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Putting the spotlight on macrophage-derived cathepsin in the pathophysiology of obliterative bronchiolitis

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New findings for the puzzle of bronchiolitis obliterans syndrome (BOS) are pointing to the role of CatB-procollagen-TGF-β signalling pathways, linked to fibrosis mechanisms and tissue damage control https://bit.ly/3qQPax9

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While the experience of lung transplantation (LTx) is growing worldwide, long-term outcomes are not improving accordingly. Next to oncological and infectious complications, chronic rejection, clinically defined as chronic lung allograft dysfunction (CLAD), remains the major bottleneck to improving long-term outcomes [1, 2]. Increased recognition of clinical phenotypes of CLAD assists in predicting patient prognosis; however, mechanistically, we are still far from unravelling the pathophysiological processes underlying CLAD. Indeed, the internationally endorsed recognition of an obstructive (bronchiolitis obliterans syndrome; BOS) and restrictive (restrictive allograft syndrome; RAS) phenotype of CLAD leads us to critically review historical mechanistic studies, as these are not focused on separate phenotypes [1, 3]. Whether both phenotypes share common pathophysiological mechanisms remains unknown; however, obliterative bronchiolitis (OB), pathological scarring of the small airways, is found in both phenotypes in varying degrees and is therefore a major target for further research because adequate therapy is lacking [4]. One of the major reasons for this poor knowledge of the mechanism of CLAD has been the lack of an adequate animal model of CLAD. Indeed, animal models are key for our further understanding of pathophysiological mechanisms. Although the initially proposed heterotopic trachea transplant model has its merits, the scientific community was especially intrigued by the murine orthotopic left LTx, as this was regarded as the ultimate model of CLAD. Key pathological findings include peribronchial inflammation, peribronchial thickening, vascular rejection and alveolar fibrosis.