



Authors' response to the commentary by Bonaventura and Montecucco on: 'Characterization of circulating leukocytes and correlation of leukocyte subsets with metabolic parameters 1 and 5 years after diabetes diagnosis'

Maria Apostolopoulou^{1,2,3} · Michael Roden^{1,2,3}

Received: 2 September 2018 / Accepted: 4 September 2018 / Published online: 15 September 2018
© Springer-Verlag Italia S.r.l., part of Springer Nature 2018

Dear Editor,

We would like to respond to the stimulating commentary by Dr. Bonaventura and Dr. Montecucco [1] on our article 'Characterization of circulating leukocytes and correlation of leukocyte subsets with metabolic parameters 1 and 5 years after diabetes diagnosis'. These authors not only elegantly summarize the main results of our study [2], but also discuss accumulating data on the role of neutrophils in the pathogenesis of type 1 diabetes (T1D). Recently, peripheral neutropenia has been proposed to precede and accompany the onset of T1D, mainly resulting from increased infiltration of small pancreatic blood vessels by neutrophils [3]. Neutrophils—a rather unexplored player in T1D pathogenesis—could initiate T-cell response and promote T1D development, indicative of a crosstalk between innate and adaptive immunity in the early stages of T1D, as summarized by recent studies [4, 5].

Our new data reveal that in a rather large, comprehensively phenotyped cohort, neutrophil count was already lower in T1D than in type 2 diabetes patients at the time of clinical diabetes diagnosis, but also at 5 years after diabetes diagnosis [2]. Also, neutrophil count correlated positively

with C-peptide levels at 5 years of T1D duration, suggesting the presence of more profound neutropenia among patients with very low β -cell secretory capacity. We agree that the role of innate immunity and the crosstalk with the adaptive immune system will require detailed future studies not only for the better understanding of pathogenic mechanisms of T1D, but also for examining, whether neutrophils may serve as a marker for prediction of disease onset and—as supported by our study—of disease progression and β -cell secretory capacity during the years after T1D diagnosis.

Author contributions

MA wrote the response and MR read and critically reviewed the response.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest for this work.

Statement of human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent Informed consent was obtained from all patients for being included in the study.

Managed by Massimo Federici.

✉ Michael Roden
michael.roden@ddz.uni-duesseldorf.de

- ¹ Division of Endocrinology and Diabetology, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
- ² Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich-Heine University Düsseldorf, Auf dem Hennekamp 65, 40225 Düsseldorf, Germany
- ³ German Center for Diabetes Research, Partner Düsseldorf, Düsseldorf, Germany

References

1. Bonaventura A, Montecucco F (2018) Comment on "Characterization of circulating leukocytes and correlation of leukocyte subsets with metabolic parameters 1 and 5 years after diabetes diagnosis". *Acta Diabetol*. <https://doi.org/10.1007/s00592-018-1229-5>
2. Apostolopoulou M, Menart-Houtermans B, Ruetter R et al (2018) Characterization of circulating leukocytes and correlation of leukocyte subsets with metabolic parameters 1 and 5 years after diabetes diagnosis. *Acta Diabetol* 55:723–731

3. Valle A, Giamporcaro GM, Scavini M et al (2013) Reduction of circulating neutrophils precedes and accompanies type 1 diabetes. *Diabetes* 62:2072–2077
4. Huang J, Xiao Y, Zheng P et al (2018) Distinct neutrophil counts and functions in patients with newly diagnosed type 1 diabetes, latent autoimmune diabetes in adults, and type 2 diabetes. *Diabetes Metab Res Rev*. <https://doi.org/10.1002/dmrr.3064>
5. Battaglia M (2014) Neutrophils and type 1 autoimmune diabetes. *Curr Opin Hematol* 21:8–15