

***MCP-1* Promoter Polymorphism at -2518 is Associated with Metastasis of Nasopharyngeal Carcinoma after Treatment**

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Nasopharyngeal Carcinoma (NPC) is more prominent in southeastern Asia including southern China, Hong Kong and Taiwan. It is a multifactorial disease, whose etiologies includes EBV infection, genetic, and environmental factors [1]. Histopathologically, NPC is heavily infiltrated with leukocytes, particularly by macrophages and T lymphocytes. Monocyte Chemoattractant Protein-1 (MCP-1) is a proinflammatory chemokine involved in the recruitment of T lymphocyte and monocyte/macrophages from circulation to the sites of inflammation [2]. Overexpression of MCP-1 has been reported in a variety of diseases characterized with intensive macrophages infiltration such as atherosclerosis, arthritis, idiopathic pulmonary fibrosis and various tumors. It is known that MCP-1 expression in response to a variety of inflammatory molecules can be modulated by a functional single nucleotide polymorphism (SNP), -2518G/A, located at the distal regulatory region of MCP-1 promoter [3]. Through global gene expression analysis of NPC tumor cells and adjacent normal nasopharyngeal tissue by Affymetrix microarrays, MCP-1 was overexpressed in 6 out of 9 NPC samples examined, and was further confirmed by IHC. Previous literatures have shown that the MCP-1 SNP-2518 is associated with susceptibility and severity of human diseases. The purpose of this study is to evaluate the associations of MCP-1 SNP-2518 with NPC prognosis.

Genomic DNA collected from 411 NPC patients who had been admitted to CGMH, Lin-Kou, from March 1994 to November 2004 were subjected to this study. The *MCP-1* SNP-2518 genotype was determined by TaqMan[®] genotyping kit and statistical analyses were conducted. We compared the risks of disease relapse among genotype groups after initial treatment, we found that patients with AA or AG-genotype are prone to develop distant metastasis (AA vs. GG HR=2.21, $P=0.017$; AG vs. GG HR=2.23, $P=0.005$); on the other hand, patients of AA-genotype had a reduced risk of developing local recurrence when compared with patients with GG –genotype (AA vs.GG HR=0.53, $P=0.05$). Here is the first report showing that MCP-1 SNP-2518 is an independent genetic risk predictor for developing distant metastasis after complete treatment in NPC patients. This finding may help to develop personalized therapy, and validation study is awaited.

Reference

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Figure 1 The Distant Metastasis-free survival of NPC patients with different *MCP-1* SNP-2518 genotype was compared using Kaplan-Meier survival curves.

