identified and prevalence was compared to general population data.

**Results:** Average age was 47.6 ±13.8 years (19-74). Prevalence of CTS was 13.8% (n=15). In the CTS group, eleven subjects presented with physician confirmed diagnosis of CTS that led to surgical release, one had EMG documented CTS and three had a physician confirmed diagnosis of CTS with no surgery to date. The prevalence of clinically certain CTS in the general population ranges from 3.8% to 7.8%.

**Conclusion:** CTS is significantly more prevalent in patients undergoing migraine surgery than the general population. (1.7- 3.5-fold). These remarkable findings warrant further exploration. We suspect that patients with nerve compression syndromes are more susceptible to development of this disease complex through shared pathogenesis, genetics and risk factors. This may have important clinical implications for evaluation of patients with CTS and/or MH.

1Gfrerer, L., Hansdorfer M., Ortiz R., Nealon K., Austen WG. Occipital neuralgia/migraine: Intra-operative evidence for extracranial pathology. Paper presented at: American Society of Peripheral Nerve Meeting; Feb 1-3 2019; Palm Desert, CA.
2Atroshi, I., Gummesson, C., Johnsson, R., Ornstein, E., Ranstam, J., Rosen, I. Prevalence of carpal tunnel syndrome in a general population. *JAMA* 1999;282:153-158.
3Dale, A. M., Harris-Adamson, C., Rempel, D., et al. Prevalence and incidence of carpal tunnel syndrome in US working populations: pooled analysis of six prospective studies. *Scand J Work Environ Health* 2013;39:495-505.

Silicone Implant Shells Increase The Rate Of Proliferation Of Patient-derived BIA-ALCL Cells But Not Primary T Cells In An Engineered Biomimetic Patient-derived Breast Tissue

*Ishani D. Premaratne, BA, Matthew A. Wright, BA, Mariam Gadjiko, BA, Daniel O. Lara, BA, Arash Samadi, BA, Paula S. Ginter, MD, Giorgio Inghirami, MD, Kristy A. Brown, PhD, Jason A. Spector, MD*  
*Weill Cornell Medicine, New York, NY, USA.*

**Purpose:** The pathogenesis of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) remains poorly understood. Our lab has demonstrated the power of studying BIA-ALCL behavior in a high-fidelity tissue engineered *ex vivo* biomimetic, three-dimensional model. Herein we use this model to compare the effect of silicone implant shell on proliferation of patient-derived BIA-ALCL cells to patient-derived T progenitor cells (from which ALCL originates) within the breast microenvironment.

**Methods:** Patient-derived breast tissue was processed for its component adipocytes, ductal organoids, and stromal vascular fraction. These were suspended within 50 µl of 0.3% type I collagen matrix, to which was added 200,000 cells/mL of either patient-derived BIA-ALCL cells or T progenitor cells. These were then plated into 6mm wells. As a control, both BIA-ALCL and T progenitor cells were suspended within type I collagen alone at the same seeding density without breast components. Before plating, wells were lined circumferentially with either textured, smooth, or no implant shell. These were 1cm by 2cm pieces dissected from the whole implant. Wells were imaged using confocal microscopy over 8 days.

**Results:** Unstimulated T progenitor cell count showed no significant increase in any of the conditions tested. The change in cell count over 8 days was 3.85% in each condition (p = 0.3352). A Tukey’s multiple comparison test comparing each condition to each other additionally revealed no significant increase in cell count over 8 days for all conditions. The mean difference in cell count between days 0 and 4 was 214.1 cells (p = 0.559, 95% CI [-244.5, 672.6]), and between days 0 and 6 it was 229.1 cells (p = 0.343, 95% CI [-148.8, 607.0]).

This can be compared to previous studies by our group where proliferation of BIA-ALCL cells was found to be significantly more robust in the biomimetic platform compared to collagen-only groups, regardless of implant shell type (p < 0.01). BIA-ALCL cells grew nearly 30% faster in textured and smooth shell biomimetic groups compared to biomimetic wells lacking implant shell.

