**THE ROLE OF LRP5 IN CALCIFIC AORTIC VALVE DISEASE: LDL-DENSITY-PRESSURE THEORY**

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Atherosclerosis and osteoporosis are the leading causes of morbidity and mortality in the World. Evidence indicates that hyperlipidemia plays a paradoxical role in both disease processes. However, the mechanism is not understood. The LDL-Density Pressure Theory hypothesizes the role of lipids activate atherosclerosis within the bone and the heart to initiate the development of diseases in both of these tissues. To test this hypothesis experimental hypercholesterolemia mouse models were tested: Lrp5(-/-) /ApoE(-/-):Lrp5(-/-) /ApoE(-/-) mice (n = 180). Group I (n = 60) normal diet, Group II (n = 60) 0.25% chol diet (w/w), and Group III (n = 60) 0.25% (w/w) chol diet + atorv for the development of calcification by MicroCT and Synchrotron MicroCT Scan and by Masson trichrome stain. Finally gene expression for Lrp5, Lrp6, and Runx2 PCR was performed to evaluate the expression in the control and the cholesterol valves. The ApoE(-/-) cholesterol treated mice developed calcification and increase in Lrp5, Runx2 (P < 0.05) as compared to control. The Lrp5(-/-) mice developed no calcification by MicroCT and Synchrotron and positive gene expression for Lrp5/6 or Runx2. The double knockout ApoE(-/-):Lrp5(-/-) developed mild mineralization in the cholesterol treated valves with an increase in Lrp6 and Runx2 expression(P < 0.05). There was no mineralization in the right sided hearts valves. In conclusion Lrp5/6 is necessary for calcification in the aortic valve in the presence of experimental hypercholesterolemia. These data demonstrate the first mouse genetic evidence for the LDL-Density-Pressure theory in cardiac valves.