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We read with great interest the article by Hayashi et al. (1), in which the authors report the generation of two new mouse strains, specifically deficient in MASP-1 or MASP-3. In their study, the authors demonstrated in mice that MASP-1 is indispensable for lectin pathway activation, and MASP-3 is responsible for proteolytic processing of zymogen FD (pro-FD) to FD, the initiating protease of the alternative pathway.

The authors' findings in these mouse models are in perfect agreement with our previous results obtained with human whole blood, plasma, and serum samples using specific human MASP-1, MASP-2, and MASP-3 inhibitors developed by directed evolution (2, 3). In our prior studies, we showed that a monospecific MASP-1 inhibitor completely prevented lectin pathway activation (2). Using a specific MASP-3 inhibitor, we also demonstrated that MASP-3 is the exclusive activator of pro-FD in resting human blood (3). A publication by another research group also highlighted the important role of MASP-3 in pro-FD activation (4).

The only apparent difference between the previous human results and the new mouse results is the role of MASP-1 in LPS-driven alternative pathway activation (5). In this respect, the mouse and the human complement systems might be different, but not necessarily at the level of MASP-1 (6–8).

In all, by comparing our and other previous human results with the new mouse results of Hayashi et al. (1), we conclude that the major functions of MASP-1 and MASP-3 have been conserved during mammalian evolution, although minor species-specific differences may exist.

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Abbreviation used in this article: pro-FD, zymogen FD.

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Response to Comment on "Cutting Edge: Role of MASP-3 in the Physiological Activation of Factor D of the Alternative Complement Pathway"

We would like to express our thanks for the comment on our current published report (1) from Dr. Gál and colleagues. In the comment, they note, "The authors' findings in these mouse models are in perfect agreement with our previous results obtained with human . . . samples," citing their previous publications in 2012 and 2016. However, we disagree with their comment on the historical background regarding MASP-1 and MASP-3 in the complement system, and it is possible that their comment may cause misunderstanding of the scientific novelty and importance of our paper in the field. In 1992, our group discovered the novel serine protease designated mannose-binding lectin (MBL)-associated serine protease (MASP) (2). In addition, we contributed to the discovery of MASP-3 in 2001 (3). Since then, we have investigated the roles of MASPs in the complement system. As a result, first, in 2008 we generated mice genetically deficient for both MASP-1 and MASP-3 and demonstrated that MASP-1 contributes to activation of the lectin pathway (LP) through the activation of MASP-2 (4). Second, in 2010 we showed that MASP-1 and/or MASP-3 plays an essential role in activation of the alternative pathway (AP) through activation of complement factor D (FD), possibly by MASP-1 (5). Third, in 2011 we revealed that MASP-3 can cleave a zymogen FD (pro-FD) to an active form FD in the presence of MBL-A and *Staphylococcus aureus* (6). That was the first demonstration of the physiological function of MASP-3. Subsequently,