Clinical impact of HyMedPoly: Drug-free strategies and their future implementation.

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Antibiotic drugs performed a triumphal procession by saving countless patients life. But in the last decades a dramatically increasing antimicrobial resistance (AMR) poses a dangerous threat to the global public health. We need new antibiotics (drugs), but additionally alternative, complementary antimicrobial strategies (drug-free) to promote the success of major surgery and the application of implants. Thus, biomaterials play an indispensable role in modern medicine. In this context drug-free antimicrobial hybrid biopolymers are becoming important for clinical applications as implant coatings, wound dressings and tissue engineering approaches to kill bacteria, prevent bacterial adhesion and biofilm formation. This will open the critical question how to evalute their biocompatibility best. The authors' hypothesis is that 3D human tissue constructs are more suitable to analyse this than 2D culture systems according to the DIN EN ISO standards only. As one example an in vitro 3D wound infection model based on human cells will be demonstrated here as an in vitro tool giving enough valuable response for the analysis of drug-free antimicrobial hybrid biopolymers. The 3D skin equivalent was obtained having both a dermal and an epidermal compartment, by embedding human primary fibroblasts in collagen type I and then seeding human primary keratinocytes on it to generate well differentiated epidermal layers. This model was specifically injured and inoculated with clinically relevant bacteria (e.g Staph. aureus) at wound site, to generate a 3D wound infection model (Figure 1). The model was comprehensively characterised by histostaining, immunohistochemical analysis (e.g. Anti-Cytokeratin 10, Cytokeratin 14, Laminin 5, Filaggrin antibodies), SEM and TEM. The bacterial adherence and localization within epidermal tissue was observed through confocal microscopy. Results demonstrated the architectural features of dermal and fully differentiated epidermal layers. Immunohistology demonstrated the details of epidermal markers and remodelled intercellular connective soft tissue. The in vitro wound infection model better relates to the in vivo situation for the evaluation of biological properties (antimicrobial activity, cytocompatibility, etc.) of drug-free antimicrobial hybrid biopolymers. Next step will be the evaluation of gene expression and cytokine levels by keratinocytes to identify model skin response to bacteria that will also help exploring host-pathogen interaction and thus the antimicrobial strategies.

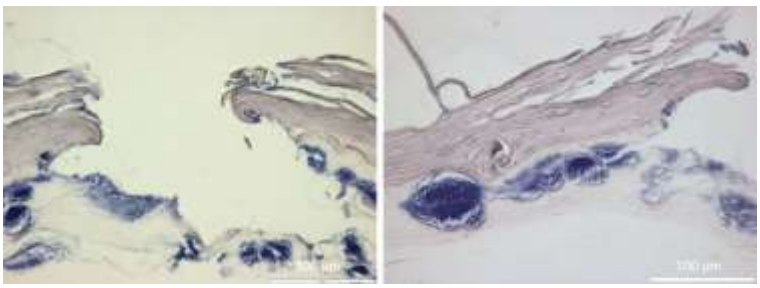

Figure 1: Cross-sections of the skin wound model inoculated with Staph. aureus. Bacteria are forming colonies in different compartments and separating the ECM and epidermal cell layers.

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