**Conclusion:** Within a tissue-engineered 3D model of the breast microenvironment, unstimulated T progenitor cells showed no significant increase in proliferation regardless of the presence or absence of implant shell. Comparatively, BIA-ALCL cells proliferated more robustly in the presence of textured and smooth implant shell. Our data suggest that silicone implant shell has a significant and quantifiable effect on cell proliferation among pathologic BIA-ALCL cells, but not their precursor T cells. Thus, these data suggest that breast implant silicone shell alone is not a
sufficient stimulus for T cell proliferation within the breast microenvironment, and imply that co-stimulatory factors are required. Further investigation into possible co-stimulatory factors are currently underway using our high-fidelity ex vivo model of the breast microenvironment.

126

Pre-clinical Application Of Tissue-engineered Human Induced Pluripotent Stem Cell-derived Epithelial Grafts In A Porcine Airway Defect Model

Ratna Varma1,2, Alba E. Marin-Araujo3,4, Sara Rostami2, Thomas K. Waddell1,2, Golnaz Karoubi1,2, Siba Haykal5,2

1Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON, Canada, 2Latner Thoracic Surgery Research Laboratories, Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, 3Department of Mechanical and Industrial Engineering, University of Toronto, Toronto, ON, Canada, 4Latner Thoracic Surgery Research Laboratories, Toronto General Hospital Research Institute, Toronto, ON, Canada, 5Division of Plastic & Reconstructive Surgery, Department of Surgery, University of Toronto, Toronto, ON, Canada.

Purpose: Tracheal injury, stenosis, and malignancy demand surgical management or transplantation, however, the latter fails due to the lack of a functioning epithelium. This issue also encompasses tissue engineering approaches such as decellularized matrices and synthetic biomaterials, wherein the absence of pseudostratified, mucociliary epithelia results in airway obstruction and life-long tracheostomies for patients. Our group has developed a composite biomaterial of Silk Fibroin and Collagen Vitrigel Membrane (SF-CVM), which provides high tensile strength for surgical manipulation and allows differentiation of primary human tracheal epithelial cells (HTECs) into functional ciliated and goblet cells. While HTECs are an endogenous source for recipient-derived grafts, they are limited in their ability to expand and differentiate reliably. Therefore, we differentiated human induced pluripotent stem cells (hiPSCs), a promising alternative, to generate functional SF-CVM-based airway epithelial grafts. We further developed a porcine airway defect model to determine graft integration and survival across 3 days.

Methods: We sequentially differentiated hiPSCs based on an established protocol towards definitive endoderm, lung progenitors, and airway progenitors, and analyzed them via flow cytometry. These airway progenitors were seeded on SF-CVM grafts under air-liquid interface culture for formation of tight junctions (ZO-1) and differentiation into ciliated (acetylated α-tubulin) and goblet cells (mucin 5AC), as assessed by immunocytochemistry.

We created a 2x4 cm tracheal defect and manipulated it according to the following four groups prior to defect closure: 1) no manipulation; 2) mucosa stripped; 3) mucosa stripped and replaced with bare SF-CVM graft; and 4) mucosa stripped and replaced with hiPSC-derived SF-CVM graft labeled with CMTMR dye. Post defect closure, all groups were wrapped in sternocleidomastoid muscle for vascularization. On post-operative day (POD) 3, all defects were assessed macroscopically, while Groups 2 to 4 were assessed for cell viability and death via calcein-AM and ethidium homodimer 1 staining, respectively.

Results: We produced 92.6±2.1% CKIT+CXCR4+ definitive endoderm, 38.1±3.9% GFP-NKX2.1+ lung progenitors, and 65.6±2.4% P63+ airway progenitors, which differentiated into 64.6±7.8% ciliated and 2.1±1.4% goblet cells on SF-CVM. This differentiation into ciliated cells on SF-CVM was significantly higher than that of HTECs (17.2±5.0%; P<0.05) and physiologically relevant, being well within the 48-70% range present in human tracheae.

There were no respiratory complications or animal mortality. Group 1 resembled native epithelium, Group 2 had granulation tissue overgrowth, while Group 3 and 4 demonstrated SF-CVM integration with the surrounding tracheal tissue. Groups 2 and 3 demonstrated epithelial infiltration with high cell mortality. Group 4 retained the CMTMR label (magenta) which co-localized with calcein-AM (green), indicating that the hiPSC-derived epithelium was intact and alive on POD3.

Conclusions: We developed functional hiPSC-derived SF-CVM epithelial grafts which survived and integrated within porcine airway defects across 3 days. This is the first pre-clinical application of biomaterials-based airway grafts generated from hiPSCs that has significant clinical