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Fibroblast growth-factor-21 is currently a weak biomarker for identifying mitochondrial and non-mitochondrial inborn errors of metabolism



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We read with interest the article by Kirmse et al. about fibroblast growth-factor-21 (FGF21) serum levels in a cohort of patients with an inborn error of metabolism (IEM) [1]. FGF21 levels were increased in IEM patients but highly variable in the various subgroups [1]. We have the following comments and concerns.

In the methods section it is mentioned that 42 patients with an IEM were investigated. However, in the result section only 38 IEM patients are mentioned. Furthermore, in figure 1 five patients with a mitochondrial disorder (MID) are presented but in the text only 4 with a MID are mentioned [1]. How to explain these discrepancies?

The authors mention that FGF21 is particularly increased in patients with a MID manifesting as myopathy [1]. How many of the four respectively five patients with a MID had myopathy? How many of the non-mitochondrial patients had muscle involvement?

According to figure 1 there were five patients from five different subgroups with FGF21 levels > 1000 pg/mL [1]. What did these five patients have in common? Myopathy? Interestingly, MID patients did not show FGF21 levels > 1000 pg/mL.

Serum lactate is regarded as a biomarker of MIDs [2]. Was serum lactate correlated with FGF21 levels at least in the mitochondrial IEM group (MITO, UCD, OA, FAO)?

Since FGF21 levels may be elevated due to various different causes, elevation of FGF21 in MIDs is non-specific. Did the authors consider causes other than "inefficient energy metabolism biochemically similar to starvation" to explain elevated FGF21 values?

Did FGF21 levels increase with age or with disease progression? Provision of age in the included probands would be helpful.

Overall, this interesting study would profit from a more homogenous study population from clarification if FGF21 was particularly elevated among those which had myopathy, and if FGF21 values were correlated with serum lactate values.

Conflicts of interest

There are no conflicts of interest.

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Author contribution

JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments.

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