A Novel Human Whole Blood Culture System Provides a Detailed and Long-Term Study of Immune Cell - Biomaterial Interactions

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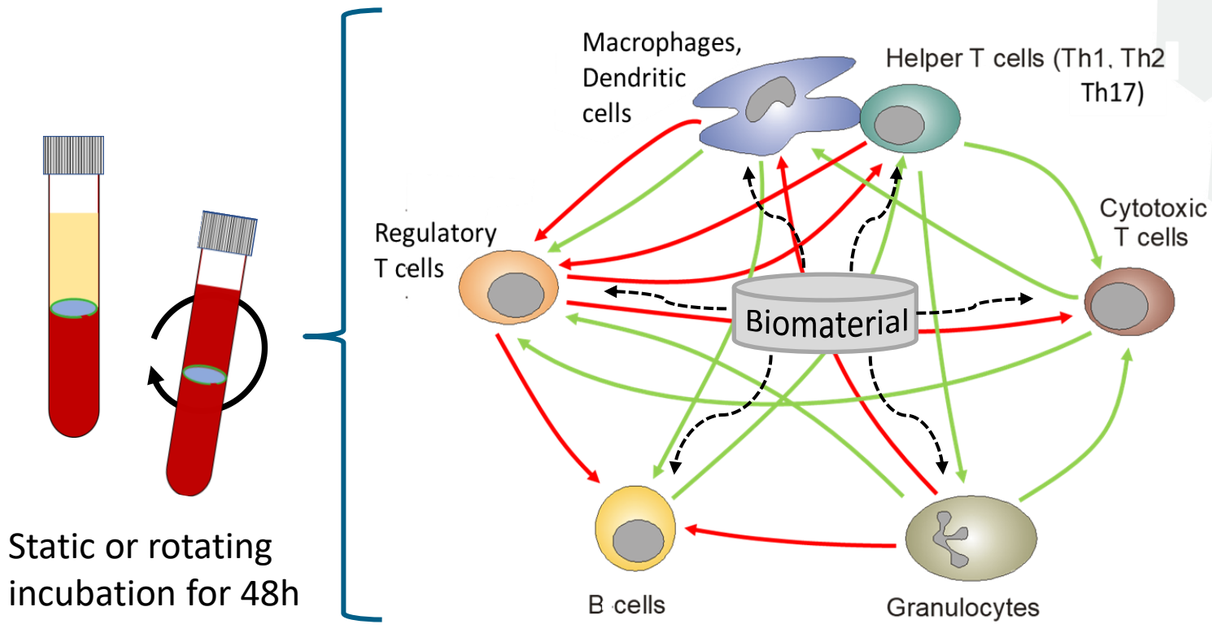
BACKGROUND & AIM

Biological evaluation is an essential part of the conformity assessment of novel implantable medical devices. Most of the described in vitro test systems are focusing on early hemocompatibility parameters. Therefore, incubation periods of > 4 hours are usually not intended.

However, interaction of immune cells with apparently hemocompatible materials over several hours or days can lead to immune cell activation, inflammation, sensitization and ultimately to rejection of implants.

Here we describe an innovative human whole blood culture model which enables long-term (up to 48h) and detailed investigation of immune cell-biomaterial interaction under in vivo like conditions.

