LETTER TO THE EDITOR

Reply to 'Islet xenotransplantation clinical trial: does histology show islet cells?'

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The question raised by Drs Salazar and Wright (1) concerning the interpretation of the histology in our study is important and one that we are happy to address. We did conduct controls for the histology, and if the positivity of the cells was due to hemosiderin, it would have also been seen in the hematoxylin-eosin staining, which it did not. We also had negative controls, one with irrelevant antibody and one omitting the primary antibody. The results were negative in both cases. The antibodies were purchased from Santa Cruz Biotechnology (Santa Cruz, CA, insulin) and Sigma (Saint Louis, MO, glucagon), the dilution was 2.5 µg/ml of antibody, and samples were inactivated with 0.3% hydrogen peroxide with 0.1% sodium azide for 10 min. The purpose of Figure 4 was to show the overall architecture of the cells, not their specific color hue, and therefore the brightness and contrast were standardized for all pictures. This would have added to possible differences between 'dark brown' and 'golden brown'. In our hands islets in neonatal pig pancreases (positive control) stain the same golden brown, which we agree is less intense than staining seen with adult human islets. Our interpretation that we were staining insulin positive cells was corroborated by at least one cell biologist and one pathologist in Mexico, and two pathologists in Canada, none of whom were

coauthors of the research, although they work in the same institutions as the authors.

We do not dismiss the suggestions that further confirmation of our observations would be of value, we would be willing to provide an independent pathologist with tissue samples for corroboration. Although our histological findings are indeed very important, the paper covered many other aspects of the results of this trial, and in particular the presence of glucose-responsive porcine insulin, which was measured by Dr Mendez in the laboratory of Dr Ricordi. The absence of porcine C-peptide could have a number of possible explanations which require detailed investigation. However, we had limited space in which to present and discuss these ideas. Nevertheless, we believe that the histological interpretation agrees both with the clinical data and with the porcine insulin detected in the patients' blood.

Reference

- 1 Salazar A & Wright JR. Islet xenotransplantation clinical trial: does histology show islet cells? *European Journal of Endocrinology* 2005 **154** 917–918.

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