Injectable Hydrogel Delivers miRNA-therapeutics to 3D-Bioprinted Calcific Aortic Valve Disease Model

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Calcific aortic valve disease (CAVD) claims 17,000 lives in the US alone, annually. No drug-based therapy is available. The only effective treatment is invasive and costly aortic valve replacement for late-stage disease patients. This study will use a novel 3D-bioprinted model of CAVD and an innovative drug-delivery platform to elucidate the underlying pathobiological mechanisms of CAVD and identify potential therapeutic targets.

Advanced imaging and nanoscale technologies at the HCBI and CNS will greatly enhance our insight into mechanisms of CAVD. To illuminate the pathobiological mechanisms of CAVD, a 3D-bioprinted CAVD model will be used to track differentially expressed microRNAs recently identified in our screening of CAVD tissues. The bioprinted CAVD model will allow us to assess the temporal association of these microRNAs with cellular changes observed in CAVD using fluorescent in situ hybridization and fluorescent phenotypic markers. We will then test whether these microRNAs can be targeted to therapeutically control CAVD cell phenotypes. Confocal microscopy will track microRNA delivery from a hydrogel drug delivery system into cells incorporated into CAVD model. Visualizing microcalcifications in the CAVD model using a near-infrared fluorescent calcium tracer will assess the functional response of calcified cells to microRNA-therapeutics.

This research will validate an innovative injectable hydrogel delivery platform in a unique 3D-bioprinted model of CAVD and identify functional combinations of miRNA therapeutics with a main goal to improve the standard of care for patients suffering from CAVD, a disease with no available drug strategies.