

Advances in Basic & Translational Research I

The role of NK cells in immune response during liver transplantation

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Natural killer (NK) cells are thought to provide a first line of defense against invading infectious microbes and neoplastic cells by exerting an effector function without the necessity for priming. They are highly heterogeneous lymphocytes with a diverse repertoire of phenotypes and functions. Their role in organ transplantation is not well defined, as it varies depending on the pathology encountered. Because NK cells are relatively unaffected by the immunosuppressive agents currently used after organ transplantation, it is important to understand how NK cells affect graft rejection and immunoregulatory mechanisms after organ transplantation.

Unlike other organs, the liver is rich in resident NK cells, and it is likely that donor liver-derived NK cells will be released into the circulating blood after transplantation and have a complex impact within the recipient immune system. We have previously demonstrated that liver mononuclear cells derived from donor liver perfusate contain a large number of NK cells that have vigorous cytotoxicity against hepatocellular carcinoma (HCC) cells with the expression of tumor necrosis factor-related apoptosis-inducing ligand, a critical molecule for NK cell-mediated anti-tumor cell killing, after IL-2 stimulation. We conducted the phase I study of the adoptive transfer of liver-derived NK cells stimulated with IL-2 in liver transplant recipients with HCC, proving that this treatment was well tolerated and reduced the HCC recurrence rate after liver transplantation. We have also proved that adoptive immunotherapy with NK cells was associated with the reduced post-transplant bloodstream infections.

In this session, I will introduce the results of our basic and clinical research on the peculiarities of liver-resident NK cells, as well as related research results by others.