Atherosclerotic lesions were present in the aortae of the ApoE$^{-/-}$ mice. A significant increase in total lesion area occupying the aorta was observed in the aged ApoE$^{-/-}$ mice compared to mice at the earlier time-point (0.11% vs. 2.78%, P = 0.006, n = 6–7 mice per group). A significant increase in the amount of PVAT surrounding the aortae of C57/BL6 mice was recorded in response to ageing (15.65 ± 2.90 mg versus 26.87 ± 2.84 mg, P = 0.02 n = 5–8 mice per group). In contrast, no differences in the amount of aortic PVAT was observed between young and ageing ApoE$^{-/-}$ mice (14.08 ± 1.64 mg versus 13.11 ± 1.78 mg, P=NS, n = 3–5). Aortic PVAT exerted anti-contractile effects in the young 8 week controls (PVAT versus no PVAT: P = 0.04, n = 6). However, the anti-contractile capacity of aortic PVAT was abolished in ageing control mice (PVAT versus no PVAT: P=NS, n = 8). The aortic PVAT from young ApoE$^{-/-}$ mice exhibited the characteristics of an aged phenotype, exerting no anti-contractile effect (PVAT versus no PVAT: P=NS, n = 8); this was sustained in ageing ApoE$^{-/-}$ mice (PVAT versus no PVAT: P=NS, n = 8). Modulations in adipokine expression were observed with ageing in both C57/BL6 and ApoE$^{-/-}$ mice.

Aortic PVAT from ApoE$^{-/-}$ mice displayed an aged phenotype even at 12 weeks of age. These findings may have important implications in the pathogenesis of atherosclerosis. Further investigation into the characteristics of aortic PVAT from ApoE$^{-/-}$ mice and the factors it releases in early and established atherosclerosis is ongoing.

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189 DIFFERENTIAL EFFECTS OF RESVERATOL ON ACETYLCHOLINE-INDUCED AND FLOW-MEDIATED DILATION OF THE MOUSE FEMORAL ARTERY

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Despite the widespread use of nutritional supplements, insight into their potential beneficial or harmful biological effects is frequently lacking. Resveratrol (RV) is a polyphenol found in berries and grape skin and is often marketed as beneficial for vascular health. Here, we tested this assumption and hypothesised that RV enhances endothelial function and flow-mediated dilation (FMD) in mouse femoral arteries.

C57BL/6 male mice (12 weeks of age) were humanely euthanised in accordance with the â€ ˜Animals (Scientific Procedures) Act 1986â€ ™ and Institutional guidelines. Sections of the femoral artery were dissected and mounted between two glass cannulae on a modified pressure myograph chamber. Arteries were pressurised to an intravascular pressure of 60 mmHg. Endothelial-dependent dilator responses to acetylcholine (ACh) and intraluminal flow in pre-constricted vessels (Phe 10^{-5} M) were assessed in femoral arteries incubated for 1 h in either 30 ÂµM RV or physiological saline solution (PSS). The contribution of different vasodilator pathways was investigated by treating sections of the femoral artery with L-NG-nitro-L-arginine (L-NNA; 100uM) or indomethacin (10 ÂµM). The drugs were applied intraluminally for 30 min using a 1-mL syringe inserted into one end of a 3â€ way luer connexion on the side of the pressure myograph chamber while incubated in PSS or RV. After 30 min incubation, dilator responses to ACh (10^{-9}–10^{-3} M) and intraluminal flow (5–10 ÂµLÂ·min^{-1}) in the presence or absence of these drugs were determined.

Maximal degrees of dilation were reached upon perfusing the arteries with of 10^{-5} to 10^{-3} M ACh. RV treatment significantly enhanced dilation in response to ACh ($p < 0.05$). Whereas dilation of the arteries in response to ACh was (mean ± SEM) 68.1 ± 13.7% (n = 9) of the passive diameter when incubated with PSS, treatment with RV resulted in dilation of 92.2 ± 13.4% (n = 6). However, RV significantly reduced FMD ($p < 0.05$); dilation in response to intraluminal flow of 8 ÂµLÂ·min^{-1} was 22.5 ± 7.1% (n = 9) and 0.67 ± 1.06% (n = 6) of the passive when the sections were incubated with PSS and RV, respectively. Incubation with L-NNA reduced dilation to ACh in the presence of RV. However, the effects of RV on ACh dilation were maintained in the presence of indomethacin. The effects of RV on FMD were not significantly modulated by L-NNA or indomethacin. The responses to intraluminal flow were still compromised and no significant dilation was present. Our data suggest that RV may have differential effects on ACh-dependent and FMD responses in the mouse femoral artery. The use of RV as a nutritional supplement still warrants caution.

190 INVESTIGATING PLATELET FUNCTIONAL HETEROGENEITY USING DROPLET MICROFLUIDICS

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Platelet activation is an important step in arterial thrombosis, the acute complication of atherosclerosis. However, current diagnostic techniques for platelet function have been shown to be inadequate to predict thrombosis. In spite of this, many patients are prescribed aspirin to prevent (further) occurrence of arterial thrombosis, introducing bleeding risk. Platelets have been shown to be heterogeneous in a number of features such as size, volume and density, and this variety may underpin overall system behaviour. Functional heterogeneity has been suggested in several studies but current methods are not suitable to reliably study single platelet function. Such a method should provide a high throughput means to profile large platelet populations for the identification of, potentially rare, hyperactive platelets. In addition, the technique must prevent paracrine signalling (platelet-mediated activation of neighbouring platelets), necessitating the isolation of single platelets. This study adapts a droplet microfluidics approach to investigate single platelet functionality.

Here, single platelet sensitivity is studied by adding the agonist (convulxin, specific ligand of the GPVI receptor for collagen) during encapsulation in droplets. After an incubation period the platelets are retrieved from the droplets into fixative, followed by flow cytometry analysis of markers for activation. The PAC-1 antibody is used to identify the active conformation of the Î ± IIbÎ²3 receptor, important for aggregation and adhesion, and anti-CD62P (p-selectin) to identify degranulation of the platelets. Platelets are identified with CD42b, which is a platelet specific receptor.