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## Effects of MFGM-providing ingredients on intestinal functions using an *in vitro* quadricellular model of intestinal epithelium

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### Abstract

Intestinal digestive, barrier, endocrine and immune functions are modulated by the nature of the food bolus. We hypothesized that dairy ingredients providing milk fat globule membrane (MFGM) could modulate these functions.

Our objective was to investigate the effects of four dairy ingredients (A, a non-enriched source of MFGM and B to D, enriched MFGM-ingredients) on gut functions in both physiological and inflammatory environments using a quadricellular (Caco-2, HT29-MTX, NCI-H716 and RajiB) model of the human intestinal epithelium.

Enriched ingredients were standardized at 1.34 mg/mL phospholipids whereas ingredient A was used at a lower concentration (0.51 mg/mL) to investigate dose-dependent effects. Inflammation was induced using TNF $\alpha$ . Cytotoxicity was evaluated by lactate-dehydrogenase release and barrier integrity by trans-epithelial electrical resistance (TEER). Expression of genes of interest was quantified by RT-qPCR.

All MFGM-ingredients significantly decreased cytotoxicity and improved barrier integrity compared to culture medium alone in the physiological state. An MFGM-dose dependent effect on TEER was observed, with the strongest effects for enriched ingredients. Ingredients B and C, both enriched in MFGM but differing in protein fraction, induced more changes in gene expression (barrier, digestive, endocrine and proliferative functions).

In the inflammatory state, all four ingredients had no effect on cytotoxicity but maintained barrier integrity. Ingredient B up-regulated several genes involved in gut barrier (claudins, mucins, occludin, ZO-1), digestive function (lactase) and induced a stronger immune response. Ingredient A, closer to ingredient B in terms of protein fraction, also modulated the expression of genes involved in digestive and immune functions, suggesting that components other than MFGM, such as proteins, could be involved in the observed effects.

These results add to the body of evidence of MFGM benefits. Further analysis is being conducted to investigate the effects of these ingredients incorporated within a model matrix and subjected to an *in vitro* digestion.