evaluated and the implants were harvested at predetermined time points for analysis (n=6 animals per group). Histology and immunohistochemistry were performed to test if PHCS can enhance the therapeutic effects of STSG.

RESULTS: The hMSCs in HCS still maintain self-renewal and differentiation capacity after extended periods of culture. The TGF-β1, ANG1 and ANG2 amount in PHCS was higher than HCS (p<0.05) whereas the VEGF amount in PHCS was significantly lower than that in HCS (p<0.05). The HCS and the PHCS implantation significantly reduced skin contraction and improved cosmetic appearance relative to the STSG control group. The PHCS group experienced the least hemorrhage and necrosis, and lowest inflammatory cell infiltration. It also induced the highest neovascularization in early stages, which established a robust blood microcirculation to support grafts survival and tissue regeneration. Moreover, the PHCS grafts preserved the largest amount of skin appendages (including hair follicles and sebaceous glands) and developed the smallest epidermal thickness. The collagen deposition and fibril morphology in PHCS grafts were also similar to normal skin, indicating a lower degree of skin fibrosis. The superior therapeutic effect seen in PHCS groups was attributed to the elevated presence of growth factors and cytokines in the pre-vascularized cell sheet, which exerted a beneficial paracrine signaling during the early stage of wound repair.

CONCLUSION: The strategy of combining autologous STSG with PHCS implantation appears to be a promising approach in regenerative treatment of full thickness skin wounds.

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Requirement Of talin1 For Cell Proliferation During Palate And Mandibular Development In Zebrafish

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PURPOSE: The role of cytoskeletal proteins in craniofacial morphogenesis remains understudied. Critical cellular processes like cell morphological change, migration, proliferation and differentiation are coordinated to mediate craniofacial morphogenesis. These cellular processes require extensive interactions between cellular junctions and the extracellular matrix. Adhesion of cells to extracellular matrix is necessary for the development of multicellular organisms both functionally and structurally during embryonic development. The integrin family of cell adhesion molecules regulates interactions between cells and extracellular matrix. Talin (tln), an adaptor protein, is one of the several proteins that link an integrin subunit to the actin filaments. This link is essential to transmit force from the actin cytoskeleton to the extracellular matrix. Gene knockout studies in mice imply that tln1 plays an important role in the early morphogenetic events during embryonic development. However, the role of tln1 in the molecular and cellular mechanisms involved in craniofacial morphogenesis is poorly understood. Given the central role of tln as a cytoskeletal protein that interface with a number of key regulatory pathways, we hypothesize that tln1 is critical in regulating cellular processes that underlie craniofacial morphogenesis.

METHODS: The tln1 mutant line was generated from an insertion mutagenesis screen. The expression of tln1 was determined by whole mount in situ hybridization (WISH) during embryogenesis, and the level of expression was analyzed by quantitative and non-quantitative PCR. Craniofacial cartilaginous structures and muscles were examined by Alcian Blue stain and in the mylz2::mCherry transgenic respectively. Cell lineage tracing, morphology characterization, proliferation and apoptosis assays were performed in sox10::kaede and sox10::mCherry transgenic animals.

RESULTS: The tln1 homozygotes exhibit microcephaly and pericardial edema, and survive until 5 days post fertilization (dpf). WISH analysis shows that tln1 is#8232;expressed in the craniofacial region starting at 48 hours post fertilization (hpf). The mutant is a loss-of-function (LOF) allele demonstrated by quantitative PCR. Analysis of the craniofacial cartilage and muscles show that the lower jaw is shorter and highly malformed, the palate is shorter and the craniofacial muscles are disorganized. There is no observed defect in cranial neural crest cell (CNCC) migration and no increased CNCC death in the mutants. Pulse-chase analyses suggest that defects in directive cell proliferation in the CNCCs may be causing the palate anomalies. Further cell proliferation experiments via EdU and BrDu labeling are ongoing to validate these results.

CONCLUSIONS: Tln1 is required for craniofacial development: in formation of the palate, Meckel’s cartilage and a number of other ventral cartilage structures and the craniofacial muscles. We hypothesize that the cytoskeleton
and the associated machinery plays a critical role in craniofacial morphogenesis. The analysis of tln1, one of the proteins that link the cytoplasmic domain of integrin to the actin cytoskeleton, will lead to a better understanding of the involvement of the cytoskeletal network in craniofacial dysmorphosis.

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Changes in Skull Dysmorphology with Age in Unilateral Coronal Synostosis

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PURPOSE: While modern research on coronal craniosynostosis has vastly widened our breadth of knowledge regarding treatment of the condition, the mechanism underlying the development of the deformity remains uncovered and largely uninvestigated. This study evaluates midface and skull base development in nonsyndromic unilateral coronal synostosis (UCS), focusing on zygomatic and cranial base anatomical changes during the first year of life. Additionally, this study seeks to chronicle the changes over time in infancy in order to characterize the mechanistic progression of facial dysmorphology.

METHODS: CT scans from 50 subjects were reviewed (25 UCS, 25 controls) and CT DICOM data was digitized and reconstructed. Patients were stratified into five age groups all under one year of age. A series of 42 measurements focusing on the zygoma, orbits and cranial base were taken from the scans using Materialise Mimics software (Leuven, Belgium). Statistical analysis was performed using SPSS (Armonk, NY).

RESULTS: Starting at less than two months of age, significant differences are noted and persist in nasal and cribiform plate deviation (p=0.003). These differences are discernible in patients as young as 19 days old, except for the contralateral zygoma length, which only became noticeably higher in patients at the one month mark. At 2–3 months of age, the distance between the ipsilateral pterion to sella is significantly increased (p=0.003) and persists over time. Significant differences in contralateral zygomatic and orbital height and length are noted to develop and persist starting at 4–6 months of age. Patients under two months of age also demonstrated significant differences in the maxillary anteroposterior length (p=0.020), sella-basion distance (p=0.024), sphenoooccipital synchondrosis-basion distance (p=0.040), more acute orbital rim angle (p=0.037), reduced orbital width (p=0.039) and higher contralateral zygoma lengths (p=0.037) with non-uniform re-development of significant differences at later time points. A feature that was prevalent across all ages was the difference in angle of the sphenoid wing between the ipsilateral and contralateral side. The sphenoid wing ipsilateral to the fused suture consistently had a more acute angle from the midline, in comparison to the contralateral side. This difference was as high as 22 degrees in some patients.

CONCLUSION: Unilateral coronal synostosis results in characteristic bony changes, but the development of this facial dysmorphology has not been chronicled over time to elucidate an underlying mechanism. This study demonstrates that the earliest changes in UCS are ipsilateral orbital changes and nasal deviation beginning before two months of age. This is then followed by changes in the contralateral zygoma and orbit. Sphenoid wing asymmetry was present in all age groups. Additionally, the ipsilateral sphenoid wing angle was consistently more acute than the contralateral sphenoid wing angle through all age groups; this further supports skull base changes as early changes in the mechanistic progression of facial dysmorphology in unilateral coronal synostosis. An understanding of the timing of development of facial features of unilateral coronal synostosis is essential for determining the optimal timeframe for intervention, and for allowing the surgeon and patient’s family to anticipate the possible need for revision surgeries for specific features.

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Ability To Cope With Chronic Pain Puts Migraine Surgery Patients In Perspective

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PURPOSE: Migraine surgery candidates are chronic pain patients. However, chronic pain analysis tools are not typically applied to migraine surgery patients. This is the first migraine study to include the Pain Self Efficacy Questionnaire (PSEQ), which is used to determine patients’ coping