CENTER FOR FLUID MECHANICS AND THE FLUIDS, THERMAL AND CHEMICAL PROCESSES GROUP OF THE DIVISION OF ENGINEERING SEMINAR SERIES

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On The role of Pulsating flow in the Morphogenesis and function of embryonic heart

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Nature has shown us that some hearts do not require valves to achieve unidirectional flow. In its earliest stages, the vertebrate heart consists of a primitive tube that drives blood through a simple vascular network nourishing tissues and other developing organ systems. We have shown that in the case of the embryonic zebrafish heart, an elastic wave resonance mechanism based on impedance mismatches at the boundaries of the heart tube is the likely mechanism responsible for the valveless pumping behavior. In this model, compared to peristalsis, fewer cells are required to actively contract in order to maintain the pumping action than are necessary in a peristaltic mechanism. When functioning normally, mature heart valves prevent intracardiac retrograde blood flow; before valves develop there is considerable regurgitation, resulting in oscillatory flow between the atrium and ventricle. As reversing flows are particularly strong stimuli to endothelial cells in culture, an attractive hypothesis is that heart valves form as a developmental response to oscillatory blood flow through the maturing heart. Here, we exploit the resonant pumping properties of the embryonic heart to reduce oscillatory flow during valvulogenesis by lowering heart rate. Reducing oscillatory flows across endocardial cushions leads to arrested valve growth. Using this assay, we identify Klf2a, a shear-responsive gene, as an essential valve inducer in the zebrafish heart. Klf2a is normally expressed in the valve precursors in response to oscillatory flow.

> TUESDAY, MARCH 4, 2008 Barus & Holley, Room 190 3:00pm