TRANSGENIC MICE WITH FLUORESCENT INTESTINAL K-CELLS

Dr Fiona Gribble and Dr Frank Reimann have developed transgenic mice with fluorescently labelled intestinal K-cells.

Uses

- Investigate the mechanisms involved in glucose-dependent insulinotropic polypeptide (GIP) secretion
- Potential to identify targets in these cells that could be exploited therapeutically for treatment of obesity
- Isolated cells suitable for electrophysiology, fluorescence calcium imaging, and expression analysis studies

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Case Ref: Gri-2367-09

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Background

Glucose-dependent insulinotropic polypeptide (GIP) is an intestinal hormone released by K cells that promotes insulin release following glucose ingestion. It coordinates the fate of dietary fat directly in adipocytes and has been postulated to link overnutrition to obesity.

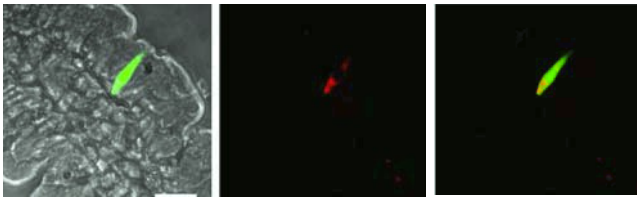
To date there has been relatively poor understanding of how K cells release GIP, largely because living enteroendocrine cells are difficult to identify. At the cellular and molecular levels very little is known about how K cells respond to glucose and other stimuli largely because there is a lack of validated cell models for studying GIP release in vitro.

Technology

Dr Fiona Gribble and Dr Frank Reimann at the University of Cambridge have made a transgenic mouse model in which GIP-secreting K cells are labelled by the yellow fluorescent protein Venus.

Expression of Venus in these transgenic mice driven by the GIP promoter and was shown to be restricted to K cells as assessed by immunofluorescence and measurements of the *Gip* mRNA and GIP protein contents of purified cells (Figure 1). From freshly isolated tissue of these transgenic mice K cells can be identified and purified.

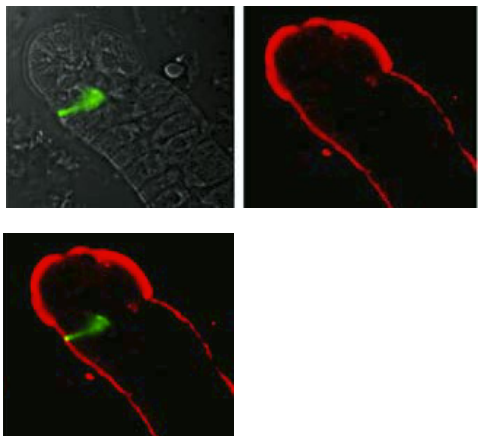
Figure 1: Colocalisation of direct Venus fluorescence (green) with GIP immunofluorescence (red) in the small intestine.



The fluorescently labelled cells will provide novel opportunities to interrogate the mechanisms of GIP secretion, for example enabling analysis of the expression of candidate glucose-sensing machinery in K cells (Figure 2).

The fluorescently tagged cells are suitable for patch clamping, single-cell dynamic calcium imaging, and cell sorting, providing a range of new and powerful techniques to interrogate the function of this enteroendocrine cell type.

Figure 2: Immunostaining for Venus (green) and sodium-dependent glucose transporter 1 (SGLT1) (red) in the duodenum/jejunum, showing the apical localisation of SGLT1 on the villus.



Publication

Nutrient-dependent secretion of glucose-dependent insulinotropic polypeptide from primary murine K cells. Diabetologia. 2009. 52(2):289

Commercialisation

These mice are available for internal research purposes on a non-exclusive basis and we are seeking licensees to apply these mice to their own research.