L997F is associated with increased susceptibility to pancreatic ductular obstruction.

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M. Gomez Lira,[1] M. G. Benetazzo,[1] M. G. Marzari,[1] C. Bombieri,[1] F. Belpinati,[1] C. Castellani,[3] G. C. Cavallini,[2] G. Mastella,[3] and P. F. Pignatti[1]

[1]*Section of Biology and Genetics, Department of Mother and Child, Biology and Genetics, and* [2]*Department of Surgical and Gastroenterological Sciences, University of Verona, and* [3]*Cystic Fibrosis Center, Ospedale Civile Maggiore, Verona*

Electronic-Database Information

The accession number and URLs for data in this article are as follows:

Cystic Fibrosis Genetic Analysis Consortium, http://www.genet.sickkids.on.ca./cftr

Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/Omim (for CF [MIM 219700])

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Address for correspondence and reprints: Dr. Macarena Gomez Lira, Section of Biology and Genetics, Department of Mother and Child, Biology and Genetics, University of Verona, Strada Le Grazie 8, I-37134 Verona, Italy. E-mail: macarena@borgoroma.univr.it

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On the Age of the Most Prevalent Gaucher Disease–Causing Mutation, N370S

To the Editor:

We have recently described a common origin for the most prevalent mutation (N370S) observed among Gaucher disease (GD) patients of Ashkenazi Jewish (AJ) and Spanish descent (Díaz et al. 1999). We also estimated the age of this mutation, using a formula described by Risch et al. (1995*b*). Unfortunately, as R. Colombo pointed out in a recent report (Colombo 2000), there was an error in the formula presented in the original publication that was never rectified. In a reply (Risch et al. 1995*a*) to criticisms raised by Zoossmann-Diskin (1995), Risch et al. made no mention of an error in the formula. The continued application of the formula by researchers who may not be well versed in the field may lead to repeated mistakes if the error remains uncorrected. We apologize for our failure to recognize the error, but we are pleased that it has been identified by Colombo, who had no difficulty in re-estimating the age of the mutation, using our data. This

reappraisal indicates that the N370S mutation may have occurred between the 11th and 13th centuries or even in the 10th century, considering 30 years per generation as suggested recently by Tremblay and Vezina (2000). This new estimated date for the mutation suggests that it occurred (or entered) the AJ population after the separation of the Ashkenazi and Sephardic Jewish traditions, which would be consistent with the apparent absence of this mutation among Sephardic patients. Using a totally different approach based on mutation detection in healthy Roman Jews, Oddoux et al. (1999) also got to the conclusion that the N370S is an old mutation. Further information on the origin of a mutation could be provided from the length of the chromosomal region noted with linkage disequilibrium (LD) and the strength of the LD. In this case, the data can be used to determine whether the N370S mutation had a Jewish or non-Jewish origin. The 3.2-cM region in LD in AJ (Díaz et al. 1999) seems to be shorter in Spanish chromosomes, as the flanking marker D1S2624 is in LD among AJ, whereas it is not in Spanish GD patients. Moreover, LD values are stronger in AJ than in Spanish chromosomes. These observations suggest that the mutation was introduced later in the AJ population, a statement that is independent of the actual age of the mutation. However, these results should be taken with caution because of the small number of Spanish chromosomes included in the study. Further work would be necessary to settle this issue which, to date, remains an open question.

ANNA DÍAZ,[1] MAGDA MONTFORT,[1] BRU CORMAND,[1] BAIJIN ZENG,[3] GREGORY M. PASTORES,[3] AMPARO CHABÁS,[2] LLUÏSA VILAGELIU,[1] AND DANIEL GRINBERG[1]

[1]*Departament de Genètica, Universitat de Barcelona, and* [2]*Institut de Bioquímica Clínica, Mejia Lequerica s/n, Barcelona; and* [3]*Department of Neurology and Pediatrics, NYU School of Medicine, New York*

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Address for correspondence and reprints: Dr. Daniel Grinberg, Departament de Genètica, Facultat de Biologia, Universitat de Barcelona, Av. Diagonal, 645, 08071 Barcelona, Spain. E-mail: danielr@porthos.bio.ub.es

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