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TRPV4-TAZ signaling in matrix stiffness and TGFβ1-induced epithelial-mesenchymal transition

Epithelial-mesenchymal transition (EMT) is an essential event in development, fibrogenesis, and oncogenesis. Emerging data support a role for both a mechanical signal, and a biochemical signal, in EMT. Here, we report evidence that transient receptor potential vanilloid 4 (TRPV4), a channel sensitive to both matrix stiffness and transforming growth factor β1 (TGFβ1) stimuli, is a likely mediator of EMT. We found that antagonism of TRPV4 blocked both matrix stiffness- and TGFβ1-induced EMT in normal human primary epidermal keratinocytes, as determined by changes in morphology and alterations in expression of EMT markers including E-cadherin, N-cadherin, and α-smooth muscle actin (α-SMA). In a murine dermal fibrosis model, TRPV4 deletion resulted in decreased expression of the mesenchymal marker, α-SMA, and increased expression of epithelial marker, E-cadherin. Furthermore, we found that: i) TRPV4 was essential for the nuclear translocation of TAZ in response to matrix stiffness and TGFβ1; ii) Antagonism of TRPV4 inhibited both matrix stiffness-induced and TGFβ1-induced expression of TAZ proteins; and iii) TRPV4 antagonism

suppressed both matrix stiffness-induced and TGFβ1-induced activation of Smad2/3, but not of AKT. Altogether, these data identify a novel role for TRPV4 in regulating EMT in response to both matrix stiffness and TGFβ1.

Speaker Biography

Shaik O Rahaman, is an assistant professor at the University of Maryland, USA. His laboratory is interested in elucidating the signaling events underlying the pathogenesis of atherosclerosis and fibrosis. Dr. Rahaman earned his PhD in Molecular Biology at Jadavpur University, and a BS in Human Physiology (Honors), and an MS in Biophysics and Molecular Biology from University of Calcutta. From 2000-2014, Dr. Rahaman worked at Cleveland Clinic, Cleveland, USA, as a Postdoctoral Fellow, eventually as a Project Scientist and Assistant Professor. He was the recipient of the American Heart Association Scientist Development Grant, NIH-R01 grant, and NSF grant. Dr. Rahaman is the author or co-author of 23 research papers in high impact international peer-reviewed journals of repute. Dr. Rahaman has given numerous invited talks nationally and internationally, and is a reviewer/editorial board member in numerous scientific journals. Dr. Rahaman also served as a reviewer for National Institute of Health (USA).

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