Fibrin Degradation Product β15-42—New Insights in an Old Pathway

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Beside the striking relevance for vascular hemostasis, the notable role of fibrinogen in inflammatory responses has long been unrecognized. In 1997, the pleiotropic functions of fibrinogen were first substantiated by demonstrating its crystal structure.[1] Ever since, fibrinogen and fibrin degradation products have been a target of multiple studies investigating their influence on hematopoietic and immune cells, particularly in the context of impaired vascular integrity following reperfusion injuries. Here, a massive disruption of the endothelium results in fibrinogen-promoted adhesion of leukocytes to endothelial cells and subsequent transmigration into affected tissues.[2] Previous studies revealed a prominent role of two fibrin-derived degradation products in these processes: the E1 fragment and the β15–42 peptide, whereby the latter was accredited to possess outstanding cardioprotective attributes by decreasing transendothelial leukocyte migration.[3] In this issue of *Thrombosis and Haemostasis*, Yakovlev et al[4] attempt to unveil the therapeutic effects of β15–42 and investigate to this end the underlying signaling pathways resulting in inhibition of leukocyte transmigration. By using state-of-the-art analytical methods such as solid-phase binding assays, endothelial permeability, and transendothelial migration assays, as well as murine knockout systems, they contradict the current literature view which claims that the β15–42 peptide competes with the fibrin degradation product E1 for binding to vascular endothelial-cadherin and eventually reduces transendothelial migration. Instead, the authors emphasize that β15–42 affects leukocyte transmigration by inhibiting the very-low-density-lipoprotein receptor-dependent pathway and thus promoting the active state of the Scr kinase Fyn. This results in an inactivation of the small GTPase RhoA, which was shown previously to be a key regulator in stress-induced opening of endothelial junctions.[5]

By adjusting and clarifying the signaling pathway of β15–42, the present study furthers our understanding of how fibrinogen degradation products influence the functions of leukocytes during inflammatory processes and introduces new targets for therapeutic interventions.

Conflict of Interest
None declared.

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