POTENTIAL MOLECULAR TARGETS FOR GASTRIC CANCER THERAPY

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Introduction:

Gastric adenocarcinoma remains one of the most aggressive cancers, being the fourth most common type of cancer and the second leading cause of cancer-related death worldwide. Our study aims to analyze molecular pathogenesis of gastric adenocarcinoma by exploring aberrant signaling pathways in gastric tumor tissues and gastric cancer cell lines.

Methods:

We collected tumor and adjacent normal tissue samples from 51 patients with gastric adenocarcinoma. cDNA and proteins have been used in exploring gene expression and signaling pathways by gene microarray and dot-blotting.

Results:

Gene expression analysis has identified seven genes, significantly up-regulated, that seems to be associated with tumor progression: KRT17, COL10A2, KIAA1199, SPP1, IL11, S100A2, and MMP3. Results from proteomics highlighted STAT3 activation, simultaneously with JNK and p38 MAP kinase, Wnt/b-catenin, and Akt pathways in gastric tumor tissues. The RNA interference technology was used to inhibit S100A2, and KRT17 gene expression in two human gastric cancer cell lines in order to investigate the biologic significance of these two genes in gastric cancer pathogenesis; genes were selected based on their high expression level on gastric adenocarcinoma samples. The inhibition of specific mRNA expression was determined by quantitative PCR and the effect of gene down–regulation on signaling pathways was assessed by dot-blotting.

Conclusion:

The results showed that siRNA knockdown of S100A2, and KRT17 genes decreased signaling on the pathways associated with proliferation, migration and angiogenesis, and these genes may be potential targets for developing new therapeutical strategies in gastric cancer. **Acknowledgements:**

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