Interleukin-21-Mediated TLR4 Activation in Celiac Disease

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Dear Editor,

We read with great interest the recent contribution by Eiró et al. [1]. They reported that celiac disease (CD) patients with high levels of toll-like receptor 4 (TLR4) showed high levels of interleukins (IL-1, IL-6, IL-8, and IL-17) as well as transcription factors. However, unfortunately, they did not analyze the expression of IL-21. We would like to specify the pathomechanism of CD that results from TLR4 activation.

Recently, Junker et al. [2] reported that wheat α -amylase-trypsin inhibitors induce innate immune responses by activating TLR4 and eliciting proinflammatory cytokines in susceptible people who express HLA-DQ2 and HLA-DQ8. Furthermore, Fallang et al. [3] found that DQ2.5(+) antigen-presenting cells had greater stability of bound peptides and suggested that CD is induced by an antiglutin T cell response associated with the histocompatibility antigen HLA DQ2.5. This was consistent with the study by van Heel et al. [4], who also demonstrated that HLA-DQ2.5cis is the most common HLA-DQ2 haplotype associated with CD. Combined intracellular cytokine staining with DQ2- α -II gliadin peptide tetramer staining of intestinal polyclonal T cell lines, HLA-DQ2-restricted gluten-specific T cells, produced IL-21 [5].

In CD, IL-21, a cytokine that regulates T cell activation, contributes to the mucosal T helper cell type 1 (Th1) response

[6] and induces the expression of TLR4 [7]. TLR4 signaling enhanced both CD4(+) T-cell proliferation and survival in vitro and promoted autoimmune inflammation [8].

Therefore, there is a possibility that gluten-reactive CD4(+) T cells activate TLR4 through the production of IL-21 in susceptible CD patients with HLA-DQ2.5. Blockade of IL-21 activity in CD patients should further be studied as a treatment option.

Conflict of interest None.

References

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