surgeries are: 1 day, 1 week, 1, 3, 6, 12 months post surgery. CS and DELP metrics are measured at each visit. For study interventions, all subjects (from both arms) will undergo the same series of tests, in the same sequence at each visit. Phase 1 of the visit focuses on CS and phase 2 on DELP. These interventions are as follows: first, subjects will receive Drop A; Drop A will be administered in a randomized, double-blinded manner at each visit to either balanced salt solution (control) or Muro 128 5% hypertonic saline (experimental). Drop A will be administered to both eyes. After receiving the drops, subjects will complete a visual analog scale questionnaire to grade their corneal sensitivity. Next, subjects will undergo a five minute washout. After the washout, subjects will receive Drop B; Drop B will be whichever drop was not administered in the Drop A phase. After Drop B is given, subjects will complete the visual analog scale. To begin phase 2, subjects will be given the Ocular Surface Disease Index to record dry eye signs and symptoms. Finally, tear film parameters will be collected using Schirmer's tear production test and tear film breakup time. Study Population. - Inclusion criteria: For retrospective cohort studies, subjects who have undergone unilateral SB or PV in the past year. For prospective cohort studies, subjects who will undergo unilateral SB or PV in the near future, and age-matched controls. Exclusion criteria: For both retrospective and prospective arms, the same exclusion criteria apply. They include: a previous diagnosis of dry eye; current use of neuropathic pharmacotherapies (including gabapentin, pregabalin, TCAs, SNRIs, carbamazepine, and opioids). RESULTS/ANTICIPATED RESULTS: As of 11/15/18, only the scleral buckle retrospective study arm had enough subjects for any meaningful preliminary report; the arm currently has 8 subjects. Of these 8 subjects, 5/8 subjects report increased surgical-eye corneal sensitivity and 6/8 show discordant dry eye symptoms and tearfilm parameters. Our power analysis showed that N=16 subjects in a group are required to detect a statistical significant difference in corneal sensitivity response. We expect to see a relapsing and remitting pattern of pain (as measured by corneal sensitivity and dry eye questionnaire), as is typical of neuropathic pain. Regarding dry eye symptoms, we anticipate subjects will have prominent dry eye symptoms (as measured by a validated questionnarie), but show no abnormalities in tearfilm parameters. DISCUSSION/ SIGNIFICANCE OF IMPACT: To our knowledge, this is the first observational study of neuropathic pain symptoms of corneal sensitivity and dry-eye like pain, in post retinal surgery patients. We recognize the challenge of diagnosing neuropathic pain; currently the gold standard is clinical. However, symptoms of neuropathic pain are nonspecific and subtle. Identification of a population suffering from post-retinal surgery ocular neuropathic pain will provide a foundation to test topical naltrexone as a diagnostic tool. If our hypothesis is correct, topical naltrexone could serve as a cheap, easy, and quick diagnostic test for ocular neuropathic pain. We envision this diagnostic test would allow many misdiagnosed and mistreated post-surgical patients to be treated with appropriate therapies aimed at neuropathic etiologies.

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Neural connectivity mechanisms linking off-time pubertal development and depression risk in adolescence

