effects of a novel JIA risk variant at 1q24.3. METHODS/STUDY POPULATION: JIA patients meeting criteria for the two most common disease subtypes (oligoarticular and RF neg polyarthritis) were genotyped using the Immunochip, an Illumina array with dense coverage of the HLA region and 186 other loci previously reported in autoimmune diseases. Phase I association findings (Hinks, 2013) and Phase II analysis (unpublished) of an expanded cohort (4,271 JIA and 14,390 controls) identified new risk loci, including rs78037977 at 1q24.3. We prioritized rs78037977 and predicted possible impacted mechanisms based on Bayesian predictions of attributable risk, the surrounding chromatin landscape, and transcription factor binding data. A luciferase reporter assay was used to assess allele-dependent enhancer activity. RESULTS/ANTICIPATED RESULTS: rs78037977 is located between *FASLG* and *TNFSF18* at chromosome 1q24.3 is associated with JIA ($p = 6.3x10^{-09}$), and explains 94% of the posterior probability at this locus; no other SNPs in linkage disequilibrium ($r^2>0.6$). The chromatin landscape around rs78037977 contains H3K4Me1 and H3K27Ac marks, which are indicative of enhancer activity. Further, >160 transcription factors have chromatin immunoprecipitation followed by sequencing (ChIP-seq) peaks overlapping rs78037977 in various cellular contexts. In luciferase reporter assays, the region around rs78037977 containing the reference A allele had ~2-fold increased enhancer activity compared to the non-reference allele. DISCUSSION/SIGNIFICANCE OF IMPACT: This work provides *in vitro* evidence to support allele-dependent enhancer activity of a novel JIA-risk variant at 1q24.3. Our ongoing work investigates the effect of the DNA-containing region of rs78037977 on gene expression and differential transcription factor binding at rs78037977.

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HIV-Associated Myocardial Diastolic Dysfunction and Soluble ST2 Concentration in Tanzanian Adults: A Cross-Sectional Study

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OBJECTIVES/GOALS: To determine the prevalence of myocardial diastolic dysfunction (DD) and association of serum concentration of the cardiac biomarker serum soluble ST2 in HIV-infected as compared to uninfected Tanzanian adults at the time of HIV diagnosis. METHODS/STUDY POPULATION: In this cross-sectional study we consecutively enrolled HIV-infected participants and uninfected controls at a large, referral HIV clinic in Mwanza, Tanzania. Standardized history, physical examination, echocardiography and serum samples were obtained. The primary outcome was prevalence of myocardial diastolic dysfunction in HIV-infected as compared to uninfected adults. The secondary outcome was the association of baseline serum sST2 concentration with diastolic dysfunction prevalence. Regression models were used to quantify the associations. RESULTS/ANTICIPATED RESULTS: We enrolled 388 HIV-infected, ART naïve and 461 HIV-uninfected controls. Participants with HIV had a higher prevalence of DD (OR = 2.44, p = 0.001, controlled for age, sex, hypertension and BMI) and more severe dysfunction (66.7% vs 42.5%, p = 0.056) at an earlier age. Baseline serum sST2 concentration was significantly associated with DD in HIV-infected but not uninfected participants (p = 0.04 and 0.90, respectively). More HIV-infected adults with concurrent DD exceeded the threshold of 35ng/mL as compared to controls (15.7% vs 5.3%, p<0.0001). Additionally, a significant population level shift to higher sST2 concentration was observed in HIV-infected adults with dysfunction as compared to both HIV-infected without and HIV-uninfected adults with dysfunction (Kolmogrov-Smirnov test: p = 0.02 and 0.04). DISCUSSION/SIGNIFICANCE OF IMPACT: In a large population of HIV-infected adults in sub-Saharan Africa, HIV infection is associated with myocardial diastolic dysfunction. This dysfunction is associated with higher sST2 concentrations. Therefore, we conclude that the sST2 pathway may provide insight into the pathophysiologic mechanisms of dysfunction in HIV-infected adults.

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Identification of distinct fibroblast populations with unique roles in pancreatic cancer progression and tumor immunity

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OBJECTIVES/GOALS: The desmoplastic reaction in PDAC involves a significant accumulation of immune cells and fibroblasts.The functional diversity of carcinoma associated fibroblasts (CAFs) remains largely unknown, and identification of immune regulating subsets would have a substantial impact in augmentation of immunotherapy efficacy. METHODS/STUDY POPULATION: Employing histology, FACs, multiplex immunohistochemistry, single cell RNA sequencing (sc-RNA-seq) and genetically engineered mouse models, we demonstrate that $aSMA^+$ cells are a dominant CAF population in PDAC with tumor restraining properties (TS-CAFs), as opposed those of the FAP^+ CAFs, which demonstrate tumor promoting activity (TP-CAFs). RESULTS/ANTICIPATED RESULTS: Analysis of bulk tumor depleted of either TS-CAFs or TP-CAFs showed that TS-CAFs predominantly modulate extracellular matrix (ECM) production, facilitate cell-ECM adhesion and regulate adaptive immunity, while TP-CAFs exhibit a lineage that is skewed towards a pro-inflammatory, chemokine secreting phenotype. Further, scRNA-Seq analyses demonstrate that CAFs share distinct gene expression profiles characteristic of lymphocytic and myeloid lineages. Together our data distinguish two populations of CAFs, one which is tumor suppressing with roles in ECM remodeling and another which is tumor promoting with roles in cytokine production, both with immune modulating capabilities. DISCUSSION/SIGNIFICANCE OF IMPACT: Our study identifies a complex network of functionally heterogeneous fibroblasts during PDAC progression with significant immunotherapeutic implication. The identification of distinct fibroblast subsets will allow us to discriminately target fibroblast populations to augment immunotherapy efficacy in pancreatic cancer.

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