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主要研究兴趣为 NK 细胞生物学研究、肝脏免疫学研究和新型生物治疗技术及产品研制。1989 年国内较早开展 NK 细胞研究,发现肝脏特有 NK 细胞及其肝内发育分化新途径,提出"肝脏也是天然免疫器官";发现 NK 细胞可通过分泌细胞因子对免疫系统行使整体调节,提出存在"调节性 NK 细胞(Regulatory NK Cell)";揭示肝脏乙肝病毒诱发 NK 细胞免疫耐受,提出"NK 细胞识别受体异常可导致肝脏疾病"。试图从 NK 细胞角度解析肝脏"免疫耐受"奥秘并重新认识肝脏疾病。受行业专项委托制定国家 NK 细胞临床应用技术标准,建立可临床应用的国人首株 NK 细胞系和多种基因修饰亚株、创建自身 NK 细胞体外千倍级扩增技术、研制 NK 细胞刺激因子(Interleukin-12)重组蛋白药物等,已进入临床试验申报阶段。

NK Cells and Liver Disease

Liver was recently recognized as an innate immune organ since its high content of NK cells, NKT cells and $\gamma\delta T$ cells in addition to monocyte-derived Kupffer cells. The key immunologic features of liver are considered to be immunotolerant, which keeps liver homeostasis and safeguards its pivotal function. In the last two decades, we tried to explore the liver-specific NK subset, and to clarify its biological, physiological and pathological role in liver tolerance and homeostasis. Recently, we found a liver-resident NK cells which occupys almost 50% of all hepatic NK cells (the rest of NK cells coming from blood circulation, called conventional NK cells), characterized with an unique surface phenotype, absolute localization in liver and development from adult liver heamatopoietic progenitor cells (Liver-HPC). The importance of this liver-resident NK cell, and also other possible liver-HPC-derived innate lymphoid cells such as NKT cells, $\gamma\delta T$ cells and ILC1, in HBV infection, viral hepatitis and HCC is also discussed. I will present some evidences to demonstrat that like CTLs, NK cell exhaustion also existes in tumor, and chekchpoint molecules found through liver NK cell study play a critical role in immunotherapy.