"Rapid Cloning of T Cell Receptors"

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Technology description

Rapid Cloning of T Cell Receptors (TCRs) (SJ-16-0001)/ (Rapid cloning, expression, and functional characterization of paired αβ and γδ TCR chains from single cell analysis)
St. Jude Reference #SJ-16-0001
Description: Transgenic expression of antigen-specific T cell receptor (TCR) genes is a promising approach for immunotherapy against infectious diseases and cancers. A key to the efficient application of this approach is the rapid and specific isolation and cloning of TCRs. Researchers at St. Jude have developed a novel method to rapidly clone, express and characterize the function of paired αβ and γδ TCR chains from single cells. The platform addresses the non-specific, labor-intensive, and time-consuming issues of traditional PCR-based cloning and it provides a relatively high-throughput, accurate, and efficient method of TCR engineering for therapeutic or research applications. The researchers demonstrated the capability of cloning influenza-specific TCRs within 10 days using single cell PCR and Gibson Assembly techniques. This process can be accelerated to 5 days by generating receptor libraries, requiring only the exchange of the antigen-specific CDR3 region into an existing backbone. The functional activity of these TCRs can be characterized in a novel reporter cell line for screening of TCR specificity and avidity. By generating a library of specific TCR constructs reactive against a range of viruses and HLA types, TCR-directed therapies could be used prophylactically or immediately at the earliest signs of viral reactivation or to target conserved or patient-specific tumor antigens. In addition to therapeutic applications, the protocol significantly improves the workflow for cloning and expressing TCRs for study in vitro.

References

Xi-zhi J Guo, Pradyot Dash, Matthew Calverley, Suzanne Tomchuck, Mari H Dallas, and Paul G Thomas, Rapid cloning, expression, and functional characterization of paired αβ and γδ T-cell receptor chains from single-cell analysis. Mol Ther Methods Clin Dev. 2016; 3: 15054. Published online 2016 Jan 27.
Wang, G.C., Dash, P., McCullers, J.A., Doherty, P.C., and Thomas, P.G., T cell receptor αβ diversity inversely correlates with pathogen-specific antibody levels in human cytomegalovirus infection. Sci Transl Med 4, 128ra42 (2012). Han, A et al., Linking T-cell receptor sequence to functional phenotype at the single cell level. Nature Biotech. 32(7): 684-692 (epub June 22, 2014).

Advantages

This invention enables a reduction in cost, time and reagents can get the cost per cell to under $1 per cell, compared with the standard sequencing technique which is now typically $6 per cell, it may be able to be used for cytomegalovirus (CMV) or other herpesvirus-positive patients and cancer patients in patient specific therapy, or it may be used as a molecular tool (i.e. metrics of immune health; better indicator of potent immune status) for drug development.

Institution

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