

Project Number: CC001

Title: Cellular characterisation of the human cleft palate with clinical correlation

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Scientific Outline:

Complications after cleft palate repair occur in 15-20% of patients and require extensive surgery, however currently it is unpredictable which patients might develop them. This study aims to investigate the cellular and molecular mechanisms and interactions involved in human cleft palate development and its healing following surgery, including examination of the activity and role of the TGF- β superfamily of growth factors, which are involved in palatal fusion, in a novel model system. Cells isolated from patients with cleft palate in isolation (CP), where partial midline fusion has occurred, and combined cleft lip and palate (CLP), where no midline fusion has occurred, will be characterised and correlated with short-term clinical outcomes (fistula formation). We aim to establish 3D co-culture organotypic model of the human cleft palate to investigate palatal wound healing so predictors of surgical outcome can be translated into future treatment plans and risk assessments. Such an integrated approach has not been performed using tissues isolated from human infants to date.

A unique cleft palate tissue bank has been generated at the University of Birmingham Human Biomaterials Resource Centre (HBRC). Biopsies of human palatal tissue and blood samples have been collected and linked to patient details, type of cleft and cleft measurements. Specimens have been examined in paraffin sections for biomarkers (TGF- β 1/2/3, BMP), processed for gene expression analysis using real-time polymerase chain reaction (qRT-PCR) and will be used in cell culture studies to develop a 3D co-culture model of the human cleft palate. Cellular and tissue architecture analysis will be performed with digital image processing to investigate the interactions of epithelial and mesenchymal tissues, while 2D time-lapse microscopy will be used to assess healing characteristics (scratch-wound assay) of the cell types derived from the tissue bank. The short-term clinical outcomes (oronasal fistulae, developing within weeks of surgery) will be recorded and compared with experimental findings. The specimens from the Cleft Collective will be used as a comparator to the samples collected in Birmingham.