Abstract n SO1_5 - Presenting author **Alice Colombo**

CORONARY ATHEROSCLEROSIS AND SYSTEMIC INFLAMMATION IN HDL DEFICIENT MICE

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Aim. HDL and its main protein component, apolipoprotein A-I, exert a pivotal role in regulating cell cholesterol homeostasis and in modulating inflammatory response and immune cell activation. In the present study, we investigated the impact of genetic manipulation of HDL/apoA-I levels on lipid accumulation in skin and heart vessels in relation to local and systemic immune-inflammatory activation.
Methods. ApoE deficient (EKO) mice, apoE/apoA-I double deficient (DKO) mice, DKO mice overexpressing human apoA-I (DKO/hA-I) and C57Bl/6 control mice were fed chow diet until 30 weeks of age. Plasma lipids were quantified, atherosclerosis development at the aortic sinus and in coronary arteries was measured, skin ultrastructure was evaluated by electron microscopy. Blood and lymphoid organs were characterized through histological, immunocytofluorimetric and whole transcriptome analyses.
Results. DKO mice were characterized by an almost complete lack of HDL and by plasma total cholesterol levels comparable to those of control mice. Only DKO mice showed xanthoma formation and deep alterations in the skin-draining lymph nodes, whose transcriptome analysis revealed increased activation of the immune system and an unbalanced expression of genes involved in energy metabolism. An increased presence of $CD4^+$ T effector memory cells was detected in blood, spleen and in the skin-draining lymph nodes of DKO mice. A worsening of atherosclerosis at the aortic sinus and coronary arteries was also observed in DKO mice vs EKO mice. Human apoA-I overexpression in the DKO background was able to rescue the skin phenotype and to halt atherosclerosis development.
Conclusions. HDL deficiency, in the absence of hyperlipidemia, is associated with severe alterations of skin morphology, coronary atherosclerosis, local and systemic inflammation.