effects of ADM can serve to improve TE in compromised tissue beds, as seen in patients undergoing TE concurrent with perioperative radiation therapy.

FRIDAY, JUNE 11, 2021: BREAST/AESTHETIC/GENDER AFFIRMATION TOP SCORED ABSTRACTS

1

Iqgap1 Signaling Promotes Foreign Body Response To Biomedical Implants

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Purpose: The longevity of biomedical implants is limited by adverse implant-tissue interactions leading to implant failure. In almost all cases, implant failure occurs due to a phenomenon known as the foreign body response (FBR). FBR is characterized by fibrous capsule formation around implanted devices, leading to implant malfunction as well as distortion of the surrounding tissue. In the context of breast implants, FBR leads to capsular contracture, which is the cause of a significant proportion of all breast implant failures. Despite the high prevalence of FBR-mediated implant failure, the underlying mechanisms of FBR are incompletely understood. Our work utilizing mass spectrometry has demonstrated that when compared to healthy subcutaneous tissue, foreign body capsules in mice and humans display an up-regulation of IQ Motif Containing GTPase Activating Protein 1 (IQGAP1), a scaffolding protein involved in multiple mechanotransduction pathways. Based on these findings, we sought to investigate which cellular subpopulations express IQGAP1 as well as its role in mechanotransduction pathways mediating the development of FBR.

Methods: To verify the importance of IQGAP1-mediated signaling in FBR, we employed a murine model of mechanically stimulated silicone implants (MSI), which were implanted subcutaneously in wildtype (WT) and IQGAP1+/- haplo-insufficient mice to compare the effect of human levels of mechanical stress on FBR. Homozygous IQGAP1 KO mice have been previously reported to harbor a fragile phenotype, more prone to pulmonary vascular damage and gastric pathologies. Haplo-insufficient mice were utilized in these experiments in order to prevent potential systemic complications from elevated levels of mechanical stimulation produced by the MSI model. We explanted the foreign body capsules from IQGAP1+/- haplo-insufficient and WT mice and performed single-cell RNA sequencing (sc-RNA-seq) on cells isolated from the capsules. We histologically assessed the quantity as well as maturity of collagen deposition using Masson’s Trichrome and Herovici staining of tissue sections from explanted foreign body capsules. Moreover, immunostaining for the mechanotransduction related proteins alpha-smooth muscle actin (α-SMA), phosphorylated focal adhesion kinase (p-FAK), phosphorylated cell division control protein 42 (p-cdc42), and phosphorylated extracellular signal-regulated kinase (p-ERK1/2) was performed to assess the impact of IQGAP1-deficiency on the protein level.

Results: We found that IQGAP1-deficient mice displayed a significantly reduced FBR as evidenced by thinner capsules, lower levels of collagen deposition, collagen maturity, and myofibroblast activation. Our scRNA-seq analysis revealed a depletion of mechanoresponsive myeloid cells in IQGAP1-deficient mice. This was confirmed on the protein level by a significantly reduced expression of α-SMA, p-FAK, p-cdc42, and p-ERK1/2 in foreign body capsule tissue from IQGAP1-deficient mice compared to WT mice.

Conclusion: Our results highlight the important role of IQGAP1 as a critical early stage mediator of mechanotransduction pathways contributing to the development of FBR. Further, we show that IQGAP1 plays a role in modulating the innate immune response to synthetic implants. Therefore, IQGAP1 may be a promising target for the development of novel therapeutics to limit the development of FBR around biomedical implants.

2

Tranexamic Acid Is Associated With Decreased Intraoperative Blood Loss And Wound Healing Complication Rate In Penile Inversion Vaginoplasty

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Purpose: Penile inversion vaginoplasty (PIV) is the most common gender affirming genital procedure for transfeminine patients. The purpose of this study was to investigate the impact of tranexamic acid (TXA), an antifibrinolytic, on bleeding and bleeding-related complications in vaginoplasty surgery.

Methods: Retrospective chart review was performed on patients undergoing PIV from February 2018 through March 2020 by the senior author (K.G.) at the University of Wisconsin Hospital and Clinics. Patients who received TXA received a combination of topical and intravenous TXA. Data collected includes patient demographics (age, body mass index, race, comorbidities, and tobacco and illicit drug use), intraoperative data (duration of surgery, estimated blood loss, fluid administration, TXA use and dose, and complications), and postoperative data (drain output, complications within 30 days, and revision surgery). Subgroup analysis on the effect of TXA was performed using independent sample t-test.

Results: Seventy-four patients were included in this study with 56 patients receiving TXA and 18 patients who had surgery prior to initiation of TXA protocol. There were no thromboembolic events observed in the TXA or the non-TXA group. Ninety percent of all complications were Clavien-Dindo Grade 1 and did not require intervention. There was a significantly lower EBL in the TXA group compared to the no TXA cohort (299.1 ± 64.3 vs. 347.2 ± 84.8, p=0.013). Patients who received TXA had significantly fewer wound related complications than those who did not receive TXA (21.4% vs. 66.7%, p<0.0001). Similarly, there were fewer neo-vagina skin graft failures in the TXA group, though this did not reach significance (0.0% vs. 11.1%, p=0.057). There was no significant difference in drain output between the two groups.

Conclusion: No thromboembolic events were observed with intravenous and topical tranexamic acid use in transfeminine patients undergoing penile inversion vaginoplasty surgery. TXA was also associated with lower intraoperative blood loss as well as fewer wound healing complications. Further research is needed to further study its use in gender affirmation surgery.

3

Vitamin D Improves Autologous Fat Graft Retention

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Purpose: Autologous fat grafting is a widely used technique in aesthetic and reconstructive surgery, however, unpredictable volume reabsorption may lead to unsatisfactory outcomes. Previously, we demonstrated that a fat-soluble Vitamin D3 analogue, calcitriol, significantly improved fat retention in a xenograft mouse model by 25% across multiple donors when injected systemically (p < 0.05). While calcitriol has minimal toxicity, is FDA approved, and has positive immunomodulatory and antioxidant properties, systemic administration bypasses key Vitamin D synthesis regulatory steps, thus increasing risk with high-dose use. We hypothesize that systemic supplementation with Vitamin D3 (cholecalciferol) will likewise improve fat-graft retention similar to calcitriol while avoiding potential regulatory and iatrogenic risk. In this study we compared in vivo human fat graft retention in mice treated with systemic cholecalciferol, calcitriol or vehicle control in a mouse xenograft model. In vitro adipose lipoaspirate culture was used to interrogate the therapeutic mechanism of action.

Methods: Lipoaspirate was harvested from 6 unique donors using a 2mm cannula and used in parallel for both in vitro and in vivo studies. In vivo: 0.3mL of lipoaspirate was injected bilaterally on dorsal flanks of homozygous Foxn1nu immunocompromised mice. Calcitriol (50ng), cholecalciferol (50ng, 500ng, 5000ng) or vehicle control was administered thrice weekly by IP injection. Graft volume retention was measured at 12 weeks. In vitro adipose lipoaspirate culture was used to interrogate the therapeutic mechanism of action.

Terminal analyses include tissue weight, stromal cell viability, concentration of active vitamin D metabolite (1,25(OH)2D3), and gene upregulation by qRT-PCR.