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BASIC RESEARCH

Human Whole Blood Culture System Provides Insights into Biological and Immunomodulatory Properties of Implants Used in Oral and Maxillofacial Surgery

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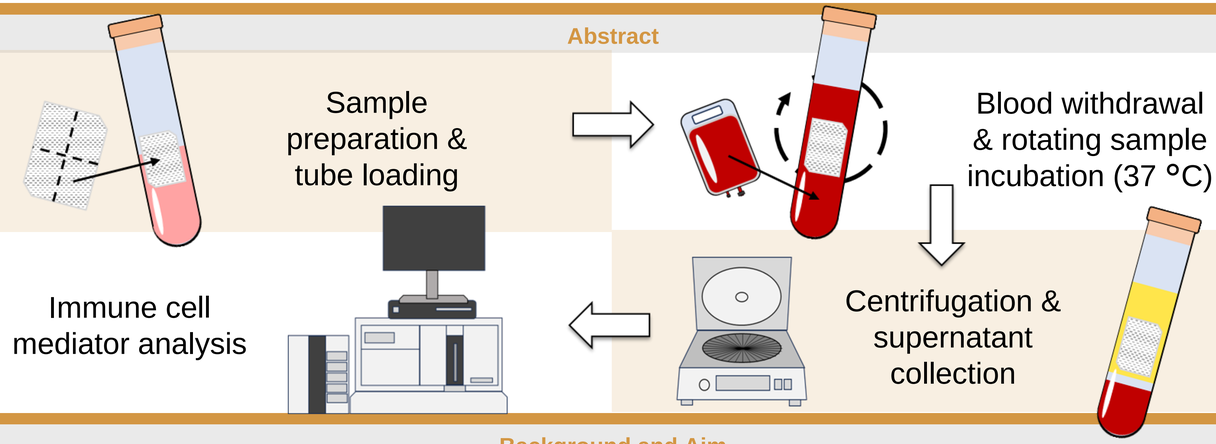
Abstract



Background and Aim

Predicting material-related responses *in vivo* remains a major problem in implant development. This is mostly related to the limited complexity of the used *in vitro* test systems (e.g. lacking of specific immune cell types), not allowing natural = complex cell-to-cell interactions and the investigation of a complete, *in vivo*-like reaction profile of the materials.

Here we present a novel whole blood culture system (tested with approved barrier membranes, used in oral and maxillofacial surgery), that provides an *in vivo*-like complexity to reliably reveal relevant insights in implant-immune cell interactions.

Methods and Materials

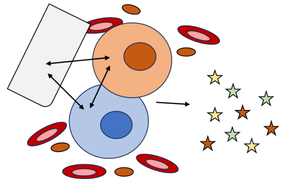
- All test membranes (Cytoplast: PTFE; Bio-Gide & OSSIX PLUS: Collagen; Tisse OS: PLGA) were incubated for 48 h at 37 °C in 3 ml tubes containing 2 ml of a custom-made cell culture medium and 1 ml fresh heparinized (50 IU/ml) human whole blood.
- LPS/TStim in suboptimal concentrations was used as stimulation control and to imitate inflammatory processes in oral tissue.
- Mediator adsorption was analysed using pre-stimulated supernatant pool of 3 donors.
- A total of 31 mediators were measured using ELISA or multi analyte profiling (MAP).

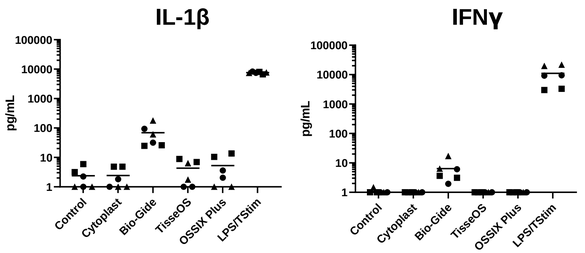
Conclusion

This novel human whole blood test system combines an *in vivo*-like complexity with an extended incubation time (48 hours) compared to most other *in vitro* test systems. This provides a reproducible and highly reliable method to sensitively detect immunomodulatory effects and complex reaction profiles of implant materials such as barrier membranes after contact with human whole blood.

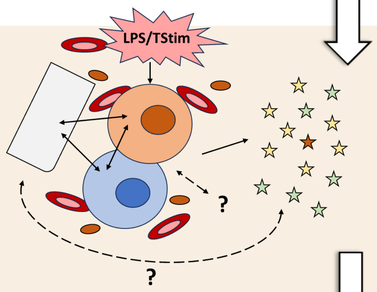
Results

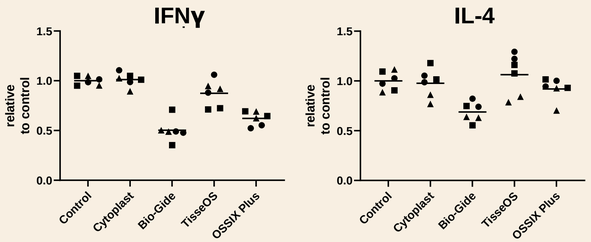
Barrier membranes reveal material-dependant mediator release in whole blood cultures



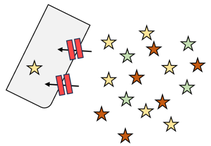


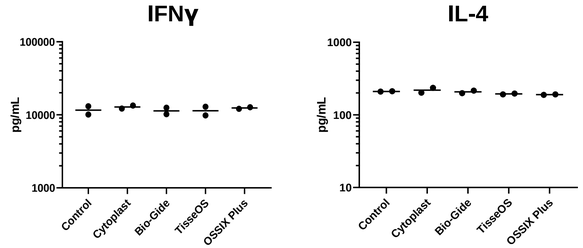
Material dependant reduction of T cell associated mediators under inflammatory conditions (LPS/TStim stimulated cultures)



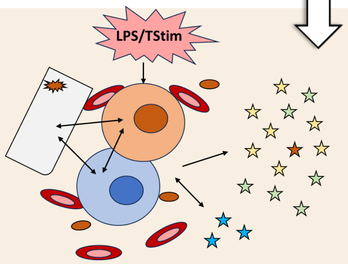


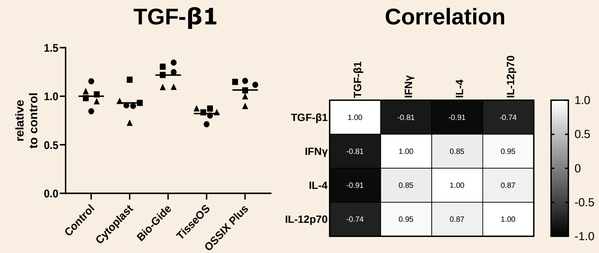
Reduction of T cell associated mediators is not related to adsorptive properties of the barrier membranes





Elevated TGF-β1 levels indicate a material-dependent balanced release between anti-inflammatory TGF-β1 and T cell associated mediators





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