cells in response to distraction. Activation of this pathway induces a more primitive neural crest gene expression network, and the reversion of *d*-SSCs to a more developmental, NCC-like state is mechanoresponsive via FAK.

CONCLUSIONS: Here we provide evidence, for the first time, that controlled mechanical advancement of the lower jaw activates FAK signaling events which unlock gene regulatory programs normally active in cranial neural crest cells during facial morphogenesis, leading to an enhanced regenerative potential of tissue-resident SSCs in the adult mandible. Mechanotransduction via FAK in skeletal stem cells during distraction activates regulatory elements normally active in primitive neural crest cells. This reversion to a more developmental chromatin state underlies the robust tissue growth that facilitates stem cell-based regeneration of this adult tissue.

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08

Risk Factors for Airway-Related Complications Following Primary Palatoplasty: An Analysis of 3,616 Cases

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PURPOSE: The present study examined risk factors associated with 30-day palatoplasty complications based on multivariate analysis of the NSQIP dataset.

METHODS: Primary palatoplasties were identified in the 2012–2015 Pediatric NSQIP database. Cases were analyzed with multivariate regression to investigate predictors for oronasal fistula/infection, airway complications (unplanned intubation or ventilation), length of stay (LOS) >3 days, and readmission. A sensitivity analysis was performed to determine whether increased operative time portends increased airway complications.

RESULTS: 3,616 patients were included. Mean age at operation was 12.2±3.8 months and mean operative time was 135.4±67.5 minutes. Thirty-day complication rate was 7.6% overall, including 3.4% oronasal fistula/infection, 2.0% airway complication, 2.4% readmission, and 0.9% reoperation. 5.1% of patients had a LOS >3 days. Oronasal fistula/infection were not predicted by comorbidities, demographics or operative time. ASA class ≥3 (OR=3.04, p=0.022) and nutritional support (OR=3.19, p=0.024) predicted airway complications; sensitivity analysis also revealed operative duration >135 minutes was predictive (OR=2.79, p=0.009), increasing further when >225 minutes (OR=5.071, p=0.001). LOS >3 days was predicted by experiencing airway complications (OR=17.37, p<0.01), but preoperative ventilator dependence was protective (OR=0.08, p=0.008). Mean LOS was 1.6±1.8 days without an airway complication versus 5.0±4.3 with. Readmissions were increased for patients with nutritional support (OR=3.14, p=0.010), but decreased with premature birth (OR=0.248, p=0.012).

CONCLUSIONS: This report represents the largest nationwide cohort of palatoplasty patients analyzed to-date. Analysis of these multi-institutional data demonstrate that airway complications with palatoplasty are increased with higher ASA class, requirement of nutritional support, and increasing operative time.

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09

Changing The Paradigm For A Rare Genetic Disease That Is Currently Contraindicated For Surgery and Lacks Alternative Treatments

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PURPOSE: Heterotopic ossification (HO) is a debilitating formation of ectopic bone restricting joint mobility and causing chronic pain. Fibrodysplasia Ossificans Progressiva (FOP) is a congenital variant of HO caused by a genetic mutation in a bone morphogenetic protein receptor that causes severe, progressive lesions resulting in immobility and often fatal mechanical respiratory failure at a premature age that currently lacks a cure. With increased proclivity for osteogenesis at baseline, surgical excision of bony lesions is contraindicated in FOP patients due to universal recurrence. We have previously shown that rapamycin is a powerful drug which can eliminate lesions in mouse models of FOP. Here, we demonstrate that combination therapy with low-dose rapamycin and the BMP receptor inhibitor LDN-212854 presents an option to prevent both primary HO and post-excision HO in an FOP mouse model.

METHODS: Within the recurrence study arm, $ACVR1^{R206H/+}$ P21 mice received inductive Ad.cre and cardiotoxin (CTX) injection in bilateral hindlimbs. Three weeks later, mice were live-scanned with *in vivo* μCT, reinjected with Ad.cre bilaterally, and underwent HO excision at the 3 week timepoint. These mice were randomized to daily rapamycin (5 mg/kg, n=12) or PBS (n=8) for 3 weeks with endpoint μCT. For low-dose rapamycin and LDN adjunctive therapy, 16 mice were stratified into low dose rapamycin (0.5 mg/kg, n=10, both hindlimbs of 5 mice), rapamycin and LDN212854 (0.5mg/kg and 0.6mg/kg respectively, n=8), and injection control (PBS, n=14) cohorts for daily injections. They were subsequently induced as previously described, with additional second and third CTX booster series on post-operative day 3 and 7. Mice were scanned with μCT 3 weeks later. Contours were drawn manually by blinded experts around HO to compute total volumes (800HU). Recurrence cohorts were analyzed by log-transform/ANOVA/post-hoc Hochberg and low-dose results were analyzed similarly with restriction to right legs only.

RESULTS: In post-surgical mice, PBS injection showed statistically similar HO volumes to baseline volumes of pre-excision mice (p=0.054). However, rapamycin treatment significantly reduced the post-surgical HO volume 11-fold (p=.044,). In the primary HO model treated with low-dose rapamycin/LDN, mice treated with rapamycin for 21 days showed 17-fold less ectopic bone (p=0.001) compared to PBS vehicle injection, paralleling a 9-fold reduction (p=.003) when treated with rapamycin plus LDN212854 adjunct.

CONCLUSIONS: These studies demonstrate that rapamycin prevents primary development of HO and is also effective in preventing post-surgical recurrence in a FOP mouse model. Furthermore, rapamycin with and without LDN adjunct remains effective at preventing primary development of HO even at lower concentrations. This study further corroborates rapamycin as a promising candidate for primary and post-surgical HO prophylaxis in children with FOP, with opportunities for subsequent dosing studies and adjunct therapies to minimize prohibitive adverse effects. Existing literature implicates similar molecular mechanisms among various etiologies of HO, suggesting a putative role for rapamycin even beyond FOP in post-traumatic and post-surgical HO patients.

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