Sensory neuropeptide CGRP and its co-receptor RAMP1 drive tumour cell growth in gastrointestinal cancers

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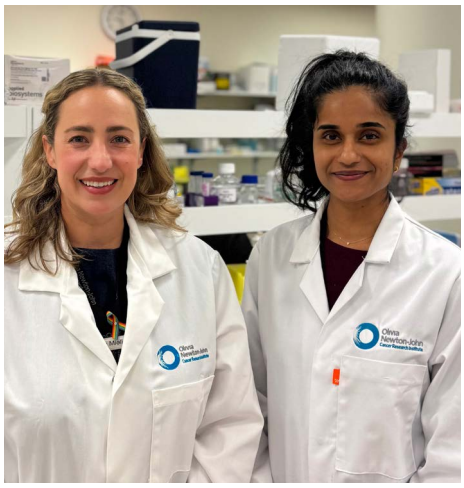
"This study reveals novel mechanisms by which the neuropeptide CGRP promotes tumour growth in GI cancers. We expand upon existing knowledge by demonstrating that tumour cells are a source of CGRP, highlighting potential therapeutic targets within the tumour–nerve axis."

🧬 What's the big idea?

The study uncovers a novel **tumour–nerve signalling axis** in gastrointestinal cancers, showing that the sensory neuropeptide **CGRP** and its co-receptor **RAMP1** actively drive tumour growth. This identifies a new, targetable pathway in the tumour microenvironment.

💊 What did the researchers do?

- Analysed **180 patient samples** of colorectal cancer (CRC), gastric cancer (GC), and CRC liver metastases using multiplex immunohistochemistry.
- Correlated **RAMP1 expression** with clinical outcomes and molecular subtypes using **the Cancer Genome Atlas data**.
- Conducted **in vitro experiments** on cancer cell lines and patient-derived organoids to test CGRP's effect on growth.
- Performed **RNA sequencing** to identify gene pathways activated by CGRP stimulation.



🔬 What did they discover?

- **High RAMP1 expression** in tumour cells correlates with poor survival in CRC and GC.
- CGRP is not only present in nerve fibres but also **produced by tumour cells**.
- CGRP stimulation **enhances tumour cell proliferation** in a RAMP1-dependent manner and activates genes linked to metabolism, angiogenesis (blood vessel growth), and migration.
- RAMP1 expression is enriched in **CRC** from tumours with microsatellite instability and in **younger GC patients**.

🚀 Why is this important?

- Reveals a **tumour–nerve interaction** that promotes cancer progression.
- Suggests therapies targeting **CGRP** (used for migraine) could potentially be used to treat GI cancers. Further research is required to determine the therapeutic potential of these therapies in GI cancers.
- Opens new therapeutic avenues targeting both **tumour growth mechanisms and microenvironmental factors**.

🧠 What's next?

- Clinical trials to test CGRP–RAMP1 inhibitors in CRC and GC.
- Explore mechanisms regulating CGRP and RAMP1 expression in tumours.
- Investigate combination strategies with immunotherapy, as CGRP may suppress anti-tumour immunity.
- Develop biomarkers for patient stratification based on RAMP1 expression.