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Contact Information:
Tom Manning, Director of Marketing Communications
Telephone: +1.630.256.7527, ext. 103
E-mail: tmanning@slas.org

Antigen Selection for Enhanced Affinity T-Cell Receptor–Based Cancer Therapies

CHICAGO – A review by Hickman et al. in the September 2016 issue of the *Journal of Biomolecular Screening* (JBS) covers recent advances in approaches to create affinity-enhanced TCRs with exceptionally high sensitivity and specificity. These high-affinity T-cell receptors (TCRs) recognize HLA-presented peptides at the target cell surface and thus access a much larger pool of intracellular targets that are not available to either antibody or small molecule based therapies.

Due to the vast array of molecular targets that are accessible to TCRs, the technology relies heavily on big 'omics' data for target discovery. This review covers the design and mechanism of action of these agents, with a particular focus on target discovery, target selection and pre-clinical safety. It describes how advances in this area are being translated therapeutically into both adoptive T-cell therapy and soluble biologic agents for the treatment of solid tumors. In recent years both soluble and cellular TCR-based therapies have entered into early clinical trials and the emerging results are showing that these agents can be well tolerated whilst delivering potent and durable therapeutic responses.

The recent success of checkpoint inhibitors, such as those targeting the PD1/PDL1 interaction or the CTLA4 pathway, has changed the way that we think about systemic immunotherapy of cancer. It has shown that by therapeutically overcoming natural immunosuppressive mechanisms, endogenous tumor-specific cytotoxic T cell responses have the potential to deliver profound clinical benefit to patients. Natural tumor-specific cytotoxic T-cells are nonetheless limited by the low affinity of their TCRs and thus they show relatively poor activity against their cognate antigens.

JBS is one of two MEDLINE-indexed scientific journals published by SLAS (Society for Laboratory Automation and Screening). Visit JBS Online at http://jbx.sagepub.com/content/21/8 to read "**Antigen Selection for Enhanced Affinity T-Cell Receptor–Based Cancer Therapies**." For more information about SLAS and its journals, visit www.slas.org/publications/scientific-journals.

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education and information exchange and to encourage the study of, and improve the practice of life sciences discovery and technology. For more information, visit www.SLAS.org.

Journal of Biomolecular Screening (JBS): *2015 Impact Factor 2.218. Editor-in-Chief Robert M. Campbell, Ph.D., Eli Lilly and Company, Indianapolis, IN (USA). In 2017, JBS's title will change to* ***SLAS Discovery*** *(Advancing Life Sciences R&D).*

Journal of Laboratory Automation (JALA): *2015 Impact Factor 1.297. Editor-in-Chief Edward Kai-Hua Chow, Ph.D., National University of Singapore (Singapore). In 2017, JALA's title will change to* ***SLAS Technology*** *(Translating Life Sciences Innovation).*