A023 Longitudinal In Vivo Atherosclerotic Disease Development in The apoE Deficient Zucker Rat

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Introduction: There are currently no well-established small animal models to study diabetes and atherosclerosis combined. Longitudinal in vivo imaging of inflammation in atherosclerosis is a promising tool to evaluate progression of cardiovascular complications. However, vascular size of current mouse models of atherosclerosis does not allow for detailed molecular imaging. Radiolabeled DANBIRT has been used as an in vivo molecular imaging tool to inflammation. Our group has modified the lipid metabolism in Lean Zucker (LZ: $Lepr^{+/?}$) rats to promote dyslipidemia and development of atherosclerosis by knocking out the apolipoprotein E (apoE) gene using CRISPR/Cas9. We hypothesize that apoE knockout,LZ rats ($apoE^{-/-}$,$Lepr^{+/?}$) will develop atherosclerosis with dietary exposure to high fat, high cholesterol (HFHC) diet.[^{111}In]-DANBIRT will be able to localize inflammation in vivo and allow longitudinal monitoring of vascular atherosclerotic disease using SPECT/CT imaging. **Methods:** $apoE^{-/-}$;LZ adult rats were imaged for 1hr post injection of ~900 µCi of [^{111}In]-DANBIRT for SPECT/CT imaging using a NanoSPECT/CT®. Rats were placed on either HFHC or standard rodent chow for 10 weeks starting at 12 weeks of age (baseline). $apoE^{+/+}$;LZ under normal and HFHC diet were used as controls. Regions of Interests (ROI) are identified and determined for muscle (background tissue), carotid arteries, aortic arch, and descending aorta. Activity is decay corrected and compared between and among experimental groups. Serum chemistry and histologic analysis of en face aortas and aortic root were performed. Mean ± SEM, two-way ANOVA with Tukey's correction was performed. **Results:** All $apoE^{-/-}$ rats developed severe hypercholesterolemia particularly under a HFHC diet. After 10-weeks of HFHC diet $apoE^{-/-}$,LZ rats have higher [^{111}In]-DANBIRT uptake in the descending aorta uniquely compared to baseline($p<0.05$) and to normal diet fed rats (ns). Histologic analysis showed $apoE^{-/-}$,LZ have increased significant atherosclerosis on the aortas and the aortic sinus, which correlates to our imaging results. $apoE^{+/+}$,LZ rats did not develop atherosclerosis disease as expected. **Conclusion:** To our knowledge, we have the first polygenic rat model able to develop atherosclerosis translationally under HFHC. [^{111}In]-DANBIRT longitudinally evidenced atherosclerotic disease in the abdominal aorta in vivo correlated to ex vivo histologic analysis. Supported by the NORC PPF (P30 DK056350) and the CRTG (Burroughs Wellcome Fund).