

## Letter to the Editor: Advances and Challenges in Gastric Cancer Research

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### Recent Research Breakthroughs

One of the significant recent findings is the discovery of the role of nociceptive neurons in gastric cancer progression. Timothy C. Wang's team from the Digestive and Liver Diseases Research Center at Columbia University in the US published a paper in *Nature* in February 2025. They found that CGRP<sup>+</sup> peptide - containing sensory neurons interact with gastric cancer cells through the CGRP - RAMP1 axis. In multiple mouse gastric cancer models, these neurons expand significantly in a NGF - TRK pathway - dependent manner. Activating these neurons promotes tumor growth and metastasis, while inhibition or ablation has the opposite effect. In human gastric cancer samples, the density of CGRP<sup>+</sup> nerves is higher, indicating its potential as a new therapeutic target [1].

In terms of treatment, the GEMSTONE - 303 phase 3 trial, published in *JAMA* in February 2025, evaluated sugemalimab, a fully human anti - programmed death - ligand 1 (PD - L1) antibody. When Combined with Capecitabine and Oxaliplatin (CAPOX) as first - line treatment for unresectable locally advanced or metastatic gastric or gastroesophageal junction adenocarcinoma patients with a PD - L1 Combined Positive Score (CPS) of 5 or greater, it significantly improved overall survival (median 15.6 months vs 12.6 months) and progression - free survival (median 7.6 months vs 6.1 months) Compared to Placebo Plus CAPOX, with a manageable safety profile [2].

### Challenges in Gastric Cancer Management

Despite these advancements, several challenges persist. The early diagnosis of gastric cancer remains difficult. Most patients are diagnosed at an advanced stage, which greatly reduces the curative potential. Symptoms in the early stages are often non - specific, and current screening methods lack sufficient sensitivity and specificity for mass screening.

Drug resistance is another major issue. As more targeted therapies and immunotherapies are developed, a significant number of patients develop resistance over time, leading to treatment failure. Understanding the underlying mechanisms of drug resistance, such as the activation of compensatory signaling pathways and the changes in the tumor microenvironment, is crucial for developing effective strategies to overcome it.

Moreover, the high heterogeneity of gastric cancer poses challenges for personalized medicine. Different patients may respond differently to the same treatment due to genetic, epigenetic, and microenvironmental differences. Identifying reliable biomarkers to predict treatment responses and guide individualized treatment is an urgent need.

### Future Perspectives

Future research should focus on developing more accurate early - detection methods. For example, exploring new biomarkers in blood, stool, or gastric juice, and improving endoscopic techniques to detect early lesions more effectively. In terms of treatment, combination therapies that target multiple pathways simultaneously may be the key to overcome drug resistance and improve treatment outcomes. Additionally, more in - depth studies on the tumor - nerve interaction discovered recently may open new doors for developing innovative therapeutic strategies.

In conclusion, while there have been remarkable advances in gastric cancer research, significant challenges remain. Continued efforts in basic research, clinical trials, and translational medicine are essential to improve the prognosis of gastric cancer patients.

### References

1. Wang T C (2025) Nociceptive neurons promote gastric tumour progression via a CGRP-RAMP1 axis. *Nature* 640: 802-810.
2. Xiaotian Zhang, Jufeng, Gang Wang (2025) First - Line Sugemalimab Plus Chemotherapy for Advanced Gastric Cancer. The GEMSTONE - 303 Randomized Clinical Trial 333: 1305-1314.

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