GLIADIN MODULATES EPITHELIAL PERMEABILITY BY STIMULATING ARGinine METABOLISM IN MACROPHAGES

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Purpose: Celiac disease (CD) is an autoimmune enteropathy, due to a permanent intolerance to gluten in susceptible individuals. A role for arginine (Arg) and its metabolites in gluten-triggered adaptive and innate immune responses has been suggested¹². Here we evaluate the role of Arg metabolism by macrophages in the onset of intestinal defects typical of CD.

Method: RAW264.7 macrophages were treated for 24h with 1 mg/ml Pepsin Trypsin Gliadin (PTG), in the absence and presence of 2-difluoromethyl-ornithine (DFMO), an inhibitor of the limiting enzyme for polyamines production, or in the absence of Arg. Polyamines production was monitored by UHPLC-MS/MS analysis. Macrophages incubation media were added to the basolateral side of polarized Caco-2 intestinal epithelial monolayers and the permeability monitored after 48h by measuring transepithelial electrical resistance (TEER).

Results: PTG-treated macrophages displayed a massive production of the polyamine putrescine, that was completely prevented by the presence of DFMO or when the treatment was performed in the absence of Arg. The addition of the incubation medium from PTG-treated macrophages on intestinal epithelial monolayers caused a significant decrease in TEER; DFMO and Arg-free medium reduced this effect.

Discussion: The treatment with PTG induces the secretion of polyamines by macrophages that in turn affect intestinal permeability in vitro.

Conclusion: Whether these events also occur in vivo deserves to be further investigated. Pathways constitutively altered in celiac cells could render CD patients more susceptible than healthy subjects to the effects of gluten, ultimately producing the well-known gluten-driven intestinal alterations typical of CD.

References