Proceedings of the Nutrition Society (2011), **70 (OCE2)**, E40 doi:10.1017/S0029665111000711

5th International Immunonutrition Workshop, 6–8 April 2011, Puerto Vallarta, Mexico

Cytokine balance of an intestinal *in vitro* model stimulated with different gliadin peptides involved in caeliac disease

J. R. Mujico*, T. Pozo*, A. Marcos and E. Nova

Immunonutrition Research Group, Department of Metabolism and Nutrition, Institute of Food Science and Technology and Nutrition (ICTAN), Spanish National Research Council (CSIC), Madrid, Spain

Celiac disease (CD) is an inflammatory disorder of the upper small intestine in which gliadin, a family of wheat proteins, acts as an essential factor in its pathogenesis[1]. Although it is generally accepted that cereal protein activation of the immune system is involved in CD progression, a non-immuno-mediated cytotoxic activity of gliadin-derived peptides on the jejunal/duodenal tract cannot be excluded[2]. Trying to understand these mechanisms, we investigated the effect of different synthetic gliadin-derived peptides on the cytokine production of a co-culture system.

PBMC (from two healthy individuals) and CaCO-2 co-cultures were incubated with 0.1 mg/ml of different gliadin peptides involved in CD[3]: one 'toxic' (α31–43) and five 'immunogenic' (α57–89, α57–89d (deamidated by tTG), α92–106d, γ138–153d, γ222–236d). Several cytokines (IL-1β, IL-6, IL-8, IL-10 and TNFα) were measured by the Cytometric Bead Array System (BD Biosciencies) and analysed by flow cytometry (FACS calibur and Cellquest software, BD Biosciencies).

Stimulation of PBMC/CaCO-2 co-cultures with the 'toxic' gliadin peptide α31–43 and the 'immunogenic' gliadin peptide α57–89 (both deamidated and non-deamidated) did not produce any cytokine marker. Nevertheless, the other gliadin peptides (α92–106d, γ138–153d, γ222–236d) clearly induced all tested cytokines by PBMC (IL-1β, IL-6, IL-10 and TNFα) and CaCO-2 cells (IL-1β, IL-6, IL-8 and TNFα).

T-cell clones allow identification of gluten peptides that stimulate T-cells[4] but do not quantify their contribution to the mucosal inflammation. Therefore, the analysis of cytokine production in the PBMC/CaCO-2 *in vitro* model is a promising technique to assess the regulatory mechanisms involved in the inflammatory response to gliadin. In future work, this model will be also applied in order to evaluate the capacity of different Bifidobacterium strains to counteract the inflammatory effects of gliadin-derived peptides and would clearly warrant further studies of its potential as a novel dietary supplement in the treatment of CD (Figs 1 and 2).

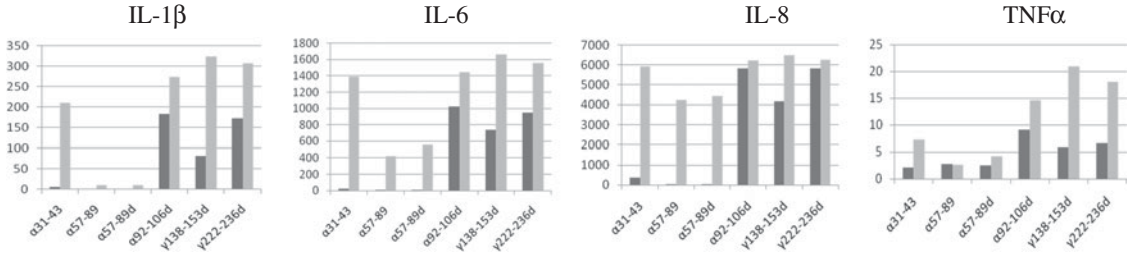

Fig. 1. Cytokine production by Caco-2 cells (pg/ml) in volunteer 1 (■) and volunteer 2 (▨).

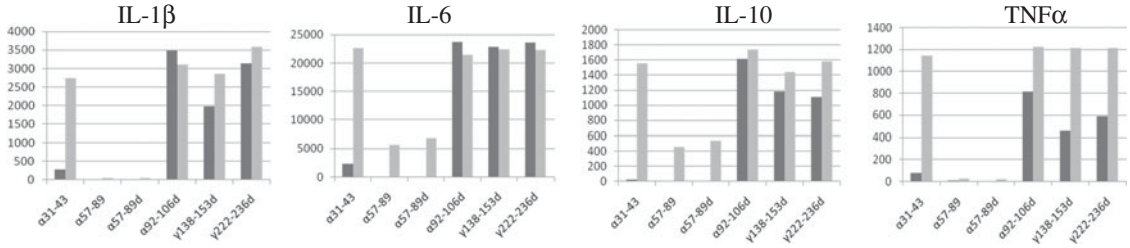

Fig. 2. Cytokine production by PBMC (pg/ml) in volunteer 1 (■) and volunteer 2 (▨).

This work was supported by grants AGL2007-66126-C03-01/ALI and AGL2007-66126-C03-02/ALI from the Spanish Ministry of Science and Innovation. T. P. was recipient of a JAE-CSIC personal grant.

1. Schuppan D, Junker Y & Barisani D (2009) *Gastroenterology* **137**, 1912–1933.
2. Maiuri L, Troncone R, Mayer M *et al.* (1996) *Scand J Gastroenterol* **31**, 247–253.
3. Ciccocioppo R, Di Sabatino A & Corazza GR (2005) *Clin Exp Immunol* **140**, 408–416.
4. Vader W, Kooy Y, van Veelan P *et al.* (2002) *Gastroenterol* **122**, 1729–1737.

*Both authors have equally contributed to this paper.