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BASIC RESEARCH PAPER

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Essential role for the ATG4B protease and autophagy in bleomycin-induced pulmonary fibrosis

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Abbreviations: ACTA2, actin, α 2, smooth muscle, aorta; ATG3, autophagy-related 3; ATG4B, autophagy-related 4B; cysteine peptidase; ATG5, autophagy-related 5; ATG7, autophagy-related 7; ATG9B, autophagy-related 9B; BAX, BCL2-associated X protein; CASP3, caspase 3, apoptosis-related cysteine peptidase; CAV1, caveolin 1, caveolae protein, 22kDa; CCL3, chemokine (C-C motif) ligand 3; CXCL1, chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity α); CXCR2, chemokine (C-X-C motif) receptor 2; DRAM2, DNA-damage regulated autophagy modulator 2; GFP-LC3B, green fluorescent protein-LC3B; IL12B, interleukin 12B; IL13, interleukin 13; IFNG, interferon, gamma; IPF, idiopathic pulmonary fibrosis; MAP1LC3B/LC3B, microtubule-associated protein 1 light chain 3 β; RELA, v-rel reticuloendotheliosis viral oncogene homolog A; SQSTM1, sequestosome 1; TGFB1, transforming growth factor, β 1; TGFBR2, transforming growth factor, β receptor II (70/80kDa); TNF, tumor necrosis factor; TUBB4, tubulin, β 4, class IV; WT, wild type.

Autophagy is a critical cellular homeostatic process that controls the turnover of damaged organelles and proteins. Impaired autophagic activity is involved in a number of diseases, including idiopathic pulmonary fibrosis suggesting that altered autophagy may contribute to fibrogenesis. However, the specific role of autophagy in lung fibrosis is still undefined. In this study, we show for the first time, how autophagy disruption contributes to bleomycin-induced lung fibrosis in vivo using an *Atg4b*-deficient mouse as a model. *Atg4b*-deficient mice displayed a significantly higher inflammatory response at 7 d after bleomycin treatment associated with increased neutrophilic infiltration and