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Revealing the role of 33-mer gliadin oligomers in gluten related disorders

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Gluten-related disorders are the most common food intolerances in Western societies, affecting around 1-7% of the general population. [1] Gluten is a complex protein matrix present in wheat, rye, barley and some varieties of oats. In wheat, gliadin is the protein associated with gluten-related disorders. [2] The gliadin protein is not fully degraded by humans producing an immunodominant fragment of 33 amino acids (33-mer) that triggers different immune responses in susceptible individuals. The cause and the early events that lead to the 33-mer intolerance are not understood. [1]

Recently, we showed that the 33-mer oligomerizes under physiological conditions forming different size oligomers and fibril-like structures. [3] During the self-assembly process, a structural transition towards the characteristic amyloid β parallel structure occurs. [4] Based on the structural and morphological similarities with amyloid aggregation, we focused on immunological aspects, reporting that only large oligomers of 33-mer induce an innate immune response in macrophages mediated by human Toll-like receptor 4 (TLR4). [5] Taking into account that oligomerization and structural transformation followed by activation of the innate immune system are hallmarks in amyloidosis diseases, our findings open a new field of research in the context of gluten-related disorders, and human health.

Here, we present insights into the supramolecular behavior of the immunodominant 33-mer *in vitro* and in the intestinal Caco 2-cell model.

Literature:

[1] K. Serwick, *Science*, 2018, 360, 848. [2] L. M. Lammers, M G. Herrera, V. I. Dodero, *ChemistryOpen* 2018, 7, 217. [3] M. G. Herrera, F. Zamarreño, M. Costabel, H. Ritacco, A. Hütten, N. Sewald, V. I. Dodero, *Biopolymers* 2014, 101, 96. [4] M. G. Herrera, L. A. Benedini, C. Lonez, P. L. Schilardi, T. Hellweg, J.-M. Ruysschaert, V. I. Dodero, *Soft Matter* 2015, 11, 8648. [5] M. G. Herrera, M. Pizzuto. C. Lonez, K. Rott, A. Hütten, N. Sewald, J-M Ruysschaert, V. I. Dodero, *Nanomedicine: NBM*. 2018, 14, 1417.