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Blood metabolomics uncovers inflammation-associated mitochondrial dysfunction as a potential mechanism underlying ACLF (vol 72, pg 688, 2020)

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Correction to ‘Blood metabolomics uncovers inflammation-associated mitochondrial dysfunction as a potential mechanism underlying ACLF’ [J Hepatol 2020 (72) 688–701]☆

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In this article, some results shown in Table S3; a paragraph of the Results section; Fig. 2A(iii) and its related part in Fig. S6; and one related sentence in the discussion are incorrect. During a routine check of the results presented in this article, we realized that patients with single organ (kidney, brain, or liver) failure or dysfunction were wrongly classified owing to an error during coding. Because of this, we computed wrong values for area under the receiver-operating-characteristic curve (AUC) assessing the discriminating accuracy of each metabolite in

differentiating single organ failure/dysfunction from acute decompensation (AD). We have now computed the correct AUC values for single organ failure/dysfunction vs. AD. All other computed values were correct, in particular the AUCs for ACLF, and therefore these errors do not change our conclusion for the differences in blood metabolome between patients with ACLF and those with AD. Herein, we show the incorrect paragraph of the Results section and sentence in the Discussion, and corresponding corrected paragraph and sentence. The Results section,

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Fig. S6, Table S3, and the Discussion have been corrected online and in the printed version. In addition, we present the corrected Fig. 2. below. We apologize for any inconvenience caused by these late corrections.

Results

Incorrect

The blood metabolite fingerprint is qualitatively similar in patients with single organ dysfunction/failure independently of the affected organ

To assess if there was a specific blood metabolite fingerprint for each category of organ failure/organ dysfunction, we compared patients with single liver-, brain- and kidney-failure/dysfunction with patients with AD without any organ failure/dysfunction, using metabolite AUCs [Fig. 2A(iii)]. The clinical phenotype and number of patients included in this analysis is depicted in Fig. S3C. The main finding of this analysis was that the fingerprint defining ACLF of any grade was also identified in the 3 categories of single organ failure/organ dysfunction, suggesting a common metabolic derangement across different organs.

Corrected

The blood metabolite fingerprint of ACLF differs across the different categories of patients with single organ failure/dysfunction

We compared patients with single liver-, brain- and kidney-failure/dysfunction with patients with AD without any organ failure/dysfunction, using metabolite AUCs [Fig. 2A(ii); Fig. S6; Table S3]. The clinical phenotype and number of patients included in this analysis is depicted in Fig. S3C. The main finding of this analysis was that the fingerprint defining ACLF of any grade was similarly present in patients with single kidney OF/OD (with most values for AUC being of 0.75 or more), but was less marked in those with single liver OF/OD (with most values for AUC being between 0.70 and 0.75) and even absent in those with brain OF/OD (with values of AUC ranging from 0.54 to 0.61). These findings indicate differences in the contribution of individual organs to the ACLF fingerprint; the kidney being a major contributor followed by the liver to a lesser extent, while the contribution of the brain was at most modest.

Discussion (First paragraph)

Incorrect

Of note, the ACLF fingerprint was independent of the type of organ failure (phenotype).

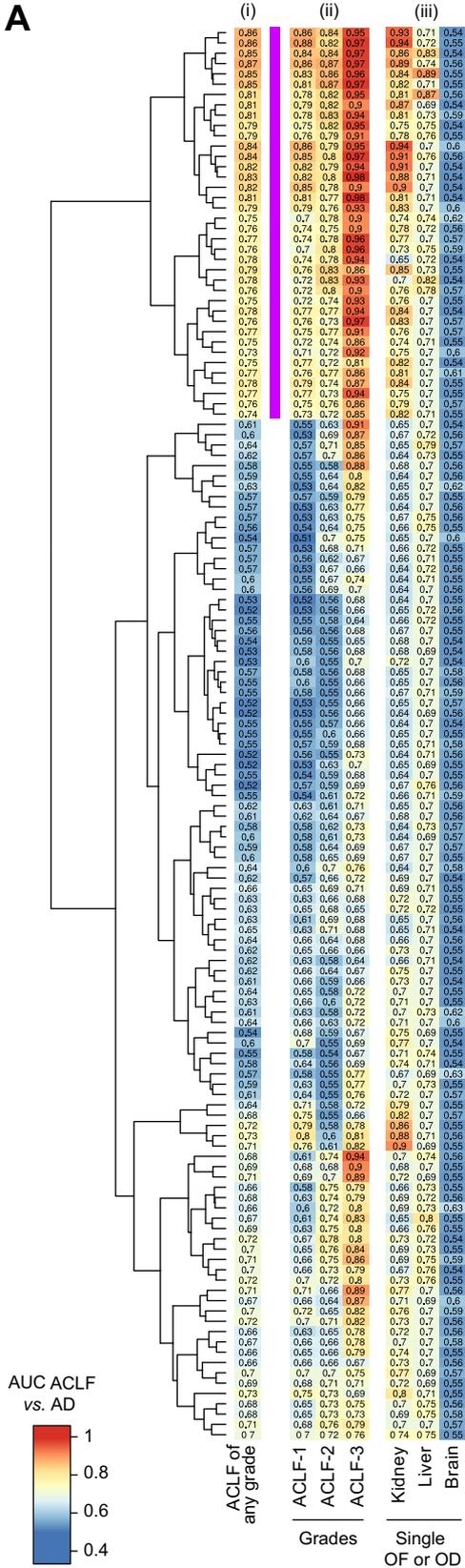
Corrected

Of note, there were differences in the contribution of individual organs to the ACLF fingerprint. The kidney was a major contributor to the ACLF fingerprint followed by the liver to a lesser extent, while the contribution of the brain was at most modest.

