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In vitro and *in vivo* insights into the digestion of a unique natural emulsion: human milk

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Human milk is the ideal food for infant nutrition. Understanding the digestive behavior of this natural complex colloidal emulsion is essential for neonatal nutrition and a key step in developing infant formulas with optimized health benefits. However, ethical reasons limit *in vivo* trials. Thus, it is important to develop relevant in vitro models. In this aim, a dynamic in vitro digestion system (DIDGI®) was applied to human milks or infant formula.

The dynamic digester parameters were based on an exhaustive literature review to mimic closely the digestion of newborns. Raw or pasteurized pooled human milks (HM) or a liquid infant formula (IF) were digested in triplicate. In parallel, *in vivo* study was conducted on preterm newborns at Rennes Hospital (NCT02112331) to validate gastric *in vitro* data. Lipolysis, liberated fatty acids and the structural changes of the matrices were evaluated along digestion.

HMs differed from IF in terms of chemical composition (specifically regiodistribution), prehydrolysis state and emulsion structure. These initial differences impacted lipolysis kinetics and deconstruction. In comparison, the pasteurization of HM only impacted emulsion disintegration, protein aggregation and the persistence of native fat globules.

Our model will be useful to the scientist community and food manufacturers who focus on neonatal digestion and infant formulas optimization.