ApoE attenuates unresolvable inflammation by complex formation with activated C1q.

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ILRS Authors

Susanne Ackermann Luke Donald Halder

Projects

Characterization of the immediate early response of human dendritic cells to *Candida albicans*
Details

The role of Apolipoprotein E in the innate immune system
Details

Abstract

Apolipoprotein-E (ApoE) has been implicated in Alzheimer's disease, atherosclerosis, and other unresolvable inflammatory conditions but a common mechanism of action remains elusive. We found in ApoE-deficient mice that oxidized lipids activated the classical complement cascade (CCC), resulting in leukocyte infiltration of the choroid plexus (ChP). All human ApoE isoforms attenuated CCC activity via high-affinity binding to the activated CCC-initiating C1q protein (KD~140-580 pM) in vitro, and C1q-ApoE complexes emerged as markers for ongoing complement activity of diseased ChPs, Aβ plaques, and atherosclerosis in vivo. C1q-ApoE complexes in human ChPs, Aβ plaques, and arteries correlated with cognitive decline and atherosclerosis, respectively. Treatment with small interfering RNA (siRNA) against C5, which is formed by all complement pathways, attenuated murine ChP inflammation, Aβ-associated microglia accumulation, and atherosclerosis. Thus, ApoE is a direct checkpoint inhibitor of unresolvable inflammation, and reducing C5 attenuates disease burden.

Identifier

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