tie-ing the antiinflammatory effect of angiopoietin-1 to inhibition of NF-κB

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latter, recent provocative evidence suggests that ABIN proteins share a sequence of homology with IKK-γ (inhibitor of kappa B kinase), a regulatory component of the IKK signalsome that is essential for phosphorylation and consequent degradation of IκB (inhibitor of kappa B), an indispensable step in NF-κB activation. This raises the interesting possibility that ABIN proteins act by binding to and competing for an upstream regulator of the IKK signalsome, thereby inhibiting its activity. One could then speculate that Ang1-stimulated recruitment of ABIN-2 in endothelial cells could facilitate this process (perhaps by leading to a conformational change in ABIN-2 or bringing it in proximity to proteins involved in IKK activation) (Figure).

In summary, the data offered by Hughes et al.21 show that the Tie2-ABIN-2 interaction is responsible for the inhibitory effects of Ang1 on stimulated NF-κB activity, implicating this novel interaction in mediating the antiinflammatory properties of Ang1. However, in addition to its role in inflammation, NF-κB has myriad effects, raising numerous questions as to how, if at all, the Tie2-ABIN-2 interaction modifies the other effects of Ang1 on endothelial cell survival26 and migration,15 both of which are critical in angiogenesis, and both of which in endothelial cells or other cellular systems involve NF-κB signaling in some fashion.27–29 Similar questions arise about the role of the Tie2-ABIN-2 interaction in molecular crosstalk with signaling pathways, such as PI3K-Akt, known to be activated by Ang1 (Figure), but that also modulate NF-κB activity.30 The answers to such questions will be crucial in determining the physiological relevance of the Tie2-ABIN-2 interaction and may provide important clues to the intricate process of blood vessel formation in normal physiology and disease states.

References


**Key Words:** angiopoietin-1 ■ Tie2 ■ nuclear factor-κB ■ endothelial cells ■ ABIN-2
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