Comprehensive mechanism of human bone mesenchymal stem cells rescuing fulminant hepatic failure in pigs

With the support by the National Natural Science Foundation of China and the National Key Basic Research Program (973 Program), the research group led by Prof. Li Jun (**李君**) and Academician Li Lanjuan (**李兰娟**) at the State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, the First Affiliated Hospital, Zhejiang University School of Medicine, cooperated with Prof. Chen Xin from the Institute of Biochemistry, College of Pharmaceutical Sciences, Zhejiang University, and reported recently on the comprehensive mechanism of human bone mesenchymal stem cells (hBMSCs) rescuing fulminant hepatic failure (FHF) in pigs, which was published online in *Gut* (2016, Feb 16, doi:10.1136/gutjnl-2015-311146).

FHF is a life-threatening condition for which orthotopic liver transplantation is currently viewed as one of the best effective treatments, but donor organ shortages and contraindications result in the death of many patients awaiting liver transplantation. Stem cell transplantation provides a promising alternative for the treatment of FHF, but the lacking of mechanistic understanding about the stem cell-recipient interaction hinders its translation in clinics. Based on their in-house translation model, in a large animal, of hBMSCs rescue in FHF pigs, the team quantitatively evaluated the comprehensive mechanism using functional synergy analysis with a huge volume of data, which should be justified with precedent. They discovered that hBMSCs transplantation immediately suppressed D-galactosamine-induced life-threatening cytokine storms and stabilized FHF within 7 days, while human-derived hepatocytes constituted only ~4.5% of the pig hepatocytes. The implanted hBMSCs altered recipients' cytokine responses to damage through paracrine effects, and they also found an important cytokine/biological process, DLL4/Notch, which may represent a novel therapeutic means for treating FHF, and validated the liver restoration effect of DLL4 in both pig and rat FHF models. This is an important study with significant clinical implications in treating FHF patients, and may open a new avenue to the discovery of single molecule-based therapeutics that simulate stem cell actions.

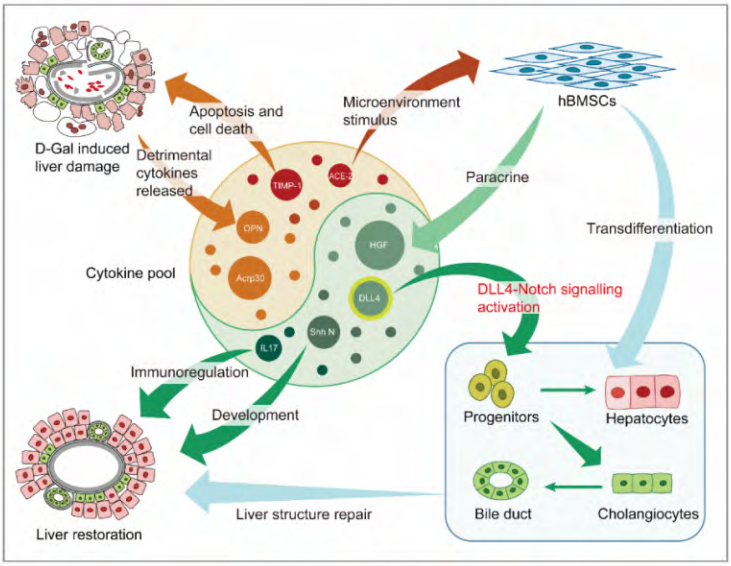

Figure Proposed mechanisms of hBMSCs action in liver restoration.