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Innate Lymphoid Cells in Mouse Models of HCC and NASH

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Innate Lymphoid Cells in Mouse Models of HCC and NASH

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Abstract

Innate lymphoid cells (ILCs) have recently gained a lot of interest in immunology since several studies have suggested that this relatively rare cell population may have master regulator functions. ILCs are divided into 3 subgroups: ILC1, ILC2 and ILC3. ILCs act T cell receptor independent but their function is mediated by cytokines. Here we study ILCs in the context of Non-alcoholic fatty liver disease (NAFLD). NAFLD is considered an important risk factor for HCC. Mice were fed either methionine-choline deficient (MCD) diet or high-fat (HF) diet to induce nonalcoholic steatohepatitis (NASH) or NAFLD. After 4 weeks or 20 weeks respectively liver showed signs of fatty liver disease. Flow cytometry was performed and group 1 ILCs were determined as CD45+, lineage-, NKp46+ and NK1.1+ or Tbet+. ILC1s were further characterized as CD49a+ and CD49b-, which are also described as liver resident NK cells (lrNK). Conventional NK cells (cNK) were defined as CD49a- CD49b+. Mice fed MCD diet showed a significant increase of cNK cells and a relative decrease of ILC1s. Mice fed high fat diet showed a relative increase of cNK and a relative decrease of lrNKs. Mice bearing AKT/CAT induced hepatocellular adenoma (HCA) showed a reduced frequency of lrNKs and MCD diet further increased cNK frequency in tumor bearing mice. Here we present a first analysis of Group 1 ILCs in the liver of mice with NAFLD and/or HCC. NK cells represent a major population in the liver of mice and human. ILC1s are closely related to NK cells and their plasticity but also their function in the setting of liver disease and HCC is not understood.