**FINDING NOVEL ANTI-FIBROTIC THERAPIES USING A DUAL-REPORTER MOUSE THAT TRACKS FIBROBLAST CELL TRANSITIONS IN VIVO AND IV VITRO**

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Cardiac fibroblasts serve important roles in cardiac structure and intercellular communication and bear primary responsibility for the maintenance of the cardiac extracellular matrix. Two critical aspects of cardiac fibroblast phenotype in response to injury are well recognized. First, the transition into the myofibroblast phenotype, so named due to their expression of contractile proteins, like smooth muscle alpha-actin which contribute to wound contracture. The myofibroblast is the primary source of collagen deposition which may persist for long periods of time following resolution of injury and scar maturation. Second, the physiologic resolution of the wound healing response requires the myofibroblast to inactivate these functions and return to the quiescent basal state. It is presumed that termination occurs by apoptosis, although the regulatory mechanisms remain undefined. Thus physiologically appropriate functions of cardiac fibroblasts require profound phenotypic transitions, and termination of the activated phenotype. Studying hepatic fibrosis, David Brenner reported on a unique transgenic reagent (RFP/GFP double reporter mice) which simultaneously express the red fluorescent protein (RFP) under control of the alpha-smooth muscle actin (aSMA) promoter and the enhanced green fluorescence protein (EGFP) under the control of collagen a1 (I) promoter. We have taken advantage of these animals to study these phenotypic transitions both in vivo and in vitro targeting the heart. For the in vitro studies we have used an automated program of “counting” red, green and yellow (red+green) cells and have subjected these cells to high-throughput screening in the presence of chemical libraries and candidates found to have the most promise with this approach in vivo. We believe this represents a unique approach for defining therapeutic approaches to studying pathologic fibrosis with great potential.