

School of Biomedical Engineering, Science and Health Systems

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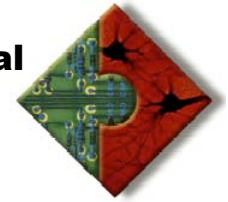
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Development of a Flow Cytometry Based Assay for Defective T Cell Signal Transduction in the Rotating Wall Vessel Bioreactor

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CLINICAL NEEDS

Dysfunction of T cell signal transduction is responsible for many immune-mediated diseases. Rotating wall vessel (RWV) bioreactors may offer a unique environment in which pathologies due to signaling dysfunction can be mimicked non-pharmacologically

GOALS

Develop a flow cytometry based assay to rapidly measure signal transduction by T cells cultured in an RWV bioreactor. Market this assay as a high throughput method for testing immune-ameliorative drugs in the RWV

APPROACH

- The RWV bioreactor prevents signal transduction through the T cell receptor (TCR, Figure 1).
- Similar inhibition gives rise to many pathological conditions (Figure 2)

This project seeks to:

- Mechanistically define signaling-inhibition in the RWV
- Identify a single “reporter” enzyme within the signaling pathway, whose activation is representative of the entire pathway
- Develop a flow cytometry based kit to rapidly measure activation of this reporter enzyme in response to stimulus administered in the RWV

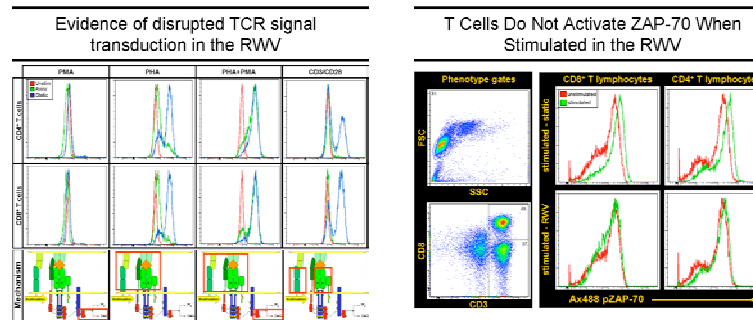


Figure 1: Culture of T cells in the RWV inhibits activation (Left) by preventing signal transduction (right)

Overview

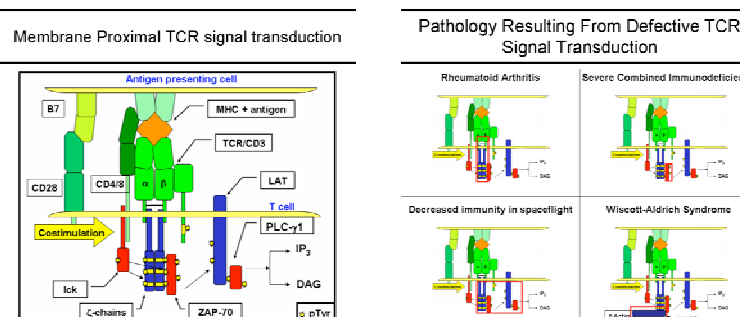
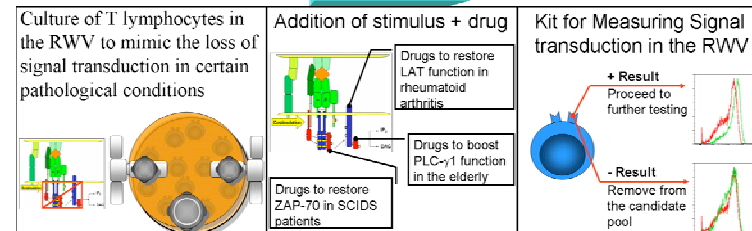


Figure 2. Signal transduction through the T cell receptor (left) is impaired in several diseases (right)

DELIVERABLES

Kit for the measurement of T cell signal transduction in the RWV including:

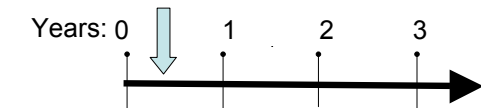
- Fixation and permeabilization reagents
- Fluorophore-conjugated primary antibody to the reporter molecule
- Bead-immobilized antibodies to CD3 and CD28 for stimulation of the cells

Timeline

Year 1: Mechanistically define the inhibition of T cell signal transduction in the RWV

Year 2: Correlate inhibition in the RWV to disease states. Identify a reporter molecule

Year 3: Final optimization of kit



Funding Required

From concept development to optimization of the product