InSyTe FLECT/CT Application Spotlight

Heart disease, cardiomyopathy

Journal: Advanced Science, 2021
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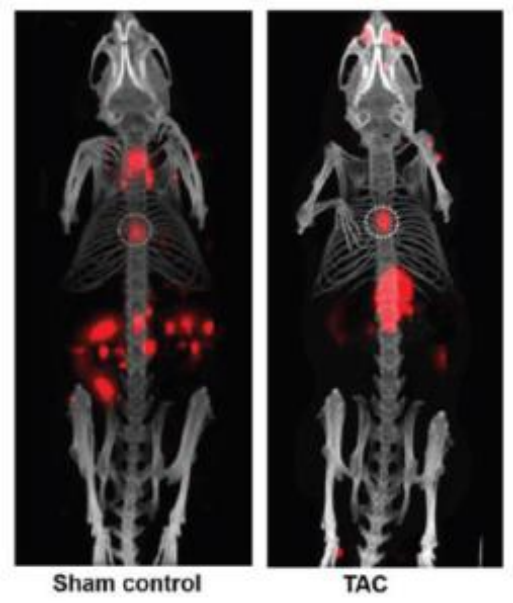
Title: Reversible Treatment of Pressure Overload-Induced Left Ventricular Hypertrophy through *Drd5* Nucleic Acid Delivery Mediated by Functional Polyaminoglycoside
Link: https://doi.org/10.1002/advs.202003706
Keywords: Heart disease, cardiomyopathy, myocardial dysfunction

Summary: Heart failure occurs when the pumping action of the heart is insufficient to keep up with the body's needs, resulting in a lack of oxygen and nutrient delivery to cells and tissues. Hypertension, or high blood pressure, is a leading cause of heart failure. In response to high blood pressure, the heart increases in size and muscle mass to increase pumping strength and counter the effects of high blood pressure. This leads to cardiac hypertrophy (enlarging of the heart) that, if sustained for a long time, may result in heart failure. Heart failure research has focused on molecular and genetic mechanisms regulating cardiac hypertrophy and recent work has shown that genetic therapy during early stages of heart failure may be successful in treating hypertrophic cardiac damage. Specifically, the dopamine D5 receptor (D5R) has been implicated in hypertension and has been shown to decrease in expression during development of cardiac hypertrophy. In this study, the researchers investigated a genetic treatment to increase D5R expression and treat cardiac hypertrophy. This treatment utilizes *Drd5* nucleic acids delivered by a non-viral delivery vector (tobramycin-based hyperbranched polyaminoglycoside, or SS-HPT). The SS-HPT and nucleic acid (SS-HPT/NA) complex was characterized in vitro, studied in vivo in an animal model of cardiac hypertrophy, and then assessed for therapeutic effect ex vivo.



The authors used the InSyTe FLECT/CT to study the biodistribution of the SS-HPT/NA complex used to deliver *Drd5* nucleic acid treatment. Images were acquired 2 weeks after transverse aortic constriction (TAC)-induced cardiac hypertrophy. The SS-HPT/NA complex was conjugated with the commonly used Cy7 near infrared fluorescent dye for FLECT contrast. The images are representative of non TAC control mice (left) versus the TAC mice (right). The authors report a twofold higher accumulation of the SS-HPT/NA complex in the heart of TAC mice compared to the control mice (circled region).

InSyTe FLECT/CT Spotlight: Using the InSyTe FLECT/CT, the research team obtained in vivo biodistribution images of the SS-HPT/NA complex in a mouse model of cardiac hypertrophy. The long wavelength, near infrared Cy7 fluorescent dye conjugated to the SS-HPT/NA complex provided fluorescence contrast and enabled the team to visualize the in vivo distribution of the nucleic acid delivery vector. They noted that the SS-HPT/NA fluorescence in vivo was twofold higher in the TAC mice with damaged hearts compared to control mice with normal hearts, though the fluorescence in the liver was comparable. These results were further confirmed in the ex vivo studies described in the publication. The in vivo imaging results from the InSyTe FLECT/CT are significant as this enabled the research team to gain an understanding of the in vivo distribution of the novel genetic therapy in the internal organs of the mouse at depths beyond 1 cm in tissue.