

Frequent Expression of C5aR in Metastatic Renal Cell Carcinoma

Introduction and Objective: Anaphylatoxin C5a is the fragment of complement 5th component, which is a potent chemoattractant for leukocytes. Recent studies showed C5a receptor (C5aR) is aberrantly expressed in human cancers, which plays a crucial role in cancer invasion via enhancing cancer cell motility. In this study, we analyzed expression of C5aR in metastatic and non-metastatic renal cell carcinoma (RCC). The possible role of C5aR in renal cancer cells was also investigated by in vitro analysis.

Materials and Methods: We retrospectively investigated data from 127 Renal Cell Carcinoma patients who received radical/partial nephrectomy or renal biopsy between 2002 and 2011. C5aR expression in renal cell carcinoma samples were examined by immunohistochemistry using Formalin-Fixed Paraffin-Embedded tissue samples, and correlation between C5aR expression and clinicopathological parameters was analyzed. In addition, murine renal carcinoma cell line RenCa was stably transfected with murine C5aR cDNA, and the effect of C5a stimulation on signal transduction and cellular morphology was investigated by western blot and immunofluorescence, respectively.

Results: The median (range) age of the patients was 62 (22-87) years. 97 patients (66 men and 31 women) had non-metastatic RCC, whose median (range) age was 63 (22-85) years, and 30 patients (20 men and 10 women) had metastatic RCC (mRCC), whose median (range) age was 59 (30-87) years. Immunohistochemical analysis showed that C5aR expression was observed in 96.7% of RCC cases that was accompanied with metastatic foci, whereas only 50.5% of non-metastatic RCC that expressed C5aR (Fisher's Exact Test, $p < 0.001$). There is no correlation between C5aR expression and other clinicopathological parameters. RenCa cells overexpressing mC5aR showed increased ERK activation upon C5a stimulation compared to control cells. F-actin staining using Alexa-conjugated Phalloidin revealed formation of actin stress fiber in mC5aR expressing RenCa cells by C5a stimulation.

Conclusions: These results suggest that C5aR expression may favor metastasis of RCC cells by ERK activation and cytoskeletal rearrangement.