likely led to massive oversights of mutations, as was, for example, the case with the mtDNA analysis of two (related) schizophrenic patients whose mtDNA fell into haplogroup I2.[19] Moreover, genuine haplogroup-specific mutations came into suspicion of being pathogenic, simply because the corresponding haplogroups were not yet fully described at the time. For example, three mutations (T3197C, A14793G, and A15218G) shared by all haplogroup U5a1 mtDNAs were targeted in that study[19] as they were found in two (unrelated) patients, and it was then believed that a 'trend towards a higher frequency of substitutions in the patients' would deserve further attention.

Nowadays, however, there is a rich body of complete mtDNA sequences and data-mining strategies available that should not be ignored.[20,21] Therefore authors of pertinent papers should make sufficient efforts to sequence entire mtDNA genomes correctly and compare them to the available database in order to avoid inadvertent interpretation of erroneous data.

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Reply to Bandelt *et al*

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We welcome the comments of Dr Bandelt *et al* on studies analyzing mtDNA in relation to the genetic bases of schizophrenia, especially those focusing on our study.

With respect to the putative technical errors that they mentioned, which could have influenced our RFLP analysis, we need to highlight that in our report, we had stated that all samples have the same concentration of DNA (10 ng/μl), spectrophotometrically measured, and that a positive control (i.e. the patient carrying the variant) was used in each analysis. Therefore, these potential problems impacting on RFLP analysis have been controlled-for in our study. No doubt, the possibility that the single occurrence of the T12096A could have spread to other samples via cross-contamination needs to be considered, even though the genetic material we analyzed was derived from 10 ml of peripheral blood samples collected and processed at different times of the study.

Patients were assigned to haplogroups H, K and W based on the presence of the variants G1719A, G4580A, C7028T, G9055A, A12308G, G13368A, G13708A and G16391A, as Huerta *et al*[1] had recently described in 250 Spanish patients diagnosed as having Parkinson's disease, and in 230 healthy individuals. Taking into account these eight variants, we could assign each sample to one unequivocal haplogroup. Unfortunately, we did not perform any phylogeny-based approaches in the analyses.

We agree that the DNA sequences of the schizophrenia patients were initially aligned to the Swedish sequence X93334 gi 1262342 and, then, only the discrepancies between the two sequences being compared to the rCRS[2] in the Human Mitochondrial Genome Database (www.mitomap.org). The alignment of the rCRS and the X93334 reveals that X93334 has 36 variant nucleotides from the rCRS, and 17 of them are present in the schizophrenia patients. This explains why some variants have been overlooked in our report. Table 1 (below) shows these 36 nucleotide variants in each of the six schizophrenia patients.

Additionally, in our article, we did not mention that the new mitochondrial DNA variants are related to the disease outcome, as Dr Bandelt *et al* indicate. Neither, would we claim that the variants we found in 'only' six mother–offspring pairs of schizophrenia patients would raise major diagnostic and clinical expectations. Indeed, we had

Table 1

Nucleotide position	Nucleotide in rCRS	Nucleotide in X93334	P1	P2	P3	P4	P5	P6
73	A	G	A	A	A	G	A	G
195	T	C	C	T	T	T	T	C
263	A	G	G	G	G	G	G	G
315	:	C	C	C	C	C	C	C
709	G	A	G	G	G	G	G	G
750	A	G	G	G	G	G	G	G
1438	A	G	G	G	G	G	G	G
1700	T	C	T	T	T	T	T	T
1780	T	C	T	T	T	T	T	T
2706	A	G	A	A	A	G	A	G
3107	N (del)	C	N (del)	N (del)	N (del)	N (del)	N (del)	N (del)
3197	T	C	T	T	T	T	T	T
3316	G	A	G	G	G	G	G	G
4769	A	G	G	G	G	G	G	G
5495	T	C	T	T	T	T	T	T
7028	C	T	C	C	C	T	C	T
8860	A	G	G	G	G	G	G	G
9477	G	A	G	G	G	G	G	G
11467	A	G	A	A	A	G	A	A
11719	G	A	G	G	G	A	G	A
12308	A	G	A	A	A	G	A	A
12372	G	A	G	G	G	A	A	G
13617	T	C	T	T	T	T	T	T
14272	C	G	C	C	C	C	C	C
14766	C	T	C	C	C	T	C	T
14793	A	G	A	A	A	A	A	A
14861	G	A	G	G	G	G	G	G
15218	A	G	A	A	A	A	A	A
15326	A	G	G	G	G	G	G	G
15924	A	G	A	A	A	A	A	A
16093	T	C	T	T	T	T	T	T
16153	G	A	G	G	G	G	G	G
16256	C	T	C	C	C	C	C	C
16270	C	T	C	C	C	C	C	C
16311	T	C	T	T	T	C	T	C
16399	A	G	A	A	A	A	A	A

rCRS, revised Cambridge Reference Sequence of the human mtDNA; X93334, Swedish reference sequence of the human mtDNA; P, patient.

indicated that further studies in larger samples are needed (Discussion section) and that our results needed to be validated and replicated in many more patient samples (Discussion section).

Unfortunately, some of the recommendations from Dr Bandelt *et al*[3,4] have been drawn from very recent articles and books, which were unavailable to us at the time of our study. Undoubtedly, in future studies, we will incorporate the data-mining strategies suggested.

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