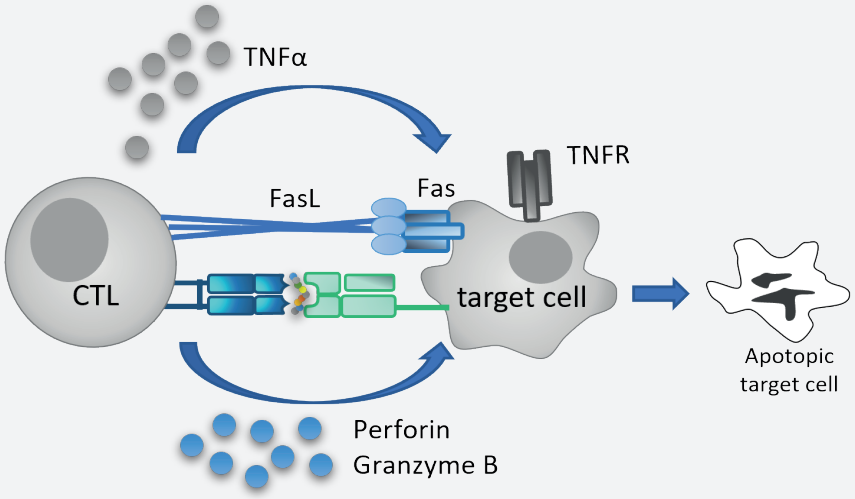
PEPperPRINT
A NEW DIVERSITY

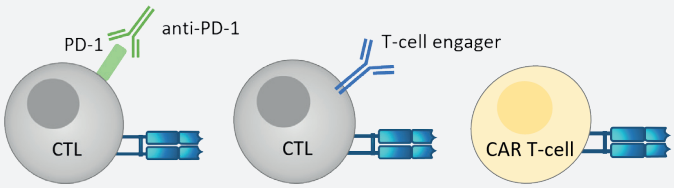
Cytotoxic T Lymphocyte-Mediated Killing Assay

Validate your new T-cell based immunotherapy by analyzing the potency of cytotoxic T lymphocyte (CTL)-mediated apoptosis of tumor cells

Cytotoxic T lymphocytes (CTLs) are a major part of adaptive immunity. CTLs are mandatory to combat tumors as they recognize and kill cancer cells via different mechanisms, and are indispensable for an effective immunotherapy. However, tumors developed different strategies to evade immunity. New therapies are based on antigen-specific activation of CTLs to increase effector function while blocking inhibitory mechanisms. The killing assays are a highly valuable tool for immuno-oncology research projects aiming to develop new anti-cancer therapeutics.



Different mechanisms of CTL-mediated killing of target cells: 1) Perforin/ Granzymes mediated killing. CTLs secrete perforin that forms pores in the target cell membrane and granzymes that subsequently induce apoptosis of cells. 2) Death receptor-mediated killing. Receptors on target cells with an intracellular death domain such as the TNF receptor 1 and the FAS receptor activate apoptotic signaling cascades when bound by their respective CTL-dervied ligands TNF alpha or FAS ligand.



