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ABSTRACTS

Gastric Cancer

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Molecular Biology: East and West

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Gastric cancers are anatomically classified as proximal and distal cancers and have marked geographic variations. While distal tumors constitute the majority of gastric cancer cases in the East, including China, Korea, and Japan, most cases in the West are proximal gastric tumors. Five-year survival rate in the West is less than 20%, whereas it is closer to 60% in Korea and Japan. It has been suggested that the higher survival rate in patients in the East than in the West might be due to differences in screening for early detection, diagnostic criteria, and staging methods, and more radical surgery in the East than in the West. However, differences between the two anatomic groups of gastric cancer have never been addressed at the molecular level.

To address these differences, we generated gene expression data from three anatomically different tumor groups of the upper gastrointestinal tract (75 distal esophageal tumors, 68 proximal gastric tumors, and 65 distal gastric tumors), and applied systems-level comparison of tumor transcriptome. As expected, overall gene expression patterns in non-tumor tissues from two different anatomic sites (proximal and distal) of stomach were very similar to each other and had distinctive patterns (unique to gastric tissues) as compared with patterns in non-tumor tissues in the distal esophagus. Surprisingly, gene expression patterns of proximal gastric tumors were more similar to those of esophageal tumors and were significantly different from distal gastric tumors, suggesting biologic differences between proximal and distal gastric cancers.

Further analysis of gene expression data identified unique gene expression signatures for proximal and distal gastric tumors, and revealed signaling pathways that are uniquely activated in the two groups of gastric cancers. Our data provide new insight on the anatomic and geographic differences between various groups of gastric tumors. In addition to differences in ethnic background between patients in the East and West, there are remarkable disparities in the treatment of gastric cancer in the two regions, including use of different staging systems, surgical methods, and chemoradiotherapy schedules. However, our data

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indicate that biologic differences between two groups of tumors as reflected in gene expression patterns may also explain the disparities in outcome in the patient populations.