Papers of the Week

Src Cannot Break Barriers Alone ♦

See referenced article, J. Biol. Chem. 2010, 285, 7045–7055

Src-induced Tyrosine Phosphorylation of VE-cadherin Is Not Sufficient to Decrease Barrier Function of Endothelial Monolayers

Many studies point to the phosphorylation of VE-cadherin by activated Src family kinases (SFKs) as a major step in promoting vascular permeability in response to inflammatory signals or growth factors. However, it’s not exactly clear how critical SFKs are as growth and inflammation factors activate other signaling pathways in parallel. In this Paper of the Week, Alejandro Adam and colleagues used three approaches to directly study SFK activity in cultured endothelial cells: knocking down the gene for the negative Src regulator C-terminal Src kinase, expressing a dominant negative Csk (DN-Csk), or expressing a constitutively active Src (caSrc). DN-Csk overexpression induced VE-cadherin phosphorylation at tyrosines 658, 685, and 731 but did not induce any changes in monolayer permeability. Similarly, Csk gene knockdown promoted VE-cadherin phosphorylation at tyrosines 658 and 731 but also did not increase permeability. caSrc expression, which promoted VE-cadherin phosphorylation on tyrosines 658 and 731, did decrease barrier function, only several hours after phosphorylation though. In addition, none of the phosphorylation sites hindered the ability of VE-cadherin to bind other adherens junction proteins or localize at the plasma membrane. Therefore, these studies by Adam and colleagues indicate that Src-induced phosphorylation of VE-cadherin by itself is not sufficient to increase vascular permeability.

DOI 10.1074/jbc.P109.079277