Methods The effect of simvastatin was assessed in HUVEC cells treated by IL-17 (100 ng/ml) alone or combined with TNFα (1 ng/ml), with or without mevalonate, a specific inhibitor of simvastatin. The effect of simvastatin on IL-17-induced cytokine or chemokine expression was assessed at the mRNA level using qRT-PCR or protein level by ELISA. Its effect on the IL-17-induced pro-thrombotic state and cell invasion was assessed using a lumiaggregometer and a matrigel assay, respectively.

Results Simvastatin decreased IL-17-induced IL-6, IL-8, CX3CL-1, RANTES mRNA and CX3CL-1 and CCL-20 production. Simvastatin restored the level of IL-33 mRNA which was decreased by IL-17. Simvastatin reduced the expression of IL-17-induced pro-thrombotic genes such as tissue factor. Simvastatin restored the level of platelet aggregation to normal levels.

Simvastatin enhanced the expression of CD39 and thrombomodulin mRNA initially reduced by IL-17 and TNFα combination. Simvastatin suppressed IL-17-induced EC invasion. All these effects were reversed by the addition of mevalonate. Finally, simvastatin had an additive effect with infliximab to decrease the effect of the combination of IL-17 and TNFα on IL-6 mRNA expression.

Conclusion These results indicate that simvastatin inhibits the pro-inflammatory, thrombotic and pro-aggregation effects of IL-17 on vessels. They provide a new understanding of the beneficial effects of statins in blood vessel inflammation.

35 SIMVASTATIN INHIBITS THE PRO-INFLAMMATORY AND PRO-THROMBOTIC EFFECTS OF IL-17 AND TNFα ON ENDOTHELIAL CELLS

Arnaud Hot, Vanina Lenief, Fabien Lavocat, Pierre Miossec *Department of Immunology and Rheumatology and the Hospices Civils de Lyon mixed research unit, Hospital Edouard Herriot, Lyon, France*

10.1136/annrheumdis-2011-201230.35

Background Inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, known as statins, are widely used for primary and secondary prevention of coronary artery atherosclerosis. Besides its lipid lowering properties, simvastatin has various anti-inflammatory effects.

Objectives The aim of this study was to assess whether simvastatin modulates the effects of IL-17, an emerging actor in atherosclerosis.