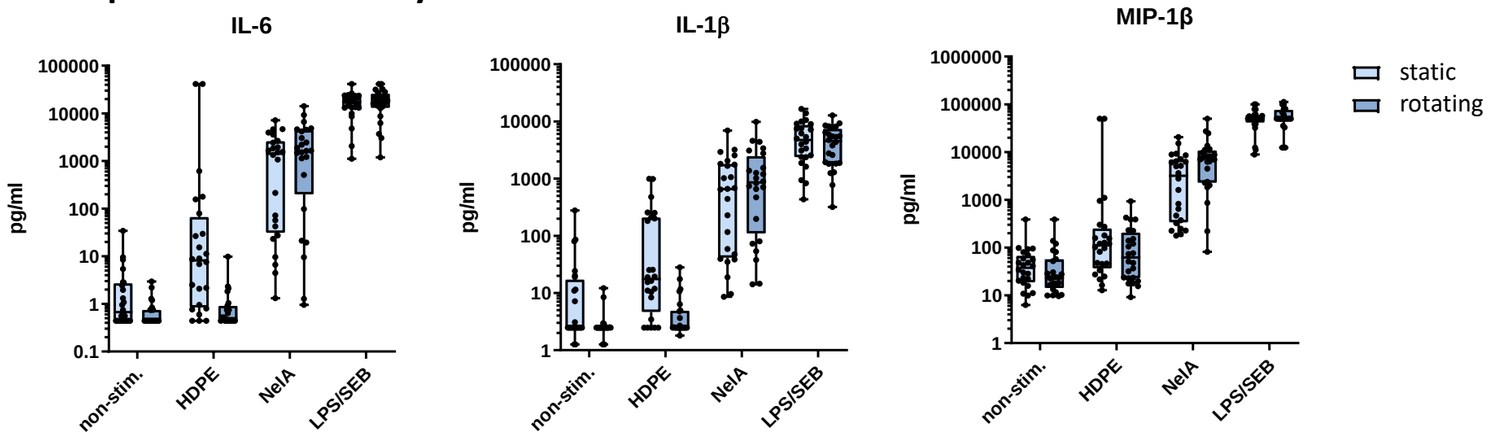
CONCEPT



Establishing a test system that provides a prolonged and complex study of immune cell - bio-material interactions.

