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TIMP-1, -2, -3, and -4 in idiopathic pulmonary fibrosis. A prevailing nondegradative lung microenvironment?

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Selman, Moises, Victor Ruiz, Sandra Cabrera, Lourdes Segura, Remedios Ramírez, Roberto Barrios, and Annie Pardo. TIMP-1, -2, -3, and -4 in idiopathic pulmonary fibrosis. A prevailing nondegradative lung microenvironment? *Am J Physiol Lung Cell Mol Physiol* 279: L562–L574, 2000.—Fibroblast proliferation and extracellular matrix accumulation characterize idiopathic pulmonary fibrosis (IPF). We evaluated the presence of tissue inhibitor of metalloproteinase (TIMP)-1, -2, -3, and -4; collagenase-1, -2, and -3; gelatinases A and B; and membrane type 1 matrix metalloproteinase (MMP) in 12 IPF and 6 control lungs. TIMP-1 was found in interstitial macrophages and TIMP-2 in fibroblast foci. TIMP-3 revealed an intense staining mainly decorating the elastic lamina in vessels. TIMP-4 was expressed in IPF lungs by epithelial and plasma cells. TIMP-2

the early stages of the disease (25). In this context, an imbalance between the synthesis and degradation of ECM molecules in the local lung microenvironment appears to be of central importance in the pathogenesis of the fibrotic component of IPF.

Matrix metalloproteinases (MMPs), the mediators of matrix degradation, are a family of zinc endoproteinases that share structural domains and are collectively capable of degrading essentially all ECM components (2). At present, the human MMP gene family contains 17 members that can be divided by structure and substrate specificity into several subgroups including collagenases, gelatinases, stromelysins, and membrane type (MT) MMPs; other MMPs do not appear to