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Overexpression of MMP9 in macrophages attenuates pulmonary fibrosis induced by bleomycin☆

Sandra Cabrera[a], Miguel Gaxiola[b], José Luis Arreola[b], Remedios Ramírez[a], Paul Jara[a], Jeanine D'Armiento[c], Thomas Richards[d], Moisés Selman[b], Annie Pardo[a,*]

[a] *Facultad de Ciencias, Universidad Nacional Autónoma de México, Mexico*
[b] *Instituto Nacional de Enfermedades Respiratorias, Mexico*
[c] *Department of Medicine, Columbia University, New York, NY, USA*
[d] *University of Pittsburgh Medical Center, Pittsburgh, PA, USA*

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Abstract

Pulmonary fibrosis is a common response to a variety of lung injuries, characterized by fibroblast/myofibroblast expansion and abnormal accumulation of extracellular matrix. An increased expression of matrix metalloprotease 9 (MMP9) in human and experimental lung fibrosis has been documented, but its role in the fibrotic response is unclear. We studied the effect of MMP9 overexpression in bleomycin-driven lung fibrosis using transgenic mice expressing human MMP9 in alveolar macrophages (hMMP9-TG). At 8 weeks post-bleomycin, the extent of fibrotic lesions and OH-proline content were significantly decreased in the TG mice compared to the WT mice. The decreased fibrosis in hMMP9-TG mice was preceded by a significant reduction of neutrophils and lymphocytes in bronchoalveolar lavage (BAL) at 1 and 4 weeks post-bleomycin, respectively, as well as by significantly less TIMP-1 than the WT mice. From a variety of cytokines/chemokines investigated, we found that BAL levels of insulin-like growth factor binding protein-3 (IGFBP3) as well as the immunoreactive protein in the lungs were significantly lower