Preface

Antibodies and liver transplantation

A few years ago, I had an opportunity to collaborate with Professor Haitao Zhao and Dr Ruoyu Miao of the Peking Union Medical College Hospital (PUMCH). To witness their superior clinical and research programs would have been reward enough for a visit to Beijing, but I was also blessed to meet Professor Yilei Mao. After I had observed him complete complex liver surgery at PUMCH, Professor Mao informed me of plans to start a new high quality journal dedicated to the science of liver disease and nutrition. I knew it would be a game-changer. Therefore, I was greatly honored to be invited to guest-edit a special issue of the journal.

In consultation with the editorial team, we chose the topic of *antibodies and liver transplantation*. We believe it is a neglected field that is ready to yield vital information regarding human physiology and the mechanism of disease. Despite knowledge that dates back over half a century, we are still uncertain of the role of the liver in humoral immunity, of autoantibodies in liver diseases, of the 'liver protective effect' on the outcome of organ transplantation, or the mechanism of the relative resilience of the liver to humoral reactions.

Human leukocyte antigens (HLA) were initially identified by crossmatching panels of human sera with patient leucocytes in a complement dependent lysis assay. In the 1970s, HLA typing was standardized through the collaboration of the major laboratories. Sensitivity was increased initially with anti-human globulin augmentation and later by the use of flow cytometry instead of complement induced lysis. Modern methods to precisely identify specific anti-HLA antibodies using antigen coated beads in a solid phase assay are reviewed by McCaughan and colleagues: while sensitivity and precision have been increased, clinical relevance needs to be reassessed (1). Xu and colleagues used these modern methods to study the impact of alloantibodies directed against the second donor on long-term outcomes of repeat liver transplantation but could detect no adverse signal (2). They recommend that the current practice of allocating liver grafts without regard for HLA matching be continued but that HLA typing and analysis also be done to unlock the differences between liver transplantation and transplantation of other organs.

Humans have 4 immunoglobulin (Ig) G subclasses, each with a different ability to fix complement, which are formed during a maturation process within the B-cell. At least two types of immune response have been described on the basis of specific cytokines produced by the T-cell and IgG subclasses by the B-cell. The type 1 response is believed to have developed to repel invaders such as viruses and may play a role in acute rejection. The type 2 response may have developed to allow successful implantation of the haplo-identical fertilized ovum in pregnancy. Either response may be the mechanism of certain auto-immune liver diseases. While deviation to the type 2 response may reduce acute rejection after transplantation, it may open the path to cholangiopathy and chronic rejection later. The current state of our knowledge of IgG subclasses in liver disease and after transplantation is reviewed in this special issue (3).

Sharma and colleagues describe a rare situation where passenger lymphocytes from a Rhesus negative liver donor produced anti-D antibody resulting in the death of the Rhesus positive recipient (4). The group also reviewed the two-way traffic between donor and recipient of antibodies active in the hematological system (5). They report that anti-D antibody, or anti-human platelet antigen-1a antibody, related passenger lymphocyte syndrome (PLS) results in a severe outcome compared to ABO PLS that appears to be self-limiting. On the other hand, Factor VIII inhibitors in the recipient, or absence of CD59, makes transplantation costly, but possible, leaving patients with their original complaint whereas liver transplantation combined with bone marrow transplantation would reverse both processes. Finally, Lazo-Langner and colleagues report a successful liver transplantation using a donor with the JAK-2 mutation (6).

This special issue demonstrates that humoral immunology remains a rich area for research in liver disease and transplantation. Unravelling mechanisms of action will not only improve outcomes of liver transplantation but may also reveal treatment options for autoimmune liver diseases and liver cancers.

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