Corrected Fig. 2. Identification of a unique ACLF-associated blood metabolite fingerprint and its behavior in different patients' groups.

(A) (i) Hierarchical cluster analysis of the area under the receiver-operating-characteristic curve (AUCs) assessing the discriminating accuracy of each of the 137 metabolites in differentiating ACLF from AD; (ii) Corresponding metabolite AUC values in assessing ACLF-1, -2, and -3, relative to AD; (iii) Corresponding metabolite AUC values in assessing single failure/dysfunction of either the liver, brain or kidney liver, relative to AD without any organ failure/dysfunction. Vertical violet bar identify the 38-metabolite cluster highly associated with ACLF of any grade and composing the ACLF-associated blood metabolite fingerprint. AUCs for each metabolite were derived from a logistic regression model (adjusted by age and sex) related to the different comparisons. (B) The eigenmetabolite₂₀ of the 38-metabolite cluster across different groups, including healthy subjects, patients with compensated cirrhosis, patients with AD of cirrhosis (without ACLF) and patients with ACLF. (C) The eigenmetabolite of the 38-metabolite cluster across four groups: AD, ACLF-1, ACLF-2, ACLF-3. (D) The eigenmetabolite of the 38-metabolite cluster across 3 groups: AD without any organ failure/dysfunction, single kidney failure/dysfunction, ACLF-2 or -3 without kidney failure/dysfunction. In (B), (C), and (D) eigenmetabolite values were compared using one-way ANOVA, followed by Student's *t* test. ACLF, acute-on-chronic liver failure; AD, acute decompensation; HC, healthy controls; KD, kidney dysfunction; KF, kidney failure; OD, organ dysfunction; OF, organ failure.

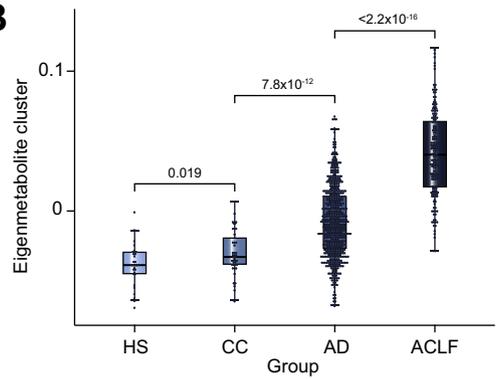
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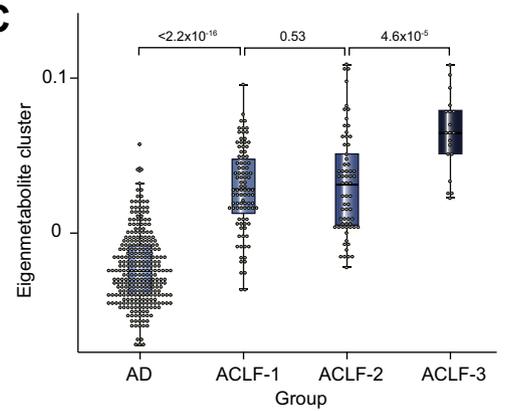
ACLF associated metabolite cluster

- β-Pseudouridine
- Pentose alcohols
- Pentose phosphates
- N-Acetyl-L-alanine
- D-Galacturonic acid
- N-Acetyl-aspartil-glutamate
- D-Glucuronic acid
- L-Kynurenine
- 4-hydroxy-3-4-methoxyphenylglycol sulfate
- N-Acetyl-L-phenylalanine
- Cystathionine
- D-Threitol
- 4-Acetamidobutanoic acid
- N-Acetylneuraminic acid
- Quinolinic acid
- Mevalonic acid
- L-Saccharopine
- Hydroxyphenylacetic acids
- Phenyllactic acid
- N-Acetyl-L-aspartic acid
- Hexanoylcarnitine
- p-Hydroxyphenylacetic acid
- 5'-Deoxy-5-(methylthio)adenosine
- N-Formyl-L-methionine
- N-Acetyl-L-tyrosine
- Related to Succinate
- 2-Heptanone
- Kynurenic acid
- N6,N6-Trimethyl-L-lysine
- Trisaccharides
- 2,2'-Thiodiacetic acid
- Octanoylcarnitine
- Pantothenic acid
- Indolelactic acid
- p-Anisic acid
- Phenol
- N-Acetyl-L-tryptophan
- L-(+)-Tartaric acid

B



C



D

