

Comment on: Keenan et al. (2010) Residual Insulin Production and Pancreatic β -Cell Turnover After 50 Years of Diabetes: Joslin Medalist Study. *Diabetes* 2010;59:2846–2853

Kristina I. Rother¹ and David M. Harlan²

We are pleased to find our previously published results (1,2) confirmed by the report of Keenan et al. (3). In their cohort of individuals with very long-standing type 1 diabetes, 67.4% of patients had residual endogenous insulin production, and in nine postmortem examinations of pancreatic tissue, insulin positive cells were found. However, we respectfully disagree that this is a surprising finding. We recently reported that many patients with long-standing type 1 diabetes maintain the capacity to secrete small amounts of insulin in a regulated manner (1,2). Their residual β -cells responded to both physiological (mixed meal) and pharmacological (arginine) stimuli. We further tested the hypothesis that expanding this residual β -cell mass might be a promising approach to treatment (1). Though our experimental conditions did not result in an improvement of β -cell mass or function, we strongly believe that expansion of remaining β -cells is a promising approach for future research.

From the ¹Clinical Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland; and the ²Diabetes Center of Excellence, University of Massachusetts, Worcester, Massachusetts.

Corresponding author: Kristina I. Rother, kr58q@nih.gov.
DOI: 10.2337/db10-1207

© 2010 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See <http://creativecommons.org/licenses/by-nc-nd/3.0/> for details.

Might the C-peptide results of the Joslin Medalists have been an underestimate of their true insulin secretory capacity? We had observed that the remaining β -cells' insulin secretion could be suppressed by exogenous insulin administration (1). Therefore, we wonder whether Keenan et al. would have found more C-peptide had the investigators tested the individuals under different conditions (some patients received insulin injections immediately before the mixed meals, which might have suppressed their C-peptide levels). The merit of the Joslin Medalist Study should, however, in no way be denigrated, especially because of its unique collection of clinical data and comparison with postmortem results.

ACKNOWLEDGMENTS

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Rother KI, Spain LM, Wesley RA, Digon BJ 3rd, Baron A, Chen K, Nelson P, Dosch HM, Palmer JP, Brooks-Worrell B, Ring M, Harlan DM. Effects of exenatide alone and in combination with daclizumab on beta-cell function in long-standing type 1 diabetes. *Diabetes Care* 2009;32:2251–2257
2. Liu EH, Digon BJ 3rd, Hirshberg B, Chang R, Wood BJ, Neeman Z, Kam A, Wesley RA, Polly SM, Hofmann RM, Rother KI, Harlan DM. Pancreatic beta cell function persists in many patients with chronic type 1 diabetes, but is not dramatically improved by prolonged immunosuppression and euglycaemia from a beta cell allograft. *Diabetologia* 2009;52:1369–1380
3. Keenan HA, Sun JK, Levine J, Doria A, Aiello LP, Eisenbarth G, Bonner-Weir S, King GL. Residual insulin production and pancreatic β -cell turnover after 50 years of diabetes: Joslin Medalist Study. *Diabetes* 2010;59:2846–2853