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IN BRIEF

STEM CELLS

Stem cell therapy for liver cirrhosis unREALISTIC?

Small-scale clinical studies have suggested that infusions of haematopoietic stem cells can reduce hepatic fibrosis and accelerate liver regeneration. However, in a multicentre, randomized controlled trial for patients with compensated chronic liver disease, no improvement in liver function and fibrosis was found for patients receiving autologous stem cell therapy compared with standard care. In the REALISTIC trial, patients were randomly assigned to a standard care group ($n = 27$) or groups receiving granulocyte colony-stimulating factor (G-CSF) with ($n = 28$) or without ($n = 26$) repeated infusions of autologous haematopoietic stem cells. No differences in MELD score were seen between the three groups after 90 days. Furthermore, serious adverse events (such as ascites, sepsis and encephalopathy) were more frequent in the G-CSF plus stem cell infusion group than in the G-CSF alone or standard care groups.

ORIGINAL ARTICLE Newsome, P. N. *et al.* Granulocyte colony-stimulating factor and autologous CD133-positive stem-cell therapy in liver cirrhosis (REALISTIC): an open-label, randomised, controlled phase 2 trial. *Lancet Gastroenterol. Hepatol.* http://dx.doi.org/10.1016/S2468-1253(17)30326-6 (2017)

DEVELOPMENTAL BIOLOGY

Stable epigenetic signatures in intestinal organoids

Intestinal epithelial organoids (IEOs) are an important tool for translational research, but many characterization studies have so far relied on gene expression analysis. Epigenetic mechanisms, such as DNA methylation, have key roles during intestinal development and homeostasis, but whether DNA methylation signatures in the intestines are cell-intrinsic or dependent on external cues was previously unknown. Now, using genome-wide DNA methylation profiling, Kraiczy *et al.* show that IEOs derived from fetal, paediatric or adult small and large bowel show stable gut segment-specific DNA methylation profiles that closely correspond to profiles from matched primary gut epithelium. Fetal IEOs showed changes in DNA methylation patterns during culture indicative of maturation that were partly regulated by TET1, a demethylating enzyme. Furthermore, distinct methylation differences were found in IEOs derived from a child with gastric heterotopia, highlighting the potential of this technology for disease-specific research models.

ORIGINAL ARTICLE Kraiczy, J. *et al.* DNA methylation defines regional identity of human intestinal epithelial organoids and undergoes dynamic changes during development. *Gut* http://dx.doi.org/10.1136/gutjnl-2017-314817 (2017)

EXPERIMENTAL MODEL

A new mouse model of Alagille syndrome

Alagille syndrome is a genetic disorder characterized by severe liver and heart abnormalities, and ocular, vertebral and craniofacial malformations. Most cases of this disease are associated with mutations in a gene encoding a Notch ligand called *JAG1*, but how signalling was affected through different Notch receptors was poorly understood and previous disease models did not recapitulate all its features. To produce the new mouse model, researchers generated mice homozygous for a missense mutation (H268Q) in JAG1 ($Jag1^{Ndr/Ndr}$) in which bile duct development is disrupted and most features of Alagille syndrome are reproduced. Using this model, the investigators studied Notch signalling and showed that the $JAG1^{Ndr}$ mutation generates a hypomorphic ligand that binds to NOTCH2 but not NOTCH1.

ORIGINAL ARTICLE Andersson, E. R. *et al.* Mouse model of Alagille syndrome and mechanisms of Jagged1 missense mutations. *Gastroenterology* http://dx.doi.org/10.1053/j.gastro.2017.11.002 (2017)