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OBJECTIVES/SPECIFIC AIMS: Earlier pubertal timing has been associated with risk for depression, particularly in girls (e.g., Keenan et al., 2014). Evidence suggests pubertal timing in girls also relates to alterations in the microstructural properties of brain white matter tracts in late adolescence (Chahal et al., 2018), and structural connectivity of cingulate and frontal regions (Chahal et al., in prep), though differences in pubertal development in both boys and girls have not been examined in the context of brain functional connectivity (FC). Individual differences in the course of puberty may have enduring effects on functional coupling among brain regions that may contribute to the risk for psychopathology. To address this question, we explored the relation between pubertal timing and tempo with depression symptoms (age 16). Then, we examined whether brain network FC (age 16) associates with pubertal indices and predicts concurrent and later depressive symptoms (age 18). METHODS/ STUDY POPULATION: Sixty-eight adolescents (37 females) completed the Mini-Mood and Anxiety Symptom Questionnaire (MASQ; Clark & Watson, 1995) at ages 14-18. Gompertz growth curve modelling of pubertal development (age 10-15; Waves 1-6) was used to estimate pubertal timing and tempo per individual, separately for males and females (e.g., Chahal et al., 2018). Resting-state MRI data (age 16) were parcellated into 264 cortical and subcortical regions to create region-to-region FC matrices based on correlations of time-series. Individual matrices were fed to the GraphVar program (Kruschwitz et al., 2015) to assess the interaction of pubertal timing and pubertal tempo with functional network connectivity using Network-based statistic (NBS; Zalesky et al., 2010). Subnetworks showing alterations in relation to pubertal timing and tempo were then examined in association with concurrent (age 16) symptoms and used to predict future depressive symptoms (age 18). RESULTS/ANTICIPATED RESULTS: In all youth, earlier pubertal timing was associated with higher depressive symptoms at age 16 ($p<.018$). This association was stronger in girls with slower pubertal tempo ($p<.039$). Interregional connectivity analyses revealed that the interaction of earlier pubertal timing and slower tempo was associated with lower FC between the left cingulate gyrus and right precuneus ($p<.0001$), regions implicated in emotion processing (i.e., Affective Processing Network) and self-referential thinking (i.e., Default Mode Network). FC of the three other emotion- and self-referential processing network regions (i.g., left insula, superior parietal lobule, and precuneus) was lower in youth with greater age 16 depressive symptoms ($p<.0001$). Finally, lower FC of of the left and right inferior parietal lobule predicted greater depressive symptoms at age 18 ($p<.0001$). In summary, FC of overlapping affective and default mode network areas was related to earlier pubertal timing and higher concurrent and future depressive symptoms. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings demonstrate individual differences in pubertal maturation are associated with depressive symptoms and differences in brain connectivity in mid-adolescence. Early pubertal development was associated with greater depression symptoms and lower FC of brain regions involved in emotion regulation and self-referential processing. Further, FC between these regions predicted higher depression symptoms two years later. These neurobiological mechanisms may, in part, underlie the link between off-time pubertal development and the risk for depression. These findings also have important implications for precision psychiatry, as we show that a risk-factor of depression (early pubertal timing) may manifest in developing neurobiology in region-specific ways. Previous network models of depression (e.g., Li et al., 2018) implicated affective network connectivity in sustained negative mood and the default mode/ self-referential network in rumination. Other networks implicated in these past models include the reward network, which may be involved in anhedonia and loss of pleasure. Our study only found associations between affective and self-referential regional connectivity, pubertal

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maturation, and depression, suggesting that pubertal risk factors may relate more closely with emotion-regulation and self-referential processing deficits.

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Optimization of chondrogenesis on 3-dimensionally printed porous tissue bioscaffolds for auricular tissue engineering

