between patients receiving energy-based device treatments and aesthetic surgery, energy-based device procedures are a useful adjunct in managing patients' aesthetic concerns.

23. COMPREHENSIVE GENOME WIDE IDENTIFICATION AND FUNCTIONAL STUDY OF EPITHELIAL MESENCHYMAL TRANSITION GENES THAT REGULATE CLEFT PATHOGENESIS AND REGENERATION

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PURPOSE: RNA makeup of epithelium is regulated by binding proteins Esrp1/2 that govern epithelial mesenchymal transition (EMT), a central cell process that underpins embryogenesis and regeneration. Loss of Esrp1/2 results in global mRNA isoform dysregulation, resulting in orofacial clefts in all vertebrates. Given the central role of Esrp1/2 to regulate EMT, there is an urgent unmet need to understand its function.

METHODS: We applied advanced long read sequencing and RNA computation to comprehensively identify RNA isoforms genome wide, between wild-type and Esrp1/2 mutant mouse and zebrafish. Differentially expressed isoforms were prioritized based on biological pathway, relative abundance and isoform differences.

RESULTS: We found that >60% of isoform switches identified involved complex or combinatorial AS patterns, which are missed by standard short-read RNA-seq. We discovered novel isoforms that were absent from existing annotations, including in genes with important EMT functions. We discovered that a key transcription factor tp63 is regulated by esrp. Over-expression of tp63 isoforms was sufficient to rescue esrp1/2 mutant clefts.

CONCLUSION: We discovered that tp63 isoforms require esrp1/2 function, and that expression of specific tp63 isoforms is sufficient to rescue cleft palate of the esrp1/2 mutant. These results provide the scientific basis of a gene therapy strategy to exploit modulation of exon usage. We have also generated a EMT long-read RNAseq atlas that will inform broad research questions in cancer, embryology and regeneration.

24. SUB NORMOTHERMIC MACHINE PERFUSION IN THE NON-HUMAN PRIMATE PARTIAL FACE TRANSPLANT MODEL: A PRELIMINARY STUDY

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PURPOSE: Vascularized composite allografts (VCAs) face substantial challenges, particularly in immunosuppression and ex vivo preservation. Subnormothermic machine perfusion (SNMP) offers a promising alternative to conventional static cold storage for preserving and reconditioning VCAs. This study investigates our extended SNMP protocol, optimized for non-human primate (NHP) VCAs, and its effects on graft immunogenicity.

METHODS: Partial facial grafts were procured from non-human primates (NHPs) weighing 4-8 kg (n=6) and perfused for 18 hours with non-recirculating Steen+ solution under a low-flow, high-oncotic protocol. Parameters including pressure, flow, weight gain, metabolic markers (lactate, pH, O_2, ions) were monitored. Pre- and post-perfusion tissue and perfusate samples were taken for analysis of the immune compartment (FACS), cytokine and gene expression profile as well as tissue histology.

RESULTS: The grafts' mean warm ischemia time was 3 hours before perfusion. Following 18 hours of continuous SNMP, mean weight gain was remained below 10%. Perfusion parameters and histology indicated stable ex vivo metabolic equilibrium and well-preserved tissues. Immune cell viability was maintained in the skin, with no major perfusion washout effect noticed, and the cellular stress response to perfusion was characterized.

CONCLUSION: We present the first application of continuous SNMP in the NHP partial face transplant model, advancing understanding of the model's response to extended ex vivo preservation and establishing a foundation for future ex vivo therapeutic uses in conjunction with tolerance induction protocols.