Response to 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

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We appreciate the response by Rother and Harlan (1) to our article (2). However, it is difficult to understand what the confirmatory aspects of the Medalist Study data are with respect to the studies of Liu et al. (3) and Rother et al. (4), which documented minimal levels of C-peptide production in individuals with a diabetes duration of 19.2 ± 11.8 years and 21.3 ± 10.7 years, respectively. Clearly, this duration is significantly lower than the Medalists' mean duration of 56.2 ± 5.8 years. Another difference is the relationship of disease duration and residual C-peptide production, which was not significant in the Medalist Study but was reported to be significant in the article by Liu et al., with a statistically higher mean duration ($P = 0.0045$) in those patients without (26.2 ± 13.1 years) than those patients with residual C-peptide production (19.2 ± 11.8 years) (3).

One of the most important components of our study is the pre- and post mortem data on nine Medalists. Ours is the first study to show a correlation between random C-peptide, physiological response to stimulation, and insulin positive β-cell mass in any human population of type 1 diabetic patients and, extraordinarily, in individuals with a mean of 55 years of diabetes. Although this part of the study included only nine patients, each had insulin positive cells even after their extreme duration of diabetes.

Although our findings of stimulated C-peptide may be an underestimation of islet secretory capacity as suggested by Rother and Harlan, because of exogenous insulin injection before the mixed-meal tolerance test, only 6 of the 31 subjects took insulin the morning of the test, and that was to bring their fasting blood glucose values to under 250 mg/dl, a safe range for the test to be performed. We hope these explanations have provided a clear differentiation between our Medalist Study and previous publications.

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REFERENCES

1. Rother KI, Harlan DM. Comment on: Keenan et al. (2010) Residual insulin production and pancreatic β-cell turnover after 50 years of diabetes: Joslin Medalist Study (Letter). Diabetes 2010;59:e26. DOI: 10.2337/db10-1207
2. 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
3. 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
4. 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 exanitide alone and in combination with daclizumab on beta-cell function in long-standing type 1 diabetes. Diabetes Care 2009;32:2251–2257

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