Cell type-specific differences in β-glucan recognition and signalling in porcine innate immune cells.

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Since the European ban on prophylactic antibiotics, efforts are ongoing to identify suitable alternatives. β-glucans are potential candidates as upon oral administration these carbohydrate polymers protected piglets from an experimental infection with enterotoxigenic *E. coli*. To further fine-tune the rational design of β-glucans as nutraceuticals, we aimed to eludicate the receptors involved in the β-glucan-mediated immunomodulation in pigs. Several receptors, such as dectin-1 and complement receptor 3 (CR3), are reported to bind β-glucans, however the contribution of these receptors in the response of innate immune cells towards β-glucans is still unresolved. Here, we report the crucial role of CR3 in β-glucan recognition by porcine neutrophils, as blocking this receptor strongly reduced the phagocytosis of β-glucans and the β-glucan-induced production of reactive oxygen species (ROS). However, in macrophages both dectin-1 and CR3 were involved in ROS production triggered by β-glucans, implying that receptor usage to recognize β-glucans is cell type-specific. Moreover, we found that β-glucan receptor engagement on neutrophils and macrophages triggers a signalling cascade, which depended on focal adhesion kinase (FAK) to elicit ROS production, while Syk kinase was only partially involved in this process. In conclusion, CR3 plays a cardinal role in β-glucan recognition by porcine neutrophils, while macrophages use a more diverse receptor array to respond to β-glucans. Irrespective of the engaged receptors, the β-glucan-triggered signalling pathway is regulated by the master switch FAK in both cell types. Our findings could accelerate the implementation of β-glucans as nutraceuticals in the swine production industry.