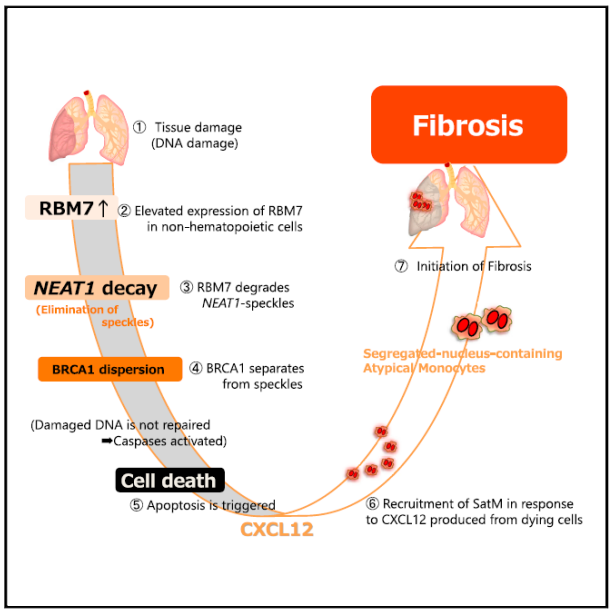
Elucidating the onset principle of fibrosis

-Discovery of the target gene Rbm7-

Fibrosis is an incurable disorder of unknown etiology. Segregated-nucleus-containing atypical monocytes (SatMs) discovered by the authors* are critical for the development of fibrosis. The research group of Kiyoharu Fukushima, Takashi Satoh and Shizuo Akira (Host Defense, IFReC, Osaka University) examined the mechanisms that recruit SatMs to pre-fibrotic areas. A screen based on cytokine expression in the fibrotic lung revealed that the chemokine Cxcl12, which is produced by apoptotic nonhematopoietic cells, was essential for SatM recruitment. Analyses of lung tissues at fibrosis onset showed increased expression of Rbm7, a component of the nuclear exosome targeting complex. Rbm7 deletion suppressed bleomycin-induced fibrosis and at a cellular level, suppressed apoptosis of nonhematopoietic cells. Mechanistically, Rbm7 bound to noncoding (nc) RNAs that form subnuclear bodies, including Neat1 speckles. Dysregulated expression of Rbm7 resulted in the nuclear degradation of Neat1 speckles, the dispersion of the DNA repair protein BRCA1, and the triggering of apoptosis. Thus, Rbm7 in epithelial cells plays a critical role in the development of fibrosis by regulating ncRNA decay and thereby the production of chemokines that recruit SatMs.



*Satoh et al. Nature 2017

The research group examined the mechanisms that recruit segregated-nucleus-containing atypical monocytes (SatMs), which are critical for fibrosis onset. They find that dysregulated expression of Rbm7, a component of the nuclear exosome targeting complex, in nonhematopoietic cells triggers apoptosis and thereby the production of chemokines that recruit SatMs.

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