UNRAVELING THE ACTIVATION AND FUNCTIONING MECHANISMS OF WNT2B+ CANCER-ASSOCIATED FIBROBLASTS IN GASTRIC CANCER PROGRESSION

Wei Kang

UEG Week Barcelona 2026 | Presentation

Mechanisms & Personalised Medicine | Stomach & H. Pylori | Digestive Oncology | Oesophagus

October 20, 2026

ZEB1-driven Wnt2b expression in cancer-associated fibroblasts promotes gastric cancer progression and angiogenesis via FZD1 in fibroblasts and FZD4 in endothelial cells, with FZD4 blockade by aptamer-based PROTAC reversing these effects and showing synergy with VEGFR inhibitors.

KEY POINTS

- Wnt2b was the most predominant Wnt ligand in progenitor-like gastric cancer CAFs and elevated Wnt2b levels were associated with poorer clinical outcomes
- ZEB1 was identified as the key transcriptional regulator of Wnt2b and ZEB1 expression in CAFs emerged as an independent prognostic indicator of unfavorable outcomes
- FZD1 on CAF membranes mediates Wnt2b pro-tumorigenic effects while FZD4 on endothelial cells promotes angiogenesis by activating both Wnt-β-catenin and Hippo-YAP1 signaling pathways
- Wnt2b deletion in transgenic mice significantly decreased xenograft growth, spontaneous tumor growth, and angiogenesis
- An aptamer-based PROTAC targeting FZD4 potently inhibited angiogenesis and xenograft growth in vivo and showed synergistic anti-tumor effects with VEGFR inhibitors
- The findings provide insights into reversing resistance to VEGF/VEGFR inhibitors by targeting the Wnt2b-FZD4 axis in the tumor microenvironment

VIEW THIS CONTENT ON GUTFLIX

https://gutflix.eu/search/d/06f198f2-d12b-11f1-819e-daaa6dbee0a2

AI-generated summary

This summary was generated by an AI large language model based on the content transcript. It is for informational purposes only and should not be considered a substitute for clinical judgment. Always rely on your professional expertise and the full clinical context when making clinical decisions.