ABSTRACT

The present inventors used a model of intrasplenically induced liver metastasis to determine whether or not NF-κB activation in the liver is involved in the onset of metastatic tumors. When IKKβ was deleted from both liver cells and hematopoietically-derived cells, the onset of tumors was reduced remarkably. Tumor cells activated neighboring bone marrow cells (Kupffer cells) and produced mitogens such as interleukin (IL)-6, and this promoted angiogenesis and growth of tumors. The mitogen production depended on NF-κB in hematopoietically-derived Kupffer cells. Furthermore, treatment with an anti-IL-6 receptor antibody decreased the degree of metastatic tumor development. That is, the present inventors showed that tumor metastasis depends on inflammation, and proinflammatory intervention that targets Kupffer cells is useful for chemical prevention of metastatic tumors. Furthermore, it was shown that inhibition of the IKKβ/NF-κB signal transduction pathway, in particular IL-6 inhibition, can be utilized for anti-metastasis agents.