Nature Reviews Gastroenterology & Hepatology **11**, 4 (2014); published online 26 November 2013; doi:10.1038/nrgastro.2013.227

LIVER

Key role for α_v integrins in myofibroblasts in liver fibrosis

New research has shown that α_v integrins are a core component of a molecular pathway that underlies the development of fibrosis in multiple organs, including the liver. "Therapeutically targeting all α_v integrins effectively treated fibrosis in multiple organs," explains author Neil Henderson, offering hope for new targeted antifibrotic therapies.

Henderson and co-workers developed a model system, using *Pdgfrb*-Cre mice, to study the effects of α_v integrins in the context of fibrosis. Depletion of α_v integrins in hepatic stellate cells (a major source of myofibroblasts in the liver) protected mice from developing liver fibrosis upon treatment with carbon tetrachloride (CCl_4). Importantly, individual depletion of multiple binding partners for the α_v subunit (β_3, β_5 and β_6 integrins, or conditional depletion of β_8 integrin on myofibroblasts) failed to protect mice from CCl_4-induced liver fibrosis—a finding that Henderson believes is because "inhibition of multiple α_v integrins is probably required to effectively treat liver fibrosis".

Crucially, use of a small-molecule inhibitor of α_v integrins (CWHM 12) substantially reduced the development of fibrosis in the liver and in the lung. Moreover, CWHM 12 reduced liver fibrosis even after the disease was well established.

"Comprehensive testing of CWHM 12 will be required before consideration of clinical trials," notes Henderson, who plans to investigate a variety of different genes in myofibroblasts in the quest for further novel antifibrotic targets.

Katrina Ray

Original article Henderson, N. C. *et al.* Targeting of α_v integrin identifies a core molecular pathway that regulates fibrosis in several organs. *Nat. Med.* doi:10.1038/nm.3282