

Regulatory CD19<sup>+</sup>CD24<sup>hi</sup>CD38<sup>hi</sup> B cells are decreased in patients with coronary atherosclerosis and have impaired interleukin-10 production in response to CpG

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**Aim:** B-lymphocytes have critical roles in the inflammatory process that drives atherosclerosis. In animal models, conventional B2 B cells promote atherosclerosis, whilst innate B1a B cells are protective. B cells with regulatory function (Bregs) have been identified in animals and humans and have been implicated in the pathogenesis of autoimmunity. Whether Bregs have a role in human atherosclerosis is currently unknown. Our aim was to characterise the frequency, phenotype and function of Bregs in atherosclerosis patients.

**Methods:** CD19<sup>+</sup>CD24<sup>hi</sup>CD38<sup>hi</sup> Bregs were quantified in patients with atherosclerosis (myocardial infarction, MI, n=60; stable angina, SA, n=40), and in healthy subjects (n=30) using flow cytometry. Interleukin-10 (IL-10) production was quantified by intracellular staining.

**Results:** The percentage and absolute number of circulating Bregs were markedly reduced in MI and SA patients compared to healthy subjects. No differences were noted in total, mature or memory B cells, suggesting a specific depletion of the Breg cell subset. Bregs from MI and SA patients produced significantly less IL-10 in response to CpG but not CD40L compared to Bregs from healthy subjects. IL-10 production by mature and memory B cells was not impaired. Molecular mechanisms that underlie defects in Bregs in patients with atherosclerosis are being characterised.

**Conclusions:** Our data show for the first time that patients with atherosclerosis harbour marked numerical and functional defects in Breg cells that may tip the balance in favour of pro-inflammatory B and T lymphocytes. A better understanding of these defects may reveal novel targets for therapies to tackle inflammation in atherosclerosis.