DR. FRANCESCO URSINI (Orcid ID: 0000-0001-8194-8642)

Article type : Letter

Correspoding Author Email Id: francesco.ursini@yahoo.it

Response to the letter to the editor by Shadmani et al – EJCI-2017-0437

Francesco Ursini

Department of Health Sciences, University of Catanzaro "Magna Graecia", Catanzaro,

Italy

Dear Editor-in-Chief.

We read with great interest the letter by Shadmani et al. regarding our recently published

article investigating the correlation between complement C3 and non-alcoholic fatty liver

disease (NAFLD) in rheumatoid arthritis (RA) patients [1].

The authors raised some technical issues about the statistical methodology of our work. We

truly appreciated the precious and highly qualified contribution - given the leading expertise of

the authors in the field of biostatistics and epidemiology - and largely agree with them that the

cross-sectional design of our study may significantly limit the ability of our results to support

definitive conclusions regarding the direction of the relationship between C3 and NAFLD.

However, we feel the need to clarify that the main aim of our manuscript was not that of

confirming a direct, unimpeachable, unidirectional causal correlation between complement C3

and the future development of NAFLD, but rather to provide a hypothesis-generating basis for

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as

doi: 10.1111/eci.12878

This article is protected by copyright. All rights reserved.

further, adequately-powered longitudinal studies aiming at investigating in details the processes linking complement system to metabolic disturbances in RA patients, as already suggested by other studies published by our group [2-4].

## References

- Ursini F, Russo E, Mauro D, Abenavoli L, Ammerata G, Serrao A, Grembiale RD, De Sarro G, Olivieri I, D'Angelo S: Complement C3 and fatty liver disease in Rheumatoid arthritis patients: a cross-sectional study. European journal of clinical investigation 2017, 47(10):728-735.
- 2. Ursini F, D'Angelo S, Russo E, Arturi F, D'Antona L, Bruno C, Naty S, De Sarro G, Olivieri I, Grembiale RD: **Serum complement C3 strongly correlates with whole-body insulin sensitivity in rheumatoid arthritis**. *Clinical and experimental rheumatology* 2017, **35**(1):18-23.
- 3. Ursini F, D'Angelo S, Russo E, Nicolosi K, Gallucci A, Chiaravalloti A, Bruno C, Naty S, De Sarro G, Olivieri I *et al*: **Complement C3 Is the Strongest Predictor of Whole-Body Insulin Sensitivity in Psoriatic Arthritis**. *PloS one* 2016, **11**(9):e0163464.
- 4. Ursini F, Grembiale A, Naty S, Grembiale RD: **Serum complement C3 correlates with insulin resistance in never treated psoriatic arthritis patients**. *Clinical rheumatology* 2014, **33**(12):1759-1764.