notropin" [Mojsov et al. *J Clin Invest*, 79:616]) are cited.

3. GLP-1 7–37 is suggested as a potential therapeutic agent for the treatment of type II diabetes. The true natural peptide GLP-1 (7–36 amide) stimulates insulin secretion with at least equal potency and, in addition, inhibits glucagon secretion, as reported by Kreymann et al. (*Lancet* 2:1300, 1987), Ørskov et al. (*Endocrinology* 123:2009, 1988), and Komatsu et al. (*Diabetes* 38:902, 1989), whereas GLP-1 7–37, at least in rats, has no effect on glucagon secretion (Weir et al. *Diabetes* 38:338, 1989). Thus, GLP-1 7–36 amide, the naturally occurring peptide, is a better candidate as a therapeutic agent for the treatment of type II diabetes.

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Reply

The comments by Holst and Ørskov on our report of the insulinotropic actions of glucagonlike peptide-I (7–37) in diabetic and nondiabetic subjects raise some interesting and important points (1). Because of the preliminary stage of our studies, the editors requested that our report be condensed. This necessitated an abbreviation of the reference list, which is quite extensive considering the many publications from United States, European, and Japanese investigators (reviewed in Fehmann and Habener 2). In our view, whether or not one or the other of the isoforms of glucagonlike peptide-I (7–37) or (7–36) amide is the predominant form of the peptide, or whether either one has unique biological actions, remains to be proven. In the rat intestine, both isoforms are expressed, and all-or-none expression of one or the other of the isoforms in the human intestine is not yet established (3). Regardless of the levels of expression of the two isopeptides, both appear to have equivalent potencies of insulinotropic actions.

The issue of whether or not glucagonlike peptide-I suppresses glucagon secretion by a direct action on α-cells or indirectly by stimulating insulin release, which in turn exerts a paracrine suppression of glucagon is unsettled (4). There is no a priori reason to believe that the two isoforms of glucagonlike peptide-I would differ in their actions, either direct or indirect, on glucagon-producing α-cells.

We are in complete agreement with Drs. Holst and Ørskov that glucagonlike peptide-I appears to be a potentially novel therapeutic agent for the treatment of NIDDM, a devastating disease for which minimal progress in treatment has been made over the last decade. Our studies, and those reported later in the year by Gutniak et al. (5), provide an impetus to pursue further the potential of glucagonlike peptide-I in the treatment of NIDDM.

Finally, in our report we had no intention of laying claim to priority of the discovery of the insulinotropic actions of glucagon-like peptide-1. Our goals are to extend understanding of the actions of the peptide and its role in the causation and treatment of NIDDM.

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Lp(a) Serum Concentrations and Metabolic Control

Epidemiological studies have identified Lp(a) as a major risk factor for coronary heart disease (1). Elevated concentrations in diabetic patients could contribute to their increased risk. Despite this possibly important link, little information is available concerning the dependence of Lp(a) on metabolic control.

Eighteen patients (9 with NIDDM, 9 with IDDM; 9 women, 9 men; mean age 45 yr, range 16–76 yr) were studied prospectively for 21 days after hospitalization for improvement of diabetic control. All of these patients suffered from long-term poor metabolic control without recent deterioration (e.g., because of infection). Lp(a) deter-