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Skin morphology in double apoA-I/apoE knock-out mice: a structural and ultrastructural study

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Apolipoprotein(apo)A-I, the main protein component of high density lipoproteins (HDLs), plays a major role in cholesterol removal from peripheral tissues and increasing evidence supports its function as an important regulator of the immune response (Annema et al., 2013).

The aim of the study was to evaluate the effect of apoA-I deficiency in dyslipidemic mice, when fed a low-fat/low-cholesterol diet. Three lines of male mice were considered: wild-type mice as controls, apoE-KO mice as dyslipidemic model (Zhang et al.,1992) and apoA-I/apoE double KO mice (DKO mice). Whereas in wild-type mice cholesterol circulates almost exclusively in HDLs, apoE-KO mice are hypercholesterolemic and cholesterol mostly circulates in low-density lipoproteins. In DKO mice, cholesterol levels are comparable to wild-type mice, but HDLs are almost absent and cholesterol entirely accumulates in low-density lipoproteins.

In the present study, all animals were maintained on a low-fat/low-cholesterol diet up to 30 weeks of age. At sacrifice, skin biopsies from two different anatomical areas (thoracic and abdominal regions) were harvested from each animal and processed for both light (LM) and transmission electron microscopy (TEM). Whereas the skin of apoE-KO mice was comparable to that of control mice, LM analysis in DKO mice revealed an increase in dermal thickness and a massive presence of foam cells and lymphocytes. TEM analysis showed the presence of cholesterol clefts in the papillary dermis and inside foam cells in the reticular dermis.

In conclusion, our results demonstrate that in DKO mice fed a low-fat/low-cholesterol diet, the lack of apoA-I is responsible for an aberrant skin morphology, with an exacerbated inflammatory response, possibly caused by a local cholesterol accumulation.

References

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