Dear Editor,

We have read with interest the letter concerning our paper titled “Histopathological liver findings in patients with hepatocerebral mitochondrial depletion syndrome with defined molecular basis”. We would like to thank Prof. Finsterer for his regard and valuable remarks. Of course, our introductory statement that mitochondrial depletion syndrome (MDS) is inherited as autosomally recessive trait is not true in all cases, and this should have been mentioned for full clarity. For some justification, MDS cases with autosomal dominant inheritance concern mostly adult patients with relatively mild clinical course, while in our study we focused on severe pediatric forms. We have discussed this issue in our latest paper on two RRM2B mutated homozygotic patients [1]. Concerning other mentions, let us say that this particular study has been intentionally directed to practising general surgical pathologists, who use standard everyday-practice lab procedures. The idea was to show that routinely processed histological biopsy and autopsy material is potentially useful in detection of rare fatal infantile liver disorders of complex pathogenetic basis. Pathologist should be aware of these pediatric diseases and consider them in corresponding clinical setting. That is why we have decided not to include non-standard pathological investigations such as electron microscopy, enzymatic histochemistry and spectrophotometry. To be exact, some investigations were not performed in routine diagnostic workout of all our patients. Full set of standard liver stains we perform in our lab (HE, PAS, PAS-D; AZAN; reticulin) was not presented due to space limitations. Since the study is addressed to general pathologists, certain clinical particulars such as detailed antiepileptic treatment scheme were not fully reported. Let us note that most of our patients were thoroughly described in earlier publications, taking into account the details you questioned. Relevant references of those three publications regarding separately three defects (DGUOK, MPV17 and POLG) are present in Table I. Answering shortly to your concerns: surgical muscle biopsy was performed in 6 out of 13 patients (in two patients with each defect). Severe mtDNA depletion in not affected skeletal muscle accompanied the depletion in the liver in four DGUOK and MPV17 mutated cases, but was not present in two examined POLG patients. Also complex IV and I deficits (usually compound) were detected only in DGUOK and MPV17 deficits, but not in POLG patients.

As regards antiepileptic treatment, in the Results and comments section we mentioned that In patients with POLG defect, severe epilepsy prevailed at the begin-
ning, and liver failure did not appear until valproate administration. This observation concerns all, and only POLG deficient patients. Their epilepsy had been uneffectively treated with all available drugs, as well as ketogenic diet. Valproate administration appeared clearly noxious, leading to fulminant liver failure and death.

Yours sincerely,
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References

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