LETTER TO THE EDITOR

Circulating levels of ghrelin in human fetuses

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In their recent interesting paper in this journal, Cortelazzi *et al.* (1) convincingly demonstrate the presence of the gastric hormone ghrelin in human fetal circulation. They also find evidence that the fetus, rather than the placenta, is the origin of the circulating hormone. We recently reported that the fetal human pancreas is a rich source of ghrelin (2). We examined fetal pancreas specimens from gestational week 18 to birth; the hormone was found to be produced by a separate, and previously unrecognized, islet endocrine cell that constitutes approximately 10% of all islet cells until birth (when gastric ghrelin cells are still very few in number) (Fig. 1A). In adult humans, on the other hand, islet ghrelin cells are few (around 1% of all islet cells) (Fig. 1B), while gastric ghrelin cells are numerous. With these observations in mind we suggest that the pancreas is a good candidate for being a source of human fetal circulating ghrelin. An interesting question for the future is whether the elevated ghrelin levels in growth-restricted fetuses, as registered by Cortelazzi *et al.* and as found in neonates by others (3, 4), reflect an exaggerated upregulation of pancreatic ghrelin or are a result of other mechanisms, e.g. altered pro-hormone processing or impaired hormone degradation.

References

- 1 Cortelazzi D, Cappiello V, Morpurgo PS, Ronzoni S, Nobile De Santis MS, Cetin I *et al.* Circulating levels of ghrelin in human fetuses. *European Journal of Endocrinology* 2003 **149** 111–116.
- 2 Wierup N, Svensson H, Mulder H & Sundler F. The ghrelin cell: a novel developmentally regulated islet cell in the human pancreas. *Regulatory Peptides* 2002 **107** 63–69.
- 3 Chanoine JP, Yeung LP, Wong AC & Birmingham CL. Immunoreactive ghrelin in human cord blood: relation to anthropometry, leptin, and growth hormone. *Journal of Pediatric Gastroenterology and Nutrition* 2002 **35** 282–286.

Figure 1 Fluorescence photomicrographs of human pancreas immunostained for ghrelin. (A) Fetus at mid-gestation with numerous ghrelin cells in islet precursors. (B) Islet of adult with few ghrelin cells at the peripheral rim.

- 4 Farquhar J, Heiman M, Wong AC, Wach R, Chessex P & Chanoine JP. Elevated umbilical cord ghrelin concentrations in small for gestational age neonates. *Journal of Clinical Endocrinology and Metabolism* 2003 **88** 4324–4327.

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