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Functional effects of TGF-beta1 on mesenchymal stem cell mobilization in cockroach allergen induced asthma

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Mesenchymal stem cells (MSCs) have been suggested to participate in immune regulation and airway repair/remodeling. Transforming growth factor β1 (TGFβ1) is critical in the recruitment of stem/progenitor cells for tissue repair, remodeling and cell differentiation. In this study, we sought to investigate the role of TGFβ1 in MSC migration in allergic asthma. We examined nestin expression (a marker for MSCs) and TGFβ1 signaling activation in airways in cockroach allergen (CRE) induced mouse models. Compared with control mice, there were increased nestin+ cells in airways, and higher levels of active TGFβ1 in serum and p-Smad2/3 expression in lungs of CRE-treated mice. Increased activation of TGFβ1 signaling was also found in CRE-treated MSCs. We then assessed MSC migration induced by conditioned medium (ECM) from CRE-challenged human epithelium in air/liquid interface (ALI) culture in Transwell assays. MSC migration was stimulated by ECM, but was significantly inhibited by either TGFβ1 neutralizing antibody or TβR1 inhibitor. Intriguingly, increased migration of MSCs from blood and bone marrow to the airway was also observed after systemic injection of GFP+-MSCs, and from bone marrow of Nes-GFP mice following CRE challenge. Furthermore, TGFβ1 neutralizing antibody inhibited the CRE-induced MSC recruitment, but promoted airway inflammation. Finally, we investigated the role of MSCs in modulating CRE induced T cell response, and found that MSCs significantly inhibited CRE-induced inflammatory cytokine secretion (IL-4, IL13, IL17 and IFN-γ) by CD4+ T cells. These results suggest that TGFβ1 may be a key pro-migratory factor in recruiting MSCs to the airways in mouse models of asthma.

Biography

Peisong Gao, MD, PhD is currently Assistant Professor of Medicine at The Johns Hopkins University School of Medicine in Baltimore, Maryland. He received his MD degree and pulmonary medicine training in The Fourth Military Medical University (FMMU), Xi'an, China. From July 1997 to January 1999, he was a visiting research fellow with Dr. Julian M Hopkin at Osler Chest Unit, Oxford University. He subsequently moved to the University of Wales Swansea with Dr. Hopkin, pursuing a PhD working in molecular genetics of asthma. In 2008, he was promoted to Assistant Professor. He is a member of the Genetics, Molecular Biology and Epidemiology Committee (GMBEC), the American Academy of Allergy, Asthma & Immunology (AAAAI), and the American College of Allergy, Asthma & Immunology (ACAAI). His research has been greatly recognized by several awards, including the 2004 Research Excellence Award, the 2007 Interest Section Award, and Outstanding Pediatric Allergy, Asthma and Immunology Award from AAAAI.

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