engineering the mAbs to have a fixed number of attachment sites for the cytotoxic agents.

Some companies, such as Ambrx Inc. and Sutro Biopharma Inc., are engineering mAbs with non-natural amino acids to specify where in the mAb the linkers and warhead should be attached to produce a homogeneous product (see BioCentury, Aug. 19).

Meditope's meditope-enabled technology is a variation on the site-specific conjugation approach.

According to scientific co-founder John Williams, his lab at City of Hope discovered a unique site within the Fab arm of Erbitux cetuximab that acts as a very specific keyhole in which a specific small peptide — known as a meditope — is able to bind non-covalently. Williams, a member of Meditope's scientific advisory board, said the binding is similar to a ligand-receptor interaction.

President and CEO Stephanie Hsieh said Meditope has been able to take this unique site from the cetuximab Fab arm and graft it into the Fab arm of any other mAb, thus enabling the antibody to interact with the small peptide key.

MEDITOPE BIOSCIENCES INC.

Pasadena, Calif.

Technology: Meditope-enabled linker technology

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2012 by John Williams, David Horne, Heng Wei Chang and Stephanie Hsieh

University collaborators: City of Hope

Corporate partners: None

Number of employees: 3

Funds raised: \$3.6 million

Investors: Angel investors

CEO: Stephanie Hsieh

Patents: None issued

"The peptide is like a trailer hitch," said Williams.

Meditope calls the resulting molecule a memAb, which can have a fixed drug to antibody ratio (DAR) that doesn't affect the binding characteristics of the original mAb.

In a recent paper in *The Proceedings of the National Academy of Sciences (PNAS)*, Williams and colleagues at the City of Hope and Thomas Jefferson University reported they were able to graft the cetuximab site onto the Fab arm of Herceptin trastuzumab and link it with a meditope peptide without affecting the binding activity of the mAb for its antigen HER2 (see SciBX: Science-Business eXchange, Oct. 31).

While Meditope is focused on ADCs, the company could use the technology for other applications. For instance, Williams said it could be used for imaging. A modified mAb would be administered without the peptide, after which the peptide conjugated to copper 64 would be administered.

Williams said the peptide would seek out the keyhole in the mAb to allow imaging of the cells of interest.

In July, Meditope raised \$3.6 million from angel investors. Hsieh said the cash would be used to continue validating the technology in vivo.

The company also will seek early partnerships for the platform and then begin developing internal programs.

“The plan is to out-license and collaborate with a partner that can fund some of the activities, and in parallel or right behind that start working on our own pipeline,” Hsieh said.

Eli Lilly and Co. and Bristol-Myers Squibb Co. market cancer drug Erbitux in North America. Merck KGaA markets Erbitux elsewhere, except in Japan where the three companies market the drug.

Roche and its Genentech Inc. unit market breast cancer drug Herceptin.

COMPANIES AND INSTITUTIONS MENTIONED

Ambrx Inc., La Jolla, Calif.

Bristol-Myers Squibb Co. (NYSE:BMJ), New York, N.Y.

City of Hope, Duarte, Calif.

Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.

Genentech Inc., South San Francisco, Calif.

Meditope Biosciences Inc., Pasadena, Calif.

Merck KGaA (Xetra:MRK), Darmstadt, Germany

Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland

Sutro Biopharma Inc., South San Francisco, Calif.

Thomas Jefferson University, Philadelphia, Pa.

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