The effects of autoimmune inflammation on proliferation, differentiation, and androgen receptor signaling in adult prostate stem cells

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OBJECTIVES/SPECIFIC AIMS: The primary goal of this project is to verify findings from a murine prostatitis model in the human setting. METHODS/STUDY POPULATION: Methods include primary cell isolation and culture, FACS, adoptive transfer, 3D cell culture, histology, immunofluorescence, xenograft, and tissue recombinant. The study population includes patients undergoing HoLEP or radical prostatectomy due to hyperplasia or indolent bladder or prostate cancer. RESULTS/ANTICIPATED RESULTS: Having verified similar sensitivities to androgen receptor (AR) inhibitors between naive murine and human basal prostate stem cells, we anticipate that autoimmune inflammation in humans affects the response of basal prostate stem cells in a manner similar to the murine setting as well. This includes increased proliferation, increased differentiation, and decreased response to AR inhibitors. DISCUSSION/SIGNIFICANCE OF IMPACT: The identification of survival mechanisms used by basal prostate stem cells in an androgen deprived environment may give insight to the process by which prostate cancer becomes androgen independent. The effect of inflammation on proliferation, survival, and AR signaling in these cells may also provide information relevant to cancer initiation and progression.

The Empower Lab: An innovative model for research experience and training for undergraduate, graduate, and medical students

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OBJECTIVES/SPECIFIC AIMS: The Empower Lab was established in 2015 with the goal of providing students with hands-on research experience in sexual and gender-based violence and health. METHODS/STUDY POPULATION: The Empower Lab consists of 10–12 undergraduate, graduate, and medical students at a time. Students undergo a rigorous application process, and agree to volunteer 8 hours per week for at least 1 year. Students are assigned to teams, and learn research skills such as literature searches, systematic reviews, research question generation, study design, IRB procedures, database creation and management, data collection and analysis, oral and poster presentation, manuscript preparation, team collaboration and communication, advocacy, and leadership. Students start as research assistants, and can be promoted to team leader, and associate director of research. A student mentor and teach each other, and are supervised by the principal investigator (PI). A survey skill self-assessment is administered to lab members on entry to the lab, every 4–6 months, and upon exit. RESULTS/ANTICIPATED RESULTS: In total, 20 students have participated in the lab to date, and 12 are currently enrolled. Eighty percent of the lab members are women. The students are 45% undergraduates, 15% graduate (nursing, social work, public health), 20% medical students, and 10% not currently enrolled in school (gap year). Twenty students completed entry surveys, 11 students have completed interim surveys, and 5 students have completed exit surveys. Examination of current surveys indicates that students are gaining skills throughout the lab experience. Free-text feedback provided further insights. Currently, the lab has 5 IRB-approved studies actively recruiting participants, 4 manuscripts being written, and 3 studies in the development phase. Students have presented at three local and 2 national meetings to date. Changes have been made to the lab structure over time in order to provide clear expectations and feedback, and strengthen student performance. DISCUSSION/SIGNIFICANCE OF IMPACT: The Empower Lab is an innovative public health lab that provides opportunities for real-world research experience for students. The teamwork, collaboration, and structure of the lab permit mentoring, support, and teaching from peers, as well as from the PI. The lab increases the PI’s productivity. Students are encouraged to develop and implement their own research ideas, further encouraging independence and initiative. Although the number of surveys is limited to date, they indicate improvement in skills and confidence among lab members. The predominance of women in the lab suggests that this is a strong model for recruitment and retention of women in STEM.
neutralizing therapies may increase risk of developing melanoma, especially in melanocytes will increase DNA repair mechanisms. DISCUSSION/SIGNIFICANCE OF IMPACT: The addition of butyrate to activated LP CD4 T cells decreases TCR-mediated activation in a dose-dependent manner, and butyrate acts directly on purified LP CD4 T cell populations independent of other cell populations. Butyrate differentially inhibited the proliferation of Th17, Th1, and Th2 subsets, with Th17 cells being the most sensitive to butyrate but increased the infection levels of all T helper subsets at low concentrations. Further studies are needed to determine the mechanism of butyrate’s actions on LP Th cells and the sensitivity of Th17 cells to the inhibitory effects of butyrate. These results could help direct targeted manipulation of the colonic microbiome of HIV-1 infected individuals to help resolve inflammation and limit the impact of the infection in the gut mucosa and systemically.

