A novel 3D skin explant model to study anaerobic bacterial infection - DTU Orbit
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Skin infection studies are often limited by financial and ethical constraints, and alternatives, such as monolayer cell culture, do not reflect many cellular processes limiting their application. For a more functional replacement, 3D skin culture models offer many advantages such as the maintenance of the tissue structure and the cell types present in the host environment. A 3D skin culture model can be set up using tissues acquired from surgical procedures or post slaughter, making it a cost effective and attractive alternative to animal experimentation. The majority of 3D culture models have been established for aerobic pathogens, but currently there are no models for anaerobic skin infections. Footrot is an anaerobic bacterial infection which affects the ovine interdigital skin causing a substantial animal welfare and financial impact worldwide. *Dichelobacter nodosus* is a Gram-negative anaerobic bacterium and the causative agent of footrot. The mechanism of infection and host immune response to *D. nodosus* is poorly understood. Here we present a novel 3D skin *ex vivo* model to study anaerobic bacterial infections using ovine skin explants infected with *D. nodosus*. Our results demonstrate that *D. nodosus* can invade the skin explant, and that altered expression of key inflammatory markers could be quantified in the culture media. The viability of explants was assessed by tissue integrity (histopathological features) and cell death (DNA fragmentation) over 76 h showing the model was stable for 28 h. *D. nodosus* was quantified in all infected skin explants by qPCR and the bacterium was visualized invading the epidermis by Fluorescent *in situ* Hybridization. Measurement of pro-inflammatory cytokines/chemokines in the culture media revealed that the explants released IL1β in response to bacteria. In contrast, levels of CXCL8 production were no different to mock-infected explants. The 3D skin model realistically simulates the interdigital skin and has demonstrated that *D. nodosus* invades the skin and triggered an early cellular inflammatory response to this bacterium. This novel model is the first of its kind for investigating an anaerobic bacterial infection.

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