Abstract BS47 Figure 2 Medin is deposited in the ECM by exosomes. A) Deposits of medin are observed in ECM from cultured VSMCs (white arrows). Fibronectin staining shows the presence of ECM. B) Medin deposits colocalise with exosome marker, CD63. Treatment with calcium and phosphate (+CaP) increases the size of medin deposits. Treatment with an exosome secretion inhibitor, spiroepoxide (+SOM), decreases the deposit size. D) The area of each medin aggregate was measured using ImageJ

and phosphate conditions. FACS was used for quantification of exosome secretion. Exosomes were isolated by differential ultracentrifugation. Extracellular matrix (ECM) was synthesised in vitro for immunofluorescence and Western blotting. Cresolphthalein assays were used to quantify calcification.

Results MFGE8, medin and calcification, shown by von Kossa staining, co-localised in the medial layer of aortas from old subjects (figure 1). Medin and calcium deposits appear predominantly extracellular. Exosome secretion is increased from senescent VSMCs and in calcifying conditions. MFGE8 was expressed by VSMCs and was secreted exclusively in exosomes and its expression and secretion increased in calcifying conditions. Immunofluorescence staining of the ECM in vitro showed medin deposits co-localise with CD63, an exosome marker. The size of medin deposits in the ECM was increased when cells were treated with calcium and phosphate and this effect was reduced with an exosome secretion inhibitor, spiroepoxide (figure 2). Treatment with spiroepoxide also decreased hydroxyapatite deposition in the ECM.

Conclusion Medin and MFGE8 are abundant in aged aortas and secreted by exosomes. The von Kossa and medin staining observed in the medial layer of aged subjects indicates co-localisation of AMA and calcification. Exosome secretion is increased with age as well as in calcifying conditions, which could contribute to the age-related deposition of medin in the

ECM. Blocking exosome release attenuates the effect of elevated calcium and phosphate on both the size of medin aggregates and the formation of hydroxyapatite in the ECM. This suggests VSMC-derived exosomes mediate both vascular calcification and medin aggregation; and conditions which induce vascular calcification also stimulate AMA formation.

Conflict of interest No conflict of interest

BS48

MICRORNA EDITING IS INTEGRAL FOR INTERLEUKIN-6 TRANS-SIGNALLING AND LEUKOCYTE TRAFFICKING TO ISCHEMIC TISSUES

¹Aikaterini Gatsiou*, ¹Simon Tual-Chalot, ²Francesca Bonini, ³Valeriana Cesarini, ⁴Almudena Ortega-Gomez, ⁵Kerida Shook, ²Jedrej Hoffmann, ⁶Shin Kwak, ⁷Craig H. Selzman, ⁸Maurizio Martini, ²Stefanie Dimmeler, ³Angela Gallo, ⁷Stavros Drakos, ⁴Oliver Soehnlein, ⁹Konstantinos Stellos. ¹Cardiovascular Research Centre, Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne; ²JW Goethe University Frankfurt, Frankfurt, Germany; ³Ospedale Pediatrico Bambino Gesù IRCCS, Rome, Italy; ⁴LMU Munich, Munich, Germany; ⁵Cardiovascular Research Centre, Institute of Genetic Medicine, Newcastle University; ⁶University of Tokyo, Tokyo, Japan; ⁷University of Utah, Salt Lake City, USA; ⁸Università Cattolica del Sacro Cuore, Rome, Italy; ⁹Cardiovascular Research Centre, Institute of Genetic Medicine, Newcastle University

10.1136/heartjnl-2019-BCS.209

Background /Aim: Adenosine to inosine RNA editing is an essential posttranscriptional RNA modification catalysed by