

# High levels of the protein SIX1 indicate that gastric cancer has grown deadly

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## Video Abstract

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# Abstract

Researchers have identified a gene important to the growth and spread of gastric cancer, opening the door to new understanding of this deadly disease. The gene, known as SIX1, has been implicated in disease progression in several cancers, but its link to gastric cancer wasn't clear. This ambiguity prompted researchers at China Medical University to take a closer look at the role of SIX1 in gastric cancer cells. The team started by measuring SIX1 protein expression in gastric tumors and adjacent non-tumor tissue collected from 208 patients. They found high levels of SIX1 in nearly half the tumor samples and virtually none in the non-cancerous tissue – a pattern suggesting that SIX1 is an important biomarker for gastric cancer. This notion was supported by the finding that patients with higher levels of SIX1 had more advanced disease than those with moderate SIX1 expression. To identify the cellular changes occurring in the presence of high levels of SIX1, the researchers turned to six commonly used gastric cancer cell lines. By either knocking out or ramping up SIX1 expression, they were able to get a clearer idea of SIX1 function. They found that boosting the levels of SIX1 led to an increase in cell division and enhanced the invasiveness of the cells – two key signs that a cancer is turning deadly. In line with these results, high levels of SIX1 also promoted the epithelial-mesenchymal transition, an important event that drives metastasis. The team also identified the other molecular players SIX1 seemed to be working with to effect these changes: the protein cyclin D1 in the case of cellular proliferation, and the protein MMP-2 in the case of cellular invasion. Overall, the results shed light on the biological and clinical significance of SIX1 in the progression of gastric cancer. They also lay a foundation for future work looking to pinpoint new drug targets for this deadly disease.