**A gut‑on‑a‑chip platform to monitor GLP-1 secretion dynamics from primary intestinal tissue**

**Background:**   Glucagon-like peptide-1 (GLP-1) is a gut-derived hormone of critical importance to metabolic homeostasis. Existing knowledge of GLP‑1 secretion largely relies on static immortalised cell lines or *ex vivo* models, which cannot capture its dynamic release. We developed a microfluidic ‘gut-on-a-chip’ (GOC) platform for monitoring of dynamic GLP-1 release from primary mouse intestinal tissue in a biomimetic setting.

**Methods:** To guide the GOC design, we first characterised the GLP-1-secreting capacity of small intestinal segments from 8‑week old male C57BL/6 mice, under a one-hour static incubation with 2.8mM taurocholic acid (TCA). Based on these findings, we fabricated the GOC platform from poly (methyl methacrylate) incorporating parallel serosal and luminal perfusion channels separated by a 2.5 × 0.5cm tissue chamber and a porous polycarbonate membrane. To evaluate its performance, we first perfused exogenous GLP‑1 (100pM) in cyclical ‘8-min on/12-min off’ intervals without tissue. We then loaded mouse duodenal tissue to assess GLP-1 release into the serosal channel in response to: (i) a 60-min continuous luminal infusion of TCA (2.8 or 10mM), and (ii) an 80-min pulsatile TCA (10mM) infusion delivered luminally or serosally.

**Results:**  Static incubation with TCA augmented GLP-1 release throughout the small intestine, most consistently from the duodenum. Without tissue, ‘on-off’ GLP-1 perfusion into the serosal channel produced oscillatory GLP-1 concentrations in the serosal efflux. With duodenal tissue, luminal TCA triggered GLP-1 release dose-dependently. Furthermore, ‘on-off’ TCA perfusion via either luminal or serosal channels induced periodic elevations in GLP-1 concentrations, with serosal perfusion triggering a more pronounced response (Figure).

**Conclusion:** This study has established a novel GOC platform that allows independent delivery of stimuli to either the mucosa or serosa surfaces of primary murine intestinal tissue and real-time monitoring of dynamic GLP-1 release. This tool has high potential to advance future mechanistic studies and drug screening for therapeutic development.

