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Evaluation of Plaque Stability of Advanced Atherosclerotic Lesions in Apo E Deficient Mice after Treatment with the Oral Factor Xa Inhibitor Rivaroxaban

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To determine whether administration of the direct factor Xa inhibitor rivaroxaban prevent the composition of advanced atherosclerotic lesions in hyperlipidemic apolipoprotein E-deficient mice. 40 26-week old female Apolipoprotein E deficient mice were fed a chow diet supplemented with Rivaroxaban 1mg/kg/d or 5mg/kg/d for 26 weeks, 19 mice received regular chow diet. At time of necropsy, the thoracic aorta was collected for subsequent real-time PCR analyze for the mRNA expression of the inflammatory cytokines .

Following perfusion fixation with formalin, innominate arteries were embedded in paraffin, cross sectioned. Morphometric analysis of maximum lesion area as well as evaluation of lesion morphology was performed following Movat's pentachrome staining. Immunhistochemistry using antibodies against alpha actin and

macrophages as well as special staining for calcium (van Kossa stain) were performed. Areas of positive staining were quantitated using computer assisted morphometry. Our study demonstrates that chronic administration of rivaroxaban does not affect lesion progress, but downregulates expression of inflammatory, mediates and promotes lesion stability in apo-E deficient mice. Direct Factor Xa inhibitors might emerge as a potential therapeutic tool in patients with established atherosclerotic disease.