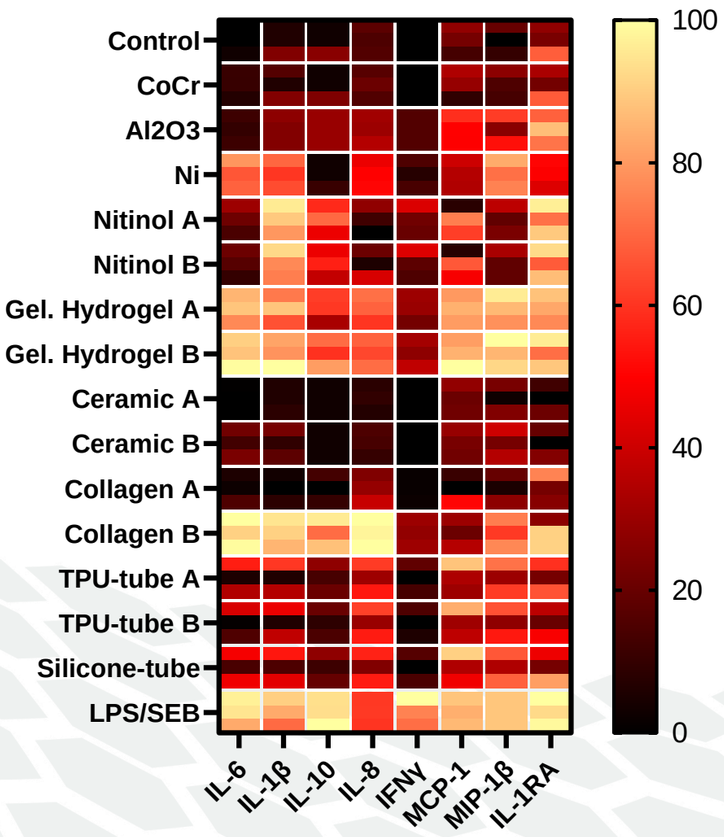
RESULTS

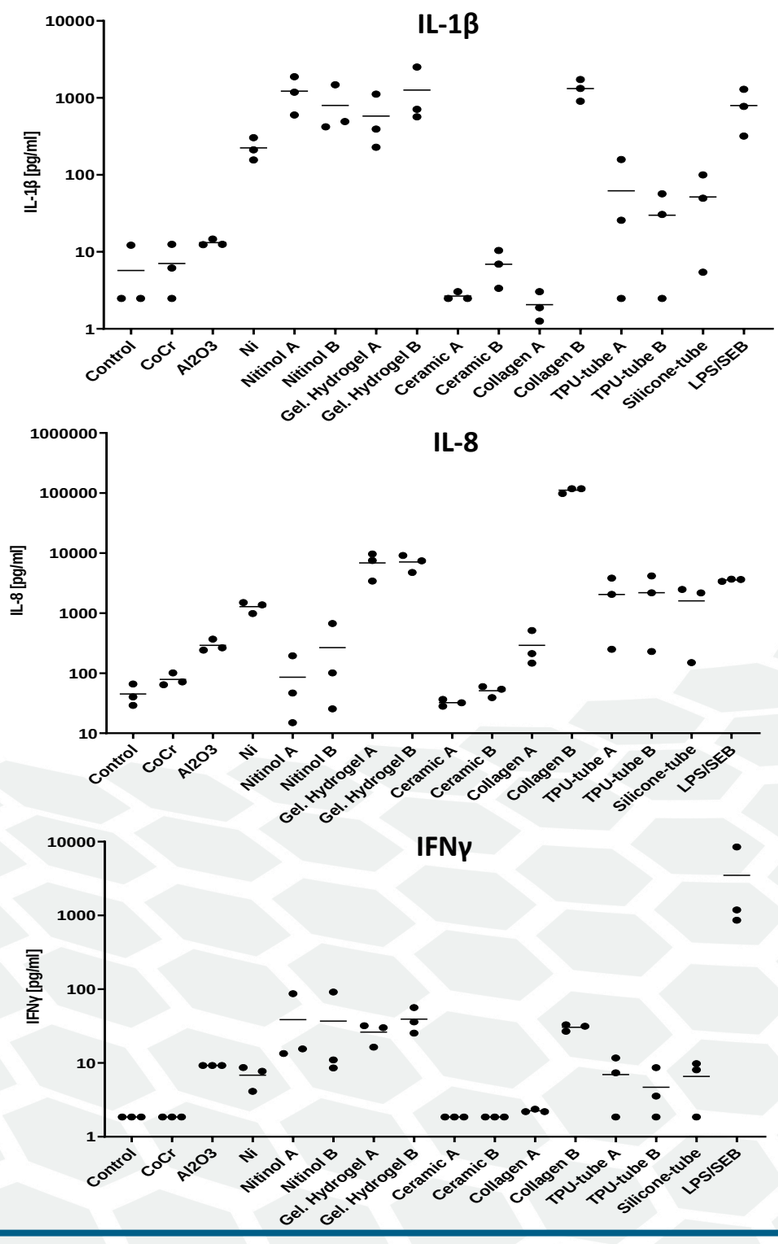
Development of the test system:



The novel test system revealed a strong and selective response to positive controls (Nel A & LPS/SEB). Switching from the static to the occasionally rotating system resulted in less activation of negative controls (non-stim. & HDPE), whereas immune cell activation by positive controls remained strong.

Investigation of representative biomaterials:





Native and surface-modified medical devices as well as raw materials were investigated in the novel test system, revealing material- and donor-specific reaction patterns of typical inflammatory cytokines and chemokines.

MATERIAL & METHODS

- **Cell culture system:**

All test materials were trimmed to fit into 3 ml tubes containing 2 ml of a custom-made cell culture medium and 1 ml fresh human whole blood.

The Tubes were incubated for 48 h at 37 °C either in a static or alternatively in an occasionally rotating system to increase immune cell contacts with the test materials.

- **Test Materials:**

Nelfilcon A and LPS/SEB Co-stimulated samples served as positive and stimulation controls. High density polyethylen (HDPE) and tubes without materials served as negative controls. All other materials were provided by different medical technology companies.

- **Blood donation:**

Heparinized blood (50 IU/ml) was collected from healthy volunteers by phlebotomy and used within 60 minutes after withdrawal.

- **Cytokine detection:**

Release of 30 mediators (e.g. IL-1β, IL-6, IL-8, IL-10, IFNγ, MCP-1, MIP-1β and IL-1RA) was measured using bead-based multiplexed sandwich immuno-assays on a Luminex 200™ analyser system.

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