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Category: Postdoc
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Title: Plakophilin-2 Deletion in Epicardium-Derived Progenitor Cells Enhances Inflammatory Cell Recruitment to the ARVC-like Myocardium
Abstract: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an under-recognized disease that contributes significantly to sudden cardiac death (SCD) in young adults. Current knowledge of ARVC disease pathogenesis is lacking and there are no disease specific pharmacologic therapies. Epicardium-derived Progenitor Cells (EPDCs) contribute to numerous cell lineages during cardiac and pulmonary development as well as injury response. Plakophilin-2 (Pkp2) is amongst the most commonly identified gene mutations in ARVC. Using an ARVC-like mouse model of Pkp2 deletion, we evaluated the contribution of Pkp2 deletion in EPDCs to ARVC disease pathogenesis. Mice deleted for Pkp2 in EPDCs alone do not demonstrate anatomic or physiologic changes. However, Pkp2 deletion in cardiac myocytes alone demonstrates an ARVC-like phenotype characterized by RV dysfunction and eventual failure. Single cell RNA-Sequencing (scRNA-Seq) identified a unique population of inflammatory fibroblasts and enhanced recruitment of inflammatory cells including B lymphocytes to the myocardium of mice deleted for Pkp2 in both EPDCs and cardiac myocytes as compared to cardiac myocyte Pkp2 deletion alone. We conclude that Pkp2 deletion in non-myocyte cardiac lineages are part of a previously unrecognized pathway for cardiac inflammation in ARVC.