Apolipoprotein(a) stimulates vascular endothelial cell growth and migration and signals through integrin alphaVbeta3.

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ABSTRACT
Elevated plasma concentrations of Lp(a) [lipoprotein(a)] are an emerging risk factor for atherothrombotic disease. Apo(a) [apolipoprotein(a)], the unique glycoprotein component of Lp(a), contains tandem repeats of a plasminogen kringle (K) IV-like domain. In the light of recent studies suggesting that apo(a)/Lp(a) affects endothelial function, we evaluated the effects of apo(a)/Lp(a) on growth and migration of cultured HUVECs (human umbilical-vein endothelial cells).
Two full-length r-apo(a) [recombinant apo(a)] variants (12K and 17K), as well as Lp(a), were able to stimulate HUVEC growth and migration to a comparable extent; 17K r-apo(a) also decreased the levels of total and active transforming growth factor-beta secreted by these cells. Using additional r-apo(a) variants corresponding to deletions and/or site-directed mutants of various kringle domains in the molecule, we were able to determine that the observed effects of full-length r-apo(a) on HUVECs were dependent on the presence of a functional lysine-binding site(s) in the apo(a) molecule. With respect to signalling events elicited by apo(a) in HUVECs, we found that 17K treatment of the cells increased the phosphorylation level of FAK (focal adhesion kinase) and MAPKs (mitogen-activated protein kinases), including ERK (extracellular-signal-regulated kinase), p38 and JNK (c-Jun N-terminal kinase). In addition, we showed that LM609, the function-blocking antibody to integrin alphaVbeta3, abrogated the effects of 17K r-apo(a) and Lp(a) on HUVECs.
Taken together, the results of the present study suggest that the apo(a) component of Lp(a) signals through integrin alphaVbeta3 to activate endothelial cells.

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