

Abstract 1

New approaches for immunological medical product testing – Analysis of macrophage phenotypes in direct contact with the material surface

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Macrophages play a central role in tissue healing and regeneration at the implant site. The transition from an inflammatory (M1) to an anti-inflammatory (M2) macrophage phenotype is required to ensure a normal wound healing process, thus promoting the functional integration and the long-term stability of the implant. The implant itself, with its physical and chemical characteristics, may influence this transition in a positive or negative way. Safety and functionality has to be demonstrated for each implantable medical product. Biological safety testing, as for example testing for cytotoxicity according to ISO 10993 thereby concentrates on two scenarios: 1) Studies on extractable and leachable substances, and 2) studies focusing on the direct cell-material-contact. With regard to macrophage activation both test scenarios are of importance as macrophage polarization might be influenced by compounds released by the implant itself as well as by physical- and chemical features of the implant surface. We concentrate on developing test scenarios and new possible analysis strategies. Especially in the field of direct implant-cell-interaction we work on new analytical methods and tools which allow for fast and automatable determination of macrophage phenotype. We here introduce our approaches that may help to develop standardizable test scenarios for bio- and immunological testing of medical products.

Abstract 2

Biomaterial Testing 2.0 – New in vitro test system for the quantification of cell response in direct contact to the material

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For biocompatibility tests scientists rely on standardized, biocompatible plastic cell culture plates with known geometry and size of culture area. However, testing of solid biomaterial and implant material in this standardized plates is often challenging. First the biomaterial has to fit in the standardized well size. One major disadvantage of placing the biomaterial into a well is that plastic culture area surrounding the biomaterial is left and needs to be taken into account when evaluating the collected data. Additionally accurate prediction of cellular behavior around the edges and the bottom side of the biomaterial is complicated. This may also be a reason why quantitative analysis of biological response of cells in the direct contact to medical products are underrepresented in the biological testing guidelines like the ISO 10993. In this work, we introduce our lab solution for creating standardized wells on a wide range of solid biomaterials, which are fully comparable to cell culture well geometry. The system is adaptable to different material sizes and roughness as well as standard plastic and glass slides. Applications like quantification of direct cell contact assays, cell secretion assays or protein adsorption assays are easy to handle in our device thereby allowing replicable and multiple assaying on the same biomaterial. Here we describe the use of our device for the quantitative testing of macrophage polarization in direct contact limited to the biomaterial surface of interest.

Abstract 3

Specific cell model for immunological medical product testing – Cell line based macrophage model (M1/M2 switch)

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One of the main reason for aseptic loosening of implants, as the most important cause for implant failure, is the unsuccessful resolution of acute inflammation after implantation. Macrophages at the implant site drive this inflammation due to their activated inflammatory phenotype. Macrophages are known to remove pathogens causing an inflammatory environment and thereby recruiting other immune cells to the area of infection. The surgery as the initial event of implantation is said to cause a sterile inflammation mainly caused by damaged cells and tissue and to a less extent by pathogens. The cell damage provides a macrophage activating environment enriched on damage associated molecular pattern (DAMPs) leading to the activation and polarization of macrophages to the inflammatory (M1) phenotype. The transition of the inflammatory M1 phenotype to an anti-inflammatory phenotype (M2) represents the successful resolution of the inflammation and the initiation of the normal wound healing process. Implant materials should therefore ideally promote this transition of M1 to M2 macrophages or at least avoid influencing it (functionality and/or safety of the implant material). Why not to test this macrophage influencing properties of implantable medical products before they get in contact with the test animal or human body at the *in vitro* cellular level? For such a test the cell model should resemble the *in vivo* like conditions at the implant site as good as possible. Thereby the test should be fast, transferable, standardized and easy to analyze. Here we describe and show first results of our test scenario, which is based on a compilation of scientific approaches. It is appropriate for the testing of macrophage modulating properties of implantable medical products in the test scenario with direct cell-material-contact as well as in the indirect material test scenario (studies on extractable and leachable substances).

Biosketch: Juliane Spohn



Dr. rer. nat. Juliane Spohn earned her doctorate in 2013 at the University of Rostock in the working group Clinical Immunology. During her postdoc phase she worked in numerous projects with industrial partners and research institutions at OUK (Orthopediatric Clinic and Polyclinic) in Rostock till 2015 and gained knowledge in the field of immunobiological testing and development of biomaterials and appropriate test methods. In addition to the subject-specific suitability in the field of implantology and immunology, she is experienced in the planning, implementation and evaluation / documentation of *in vitro* and *in vivo* examinations. Juliane Spohn has been working at the Fraunhofer IKTS since 2016 and established her own Research group “Biological Materials Analysis” at the external location (Fraunhofer Institute for Cell Therapy and Immunology, IZI) in Leipzig.