Atorvastatin enhances bone marrow endothelial progenitor cell function in corticosteroid-resistant immune thrombocytopenia patients

With the support by the National Natural Science Foundation of China, the research team directed by Prof. Huang XiaoJun (黄晓军) at Peking University People's Hospital, Peking University Institute of Hematology and Beijing Key Laboratory of Hematopoietic Stem Cell Transplantation, recently reported that Atorvastatin enhances bone marrow endothelial progenitor cells (BM EPCs) function in corticosteroid-resistant immune thrombocytopenia (ITP) patients, which was published in *Blood* (2018, 131(11): 1219—1233). The first author of the paper is Associate Prof. Kong Yuan (孔圆).

ITP, generally characterized by increased peripheral platelet destruction and reduced platelet production, is a common hematological disease. The pathogenesis of corticosteroid-resistant ITP, a clinically challenging condition in which patients exhibit either no response to corticosteroids or are corticosteroid-dependent, remains poorly understood. Murine studies suggest that BM EPCs play a crucial role in regulating megakaryocytopoiesis. However, little is known regarding the number and function of BM EPCs or how to improve impaired BM EPCs in corticosteroid-resistant ITP patients.

The research group performed a prospective case-control study and a pilot cohort study to evaluate whether the BM EPCs in corticosteroid-resistant ITP differed from those in corticosteroid-sensitive ITP, and whether atorvastatin could enhance the number and function of BM EPCs derived from corticosteroid-resistant ITP patients *in vitro* and *in vivo*. They found that reduced and dysfunctional BM EPCs play a role in the pathogenesis of corticosteroid-resistant ITP, and the impaired BM EPCs could be improved by atorvastatin. The current study indicates that the impaired BM EPCs might hamper the differentiation progress from HSCs to megakaryocytes, resulting in the occurrence of corticosteroid-resistant ITP, which is different from the immune-mediated mechanism in corticosteroid-sensitive ITP. These findings may provide new insight into the pathogenesis of corticosteroid-resistant ITP and indicate that atorvastatin represents a promising therapeutic approach for repairing impaired BM EPCs in corticosteroid-resistant ITP patients, which provided a rational for further prospective large-scale clinical trials.

Figure One representative result figure of Prof. Huang's study was utilized as the cover image of the issue of *Blood* (2018, 131(11)), which indicates that Atorvastatin treatment improves colony-forming unit—plating efficiency and promotes megakaryocytopoiesis in cultures with BM EPCs from corticosteroid-resistant ITP patients.

Prof. Ishac Nazy (McMaster University) and Prof. Adam Cuker (University of Pennsylvania) made a comment on this study, which was published in *Blood* (2018, 131(11): 1159—1161). "In this issue of *Blood*, Kong et al. show that BM EPCs in patients with corticosteroid-resistant ITP are reduced and dysfunctional but can be improved with atorvastatin, suggesting a potential novel therapy for ITP. More broadly, they serve as a reminder that ITP is not one disease but rather a heterogeneous group of diseases with varying disease mechanisms".