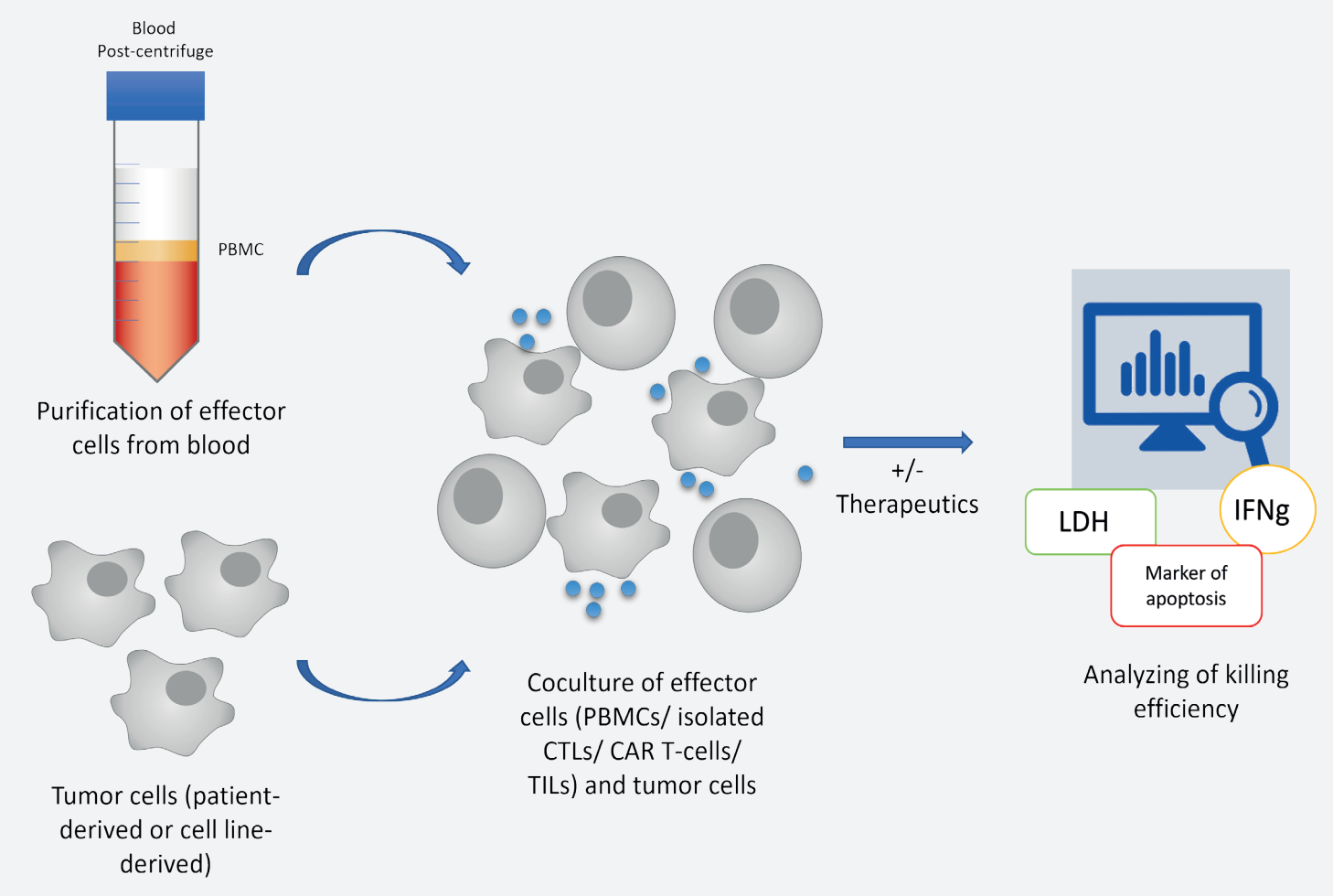
Strategies to promote tumor cell killing by CTLs: 1) Monoclonal antibodies block checkpoint inhibitors such as PD-1. 2) T-cell engaging bispecific antibodies bind a tumor antigen and a T-cell surface molecule. 3) Chimeric antigen receptor (CAR) T-cells express a synthetic receptor that binds a tumor antigen.

APPLICATIONS

- Identify immunogenic CTL epitopes
- Validate the efficiency of new immunotherapeutics
- Select the most promising drug candidates for animal studies

Assay Workflow: Cytotoxic T Lymphocyte-Mediated Killing Assays

Effector cells are isolated from blood. For the test either PBMCs or isolated CD8 T-cells can be utilized. For identification of an immunogenic epitope, effector cells are primed with the peptide candidates. As target cells tumor cells from patients or cell lines are used. Effector and target cells are cocultured with an activation mix and the peptide and/or the therapeutic drug of interest. To assess killing efficiency, different read outs can be performed such as LDH measurement and FACS-based analyses of apoptotic markers. In parallel effector cytokines of CTLs can be measured.



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Each project is different

Let's discuss how we can support your research by using our Cytotoxic T Lymphocyte-Mediated Killing Assays