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Patient-derived organoids for evaluating immunotherapies against lymphoma

Stanford scientists have developed lymphoma organoids derived from primary patient biopsies that recapitulate the tumor microenvironment. This culture system contains the diverse immune cell types present in real lymphoma tumors and allows for the testing of immune therapies that require a "competent" immune system. Patient-derived organoids can be used to accurately evaluate immunotherapies, such as bispecific antibodies and chimeric antigen receptor T-cells, in a clinical or preclinical setting.

Current lymphoma treatments frequently involve T-cell mediated immunotherapies, including bispecific T-cell-engaging antibodies and chimeric antigen receptor (CAR) T-cells. These new immunotherapies are difficult to evaluate experimentally in the traditional cell cultures that have been used to test chemotherapies. Traditional cell cultures consist of malignant B-cells only and do not contain the other immune cells present in real lymphoma tumors. Likewise, traditional cell cultures are all derived from a single sample and do not represent the diversity of real patient biology. Patient-derived lymphoma organoids can help address these issues.

Using primary lymphoma tumor biopsies to develop a patient-derived lymphoma organoid model resulted in a stable tumor microenvironment over three weeks without exogenous cytokines. Importantly, patient-derived lymphoma organoids treated with CD3:CD19 and CD3:CD20 bispecific antibodies showed B cell killing and T cell activation. Consequently, this system offers a robust platform for evaluating immunotherapies and advancing personalized medicine.

Stage of Development:
Preclinical – in-vitro (organoid) data
Continued research – Exploring other lymphoma subtypes, immunotherapies,

methods of immune microenvironment manipulation

Applications

- Assessment of new immunotherapies
- Modeling of tumor mechanisms of resistance
- Patient-specific response assessment for personalized medicine

Advantages

- Contains other immune cells that recapitulate the tumor microenvironment
- Long-term viability in culture
- The use of primary patient immune cells rather than added immune cells from other sources

Publications

- • Kastenschmidt, J. M., Schroers-Martin, J. G., Sworder, B. J., Sureshchandra, S., Khodadoust, M. S., Liu, C. L., ... & Alizadeh, A. A. (2024). A human lymphoma organoid model for evaluating and targeting the follicular lymphoma tumor immune microenvironment. Cell Stem Cell, S1934-5909

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