and efficacy of pioglitazone as a treatment for NASH.

Original article Belfort R *et al.* (2006) A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. *N Engl J Med* **355:** 2297–2307

Rapamycin therapy attenuates fibrogenesis in rats with established cirrhosis

The mammalian target of rapamycin (mTOR) activates hepatic stellate cells, which then produce extracellular matrix proteins in the fibrotic liver. Neef and colleagues investigated the effects of rapamycin, a potent inhibitor of mTOR, in two rat models of advanced liver cirrhosis.

Cirrhosis was induced in rats by either bile-duct ligation (BDL) ($n = 89$) or twice weekly 200 mg thioacetamide injections ($n = 40$). Eight control rats underwent sham BDL. Once cirrhosis was established, the rats were randomly allocated to receive 0.5 mg/kg body weight daily rapamycin, or no rapamycin, for either 14 or 28 days.

Rapamycin improved survival in BDL-treated cirrhotic rats (82% of rapamycin-treated versus 59% of rapamycin-untreated rats survived); by contrast, all the rats with thioacetamide-induced cirrhosis survived, irrespective of whether they received rapamycin. In both BDL and thioacetamide-induced cirrhosis, 14 days of rapamycin treatment prevented the accumulation of extracellular matrix proteins and suppressed interstitial matrix metalloproteinase 2 activity, which indicate preserved metabolic liver function. Rapamycin treatment for 28 days prolonged survival in rats with BDL-induced cirrhosis (but without beneficial effects on liver function); however, in rats with thioacetamide-induced cirrhosis, 28 days of rapamycin had no effect on liver function or fibrosis, compared with rapamycin-untreated rats.

The reduction in antifibrotic efficacy with time implies that compensatory mechanisms might reduce rapamycin's therapeutic value. The authors suggest that delay in the progression of cirrhosis might still be clinically useful, and propose that rapamycin should be evaluated as an antifibrotic drug in patients with cirrhosis.

Original article Neef M *et al.* (2006) Low-dose oral rapamycin treatment reduces fibrogenesis, improves liver function, and prolongs survival in rats with established liver cirrhosis. *J Hepatol* **45:** 786–796

Diet and exercise improve liver function and insulin resistance in children with NAFLD

Nonalcoholic fatty liver disease (NAFLD) is associated with obesity and insulin resistance in children. Nobili *et al.* hypothesized that oxidative stress caused by the metabolism of excess free fatty acids might contribute to the liver damage seen in NAFLD. They investigated the effect of dietary supplementation with vitamin E, an antioxidant, on liver function in children with NAFLD.

In this 12-month, double-blind study, a calorie-controlled diet and aerobic exercise plus vitamin E and C supplementation was compared with the same diet and exercise plan plus placebo, in 88 consecutive children with biopsy-proven NAFLD. No advantage for vitamin E supplementation versus placebo was seen; however, both regimens were equally effective in normalizing alanine aminotransferase levels, insulin resistance and liver brightness on ultrasound. Mean fasting insulin and glucose levels decreased in both groups. Alanine aminotransferase levels normalized in 26 of 43 patients in the placebo group and in 32 of 45 patients in the vitamin E group. Liver brightness was reduced in 37 (and eliminated in 3) placebo-treated patients, and similarly was reduced in 33 (eliminated in 3) vitamin-E-treated patients. In overweight patients, 29 of 33 in the placebo group and all 37 in the treatment group lost >20% of their excess weight.

The authors concluded that a controlled diet and exercise regimen improves liver function and insulin resistance in children with NAFLD, but that vitamin E supplementation confers no extra benefit.

Original article Nobili V *et al.* (2006) Effect of vitamin E on aminotransferase levels and insulin resistance in children with non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* **24:** 1553–1561

HMGA1 identified as a therapeutic target in pancreatic adenocarcinoma

HMGA1 encodes two transcription factors that are overexpressed in pancreatic adenocarcinomas. HMGA1 proteins are known to be involved in oncogenesis, but little is known