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# Emergent design of an hierarchically structured bio-intelligent scaffold for vasculogenesis and accelerated healing

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A novel solution has been developed for the unment clinical need for an effctive pro-angiogenic bio-intelligent biomaterial for reconstruction of skin loss wounds. Firstly the application of fibrin as a pro-angiogenic biomaterial was identified by 3D endothelial cell migration assays. A surgically feasible porous cross-linked fibrin-alginate biomaterial scaffold, Smart Matrix (SM), was formulated. Potential cytotoxicity was prevented by washing with a reducing agent, established by cytotoxicity and cell adhesion assays. Prototype material supported rapid ingress of endothelial cells in vitro. Engraftment of SM into porcine full thickness (FT) excision wounds demonstrated rapid vasculogenesis at 750 – 900µm depth from the wound bed over the first 7 days. The extent of celularisation and vascularisation in the FT model was maximised by optimisating formulation and manufacturing. Open porosity, 100µm pore diameter, enabled complete integration of 1mm thick material within 7d. This allowed a single step reconstruction with overgrafting of 150µm split-thickness skin graft. Resorption of the material takes 3-5wk which matches the rate of collagen deposition and remodelling. Wound contracture was around 35%, similar to refernece materials. The effect of SM was evaluated in a novel partial burn excision model of delayed wound healing. This demonstrated accelerated healing and switch from internal inflammatory granulation to exudatve regenerative neodermal tissue formation. This work exemplifies the value of such emergent strategies to develop bio-intelligent biomaterials. The approach has resulted in a vasculogenic bio-material which produces a non-fibrotic neodermis for full thickness skin reconstruction, with pre-clinical evidence of stimulating healing of delayed wounds.

## Biography

Julian Dye graduated in Biochemistry from The University of Oxford and gained a PhD in Physiology from Imperial College London for work on human placental mcirovascular endothelial behaviour. He then worked for a research charity in the field of reconstructive plastic surgery, where he invented a novel pro-angiogenic synthetic dermal replacement, Smart Matrix. He took the project through development, scale-up and translation to clinical cleanroom manufacuture and pre-clinical evaluation and commercialisation. Julian then joined the Open University and recently moved to a lectureship at IBME Oxford, to pursue research on bio-intelligent scaffolds.

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