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OBJECTIVES/SPECIFIC AIMS: This study's aims are to optimize the isolation and growth of chondrocytes from pig auricular cartilage; to identify the ideal seeding conditions onto 3D printed auricular bioscaffolds to maximize chondrocyte growth; and to investigate what quantity and types of host tissue can grow on the bioscaffold. Primary outcomes will include comparisons between different seeding conditions in various objective measures of bioscaffold growth and survival as listed in the methods section. Secondary outcomes will include continued optimization of bioscaffolds to minimize extrusion rates and maximize morphologic and histologic similarity to human auricular cartilage. METHODS/STUDY POPULATION: For chondrocyte-seeded scaffolds, cartilage will be collected from freshly harvested porcine auricular tissue and digested in type II collagenase. Chondrocytes derived from the harvest will be seeded into auricular PCL scaffolds using a type I collagen/hyaluronic acid composite gel, which has been previously shown to support chondrogenesis. For scaffolds containing cartilage, punch biopsies will be collected and embedded in specific areas of the scaffold previously shown to experience excessive stress/strain compared to the rest of the construct. From there, five of each chondrocyte-seeded bioscaffolds, chondrocyte-unseeded bioscaffolds, and cartilage-containing bioscaffolds will be implanted into athymic rats. Total follow up will be for six months, with outcomes as measured by clinical assessments, morphologic measurements, radiological imaging, histological analysis, biomechanical evaluation, and photodocumentation. Once these measures are obtained, we will work closely with Dr. Myra Kim, an adjunct professor with the Biostatistics Department, to appropriately analyze differences between the models. RESULTS/ANTICIPATED RESULTS: We believe that while all scaffolds (chondrocyte-seeded, chondrocyte-unseeded, and cartilage-containing) will be structurally sound, the chondrocyte-seeded scaffolds and cartilage-containing scaffolds will exhibit improved soft tissue coverage and have lower exposure and fracture rates. Additionally, between the two, we posit that there will not be appreciable differences histologically, radiologically, or morphologically. DISCUSSION/SIGNIFICANCE OF IMPACT: Auricular reconstruction is a geometrically complex and technically challenging problem. Reconstruction hinges on the physical characteristics of the deformity, patient preferences, and reconstructive materials available. The current gold standard for auricular reconstruction uses autologous rib cartilage as foundational support for overlying soft tissue and these techniques involve freehand carving of the cartilage, requiring high levels of technical skill. Harvesting the materials for this procedure is invasive, and the outcomes of the surgery are largely variable and sometimes undesirable. As alternatives, implantable scaffolds including those made from high density porous polyethylene (commercially referred to as MedPor) have been investigated. However, many of these have proven inadequate due to factors including infection, extrusion, and morphologic and biomechanical dissimilarity from native tissue. 3D printing represents an exciting new avenue through which to address many of these difficulties. Our group has previously demonstrated the successful design, production, and implantation of 3D-printed models: in auricular reconstruction, we have demonstrated the successful creation and implementation of a 3D printed ear scaffold into an athymic rodent model. We now turn our attention to optimization of seeding of our ear scaffold with chondrocytes derived from porcine auricular cartilage or with cartilage punch biopsies, all while maintaining emphasis on regulatory feasibility. With success in this arena, we will be able to provide a much less invasive and technically challenging alternative to the current gold standard, create patient-specific bioscaffolds which are more form fitting and individualized, and provide children with ear malformations better alternatives and treatments for their conditions.

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Patient Attitudes Survey to Guide Development of a Cell Replacement Device for the Management of Type 1 Diabetes

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OBJECTIVES/SPECIFIC AIMS: This study aims to estimate patient attitudes and receptiveness towards stem cell-based cell replacement devices to management Type 1 Diabetes. The primary outcomes of this study are mean response values to questions interrogating patient attitudes, knowledge, and receptiveness. METHODS/STUDY POPULATION: A RedCap survey was generated for this study. 100 participants will be drawn from Mayo Clinic Rochester, MN patients living with Type 1 Diabetes. RESULTS/ANTICIPATED RESULTS: Response values will be used to estimate broader patient attitudes. DISCUSSION/SIGNIFICANCE OF IMPACT: The response values of this survey will help inform future directions of cell replacement device development. Additionally, understanding patient attitudes may be useful in crafting more effective education strategies.

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Production of Engineered Cardiac Tissue for Disease Modeling

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OBJECTIVES/SPECIFIC AIMS: Cardiovascular diseases (CVD) is the leading cause of death worldwide in both men and women due to lack of cardiac regeneration after disease or damaged is caused. There are many challenges to studying CVD since native cardiomyocytes cannot be cultured in vitro. With the advancements in biomaterial and pluripotent stem cells research, scientists are now able to produce engineered cardiac tissue models in vitro that mimic the native myocardium. This study shows our methods for producing engineered cardiac tissue with potential applications in cardiac regeneration, disease modeling, and scalable production. METHODS/STUDY POPULATION: In this study, human induced pluripotent stem cells (hiPSCs) were combined with two different photocrosslinkable hybrid biomaterials, poly (ethylene)- glycol fibrinogen (PF) and gelatin methacrylate (GelMa), in various tissue geometries to form 3D human engineered cardiac tissues (3D-hECTs). To study

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