Evidence of a mechanosensory role for CD31 in cardiovascular disease

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CD31 (PECAM-1) has been shown to form a mechanosensory complex with VE-cadherin and VEGFR which can modulate endothelial cell (EC) responses to shear stress through NF-κB activation. Since CD31 is expressed on leukocytes, EC and platelets and has been shown to play a prominent role in the transmigration of leukocytes into sites of inflammation, we hypothesized that it might contribute to the development of atherosclerosis in a shear dependent manner. To test this hypothesis we generated Pecam¹⁻/⁻Apoe¹⁻/⁻ mice to determine the role of CD31 in an established model of murine atherosclerosis. At 10 weeks of age, Pecam¹⁻/⁻Apoe¹⁻/⁻ mice or control mice (age and sex-matched) were placed on a high fat diet (20% cocoa butter, 1.25% cholesterol) or maintained on normal chow diet, for a further 13 weeks. Aortas were then excised and stained with oil red O (ORO) to determine plaque burden and serum lipid levels and leukocyte counts taken. No differences were found in weight gain, serum cholesterol or tri-glyceride levels between CD31 deficient or control groups. Mice kept on a high fat diet showed a larger plaque burden compared to those on chow diet, but no differences were seen in percentage plaque burden between CD31 deficient or control mice in the whole aorta. Complete analysis of the aortic regions revealed a reduction in plaque burden in areas of disturbed flow (aortic arch and inner curvature) and an elevation in plaque burden in areas of steady (laminar) flow (thoracic and abdominal aortas) in Apoe¹⁻/⁻ mice lacking CD31 compared to the control groups. Thus, under conditions of laminar flow, CD31 appears to act as a mechanotransducer of anti-atherogenic signals into EC, and therefore removal of CD31 leads to an increase in plaque burden. Conversely, in areas of complex flow, CD31 transduces pro-atherogenic signals, the loss of which moderates the disease process. This indicates that the mechanosensory role of CD31 is essential in the development of atheromas at areas of disturbed flow.


Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.