The role of interleukin-23 in human melanoma
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OBJECTIVES/SPECIFIC AIMS: Interleukin-23 (IL-23) promotes differentiation of naïve T-cells into Th17 cells, which have the pathogenesis of autoimmune-inflammatory conditions such as psoriasis. IL-23-neutralizing antibody therapies are now in use for treatment of psoriasis, with promising results. Studies in mice have shown that IL-23 plays a role in inhibiting the growth, progression, and metastasis of melanomas. Thus, therapeutic neutralization of IL-23 in patients may inadvertently increase their susceptibility to development of melanoma. In this study, we aim to characterize expression of IL-23 receptors (IL-23R) in human melanocytes and melanoma cells and tissue and to study the effects of IL-23 on growth, proliferation, and tumorigenicity of these cells. METHODS/STUDY POPULATION: IL-23R expression was characterized using immunofluorescence staining, Western blot, and flow cytometric analysis. Response of melanoma and melanocytes to recombinant IL-23 treatment will be studied through similar methods in addition to assays of cell proliferation and tumorigenicity.

RESULTS/ANTICIPATED RESULTS: Preliminary immunofluorescence staining, Western blot, and flow cytometric analysis. Response of melanoma and melanocytes to recombinant IL-23 treatment will be studied through similar methods in addition to assays of cell proliferation and tumorigenicity. RESULTS/ANTICIPATED RESULTS: Preliminary immunofluorescence staining, Western blot, and flow cytometric analysis. Response of melanoma and melanocytes to recombinant IL-23 treatment will be studied through similar methods in addition to assays of cell proliferation and tumorigenicity.

The nasopharyngeal microbiome is perturbed and associated with increased clinical severity during acute respiratory viral infection
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OBJECTIVES/SPECIFIC AIMS: We sought to investigate the role of the host microbiome during severe, acute respiratory infection (ARI) to understand the drivers of both acute clinical severity and the microbial community that drive clinical severity. METHODS/STUDY POPULATION: Nasopharyngeal swabs comprised of mixed cell populations at the active site of infection were collected from 192 hospitalized pediatric patients with ARI. We combined comprehensive respiratory virus detection and virus genome sequencing with 16S rRNA gene sequencing to evaluate the microbial content of the airway during ARI. This data was coupled with 11 clinical parameters, which were compiled to create a clinical severity score. The microbiome profiles were assessed to determine if clinical severity of infection, and/or specific virus was associated with increased clinical severity. RESULTS/ANTICIPATED RESULTS: We identified 8 major microbiome profiles classified by dominant bacterial genus, Moraxella, Corynebacterium, Staphylococcus, Haemophilus, Streptococcus, Alloioiococcus, Schlegelella, and Diverse. Increased clinical severity was significantly associated with microbiome profiles dominated by Haemophilus, Streptococcus, and Schlegelella, whereas Corynebacterium and Alloioiococcus were more prevalent in children with less severe disease. Independent of the microbial community, more than 60% of patients with the highest clinical severity were infected with either respiratory syncytial virus or rhinovirus. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results suggest that both virus and microbial community may drive clinical severity during acute respiratory viral infection. It is still unclear how the complex interplay between virus, bacterial community, and the host response influence long-term respiratory impacts, such as the development of asthma. Nonetheless, during ARIs therapeutic interventions such as antibiotics and probiotics may be warranted in a subset of patients that are identified to have both a virus and microbiome profile that is associated with increased pathogenesis to limit both acute and chronic complications.

The role of lysyl oxidase in systemic sclerosis-associated lung fibrosis
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OBJECTIVES/SPECIFIC AIMS: Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology characterized by progressive fibrosis of the skin and multiple visceral organs. Effects of the extracellular matrix remodeling enzyme Lysyl oxidase (LOX) on skin fibrosis is well characterized. In the crosslinking of the extracellular matrix (ECM) due to LOX. In this study, we investigated the role of LOX in the pathophysiology of SSc. METHODS/STUDY POPULATION: LOX expression and protein levels were measured in lung tissues and primary fibroblasts from patients with SSc and healthy controls. The effects of recombinant LOX (rLOX) were measured in vitro in primary fibroblasts, ex vivo in human lung tissues and in vivo in mice given bleomycin in combination with rLOX. LOX levels and activity were evaluated in lung fibroblasts treated with an endostatin-derived peptide that ameliorates fibrosis...