PhD Project (e.g. P1)	Host institution	Start date (e.g. Month 6)	Duration (e.g. 48 months)	Supervisors (primary and co-supervisor)
P4	**FHCW**	**1**	**48**	**E. Riegel/T.Czerny/I. Giouroudi**

Project Title: Novel bioassays to predict interactions of medical devices and host cells

Hypotheses/Aims:

Novel materials or coatings for medical devices are in close contact to human tissue and for several applications (e.g., implants) and adherence and proliferation of host cells to the device/coating is essential. Standard biocompatibility tests include the analyses of migrates of the medical devices with toxicological assays. In this project we will concentrate on the cell attachment step and will establish biocompatibility assays with cells directly attached to the material or coating. For this we will adapt reporter cell lines previously developed in our group for type 4 allergy via detection of ARE pathway activity (skin sensitization; Mertl et al. 2019), inflammation via detection of NF-kB activation and genotoxicity (Pinter et al. 2021). Further, we will newly develop a dual luciferase reporter cell line for the analysis of attachment and proliferation of cells on medical devices or coatings. This should allow a direct quantification of the ability of the cells to attach and proliferate without the need of microscopy, which is often the limiting step with non-transparent materials. The use of secreted forms of luciferase for all assays will allow the study of the cellular behaviour over several days in time course experiments. The combination of bioassays covering different toxicological endpoints (skin sensitization, inflammation, genotoxicity) and markers for attachment and proliferation of cells directly in contact with the material/coating will give new insights into material-cell interactions and will allow a straight forward test regime for the development of new materials.

Short Description of the PhD project and Role of both Organizations (TUW & FH Campus):

Task 1: Adapt existing luciferase reporters for detection of pathways activities to secreted luciferases and generate new reporter cell lines in different relevant cell types (e.g., fibroblasts, muscle cells, endothelial cells). Test the novel cell lines under standard adherent conditions with model substances for each toxicological endpoint (FHCW).

Task 2: Design and test the format of material samples/coatings to apply it to the cell culture assays (TUW) and establish conditions for cell culture assays (FHCW).

Task 3: Newly generate a dual luciferase reporter for the detection of attachment and proliferation. The secreted Vargula luciferase will be expressed under a constitutive promoter and be a measure of viability, which will only be expressed by attached, living cells. A second secreted luciferase (secNluc) will be expressed under the promoter of a proliferation marker (e.g., Ki67, but other candidate genes will be tested during the project). This luciferase will therefore only be expressed by proliferating cells (FHCW).

Task 4: Generate ~10 material or coating samples (TUW) and analyse them with the newly generated test battery of luciferase assays (FHCW).

Expected Results:

- Novel assays for the analysis of the material properties to allow cell attachment and proliferation
- Novel assays for detection of material-cell interactions for the toxicological endpoints sensitization, inflammation and genotoxicity in time course experiments

Participating Faculty: E. Riegel, T. Czerny (FHCW), I. Giouroudi (TU)

Planned lab rotations:

FHCW: 42 months (Assay development and validation, sample analysis)

TUW: 6 months (3 months in year 1, 3 months in year 3): design and prepare test samples