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TRPV4 channels regulates matrix stiffness and TGFβ1-induced epithelial-mesenchymal transition

Epithelial-mesenchymal transition (EMT) has critical functions in cellular processes including development, tissue healing and oncogenesis. Emerging data support a role for both a mechanical signal, and a biochemical signal, in EMT. We report evidence showing that transient receptor potential vanilloid 4 (TRPV4) channel, is the likely mediator of EMT in response to both transforming growth factor β1 (TGFβ1), and matrix stiffness. We found that: a) genetic deficiency of TRPV4 channel blocked TGFβ1-induced EMT in normal mouse primary epidermal keratinocytes (NMEKs) as determined by changes in morphology and alterations of expression of EMT markers including E-cadherin (ECAD), N-cadherin (NCAD), and α-smooth muscle actin (α-SMA); and b) TRPV4 deficiency prevented matrix stiffness-induced EMT in NMEKs. Intriguingly, TRPV4 deficiency in mice suppressed expression of mesenchymal markers, NCAD and α-SMA, in murine dermal fibrosis model. We found an increased co-localization of TRPV4 with NCAD and decreased co-localization of TRPV4 with epithelial marker ECAD in skin tissues of bleomycin-treated wild-type mice compared to saline controls. Mechanistically, our results showed that: i) TRPV4 was critical for the nuclear translocation of YAP/TAZ (Yes-associated protein/transcriptional coactivator with PDZ- binding motif) in response to matrix stiffness and TGFβ1, ii) TRPV4 deletion inhibited both matrix stiffness- and TGFβ1- induced expression of YAP/TAZ proteins, and iii) TRPV4 deletion abrogated both matrix stiffness- and TGFβ1-induced activation of AKT, but not Smad2/3. Altogether, these data identify a novel role for TRPV4 in regulating EMT.

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. He has earned his PhD in Molecular Biology at Jadavpur University, and BS degree in Human Physiology (Honors) and MS degree in Biophysics and Molecular Biology from University of Calcutta. From 2000-2014, he has worked at Cleveland Clinic, Cleveland, USA, as a Post-doctoral 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. He is the author or co-author of 23 research papers in high impact international peer-reviewed journals of repute. He has given numerous invited talks nationally and internationally and is a reviewer and Editorial Board Member of numerous scientific journals. He also served as a Reviewer for National Institute of Health journals (USA).

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