Research Abstract
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Poly- and perfluoroalkyl substances (PFAS) are fluorinated compounds widely used in commercial and consumer products and are commonly present in our diet, drinking water, indoor air, and household dust. Due to their environmental persistence, global occurrence, and presence in nearly all human blood with relatively long half-lives, it is urgent to understand how PFAS adversely impact human health. Clinical studies show that PFAS exposure is associated with increased pancreatic cancer incidence. However, specific mechanisms of how PFAS exposure promotes pancreatic carcinogenesis remain unknown. Recent research suggests PFAS not only can generate intracellular reactive oxygen species (ROS) to activate p53-dependent pathways, but also induce alterations in the epigenetic landscape of DNA methylation. Therefore, we hypothesize that PFAS exposure can co-operate with p53 loss and/or DNA methylation changes to promote pancreatic cancer progression. The proposed study will evaluate the effect of PFAS in the pancreatic epigenome and determine if PFAS coordinate with p53 loss in disease progression by utilizing the novel 3D organoid culture system and DNA methylation sequencing.