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Remarkable properties of human milk oligosaccharides – What can we learn from Mother Nature?

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Human milk is a highly complex liquid containing thousands of biomolecules. It serves as the sole nutrition for the fast growing and vulnerable infant and has evolved under a trade-off optimization process between mother and child. The success of this evolutionary process is demonstrated by a large number of studies that show that breast-fed infants have a range of health benefits compared to formula-fed infants. Several of these benefits are assumed to be mediated through the effects of the breastmilk glycans on the commensal gut microbial flora of a healthy infant.

The free human milk oligosaccharide (HMO) fraction is the third largest component of human milk (after lactose and lipids) and is highly complex in its composition. To date, infant formula is not supplemented with glycans that are identical to the naturally occurring HMOs and much work has taken place to develop functional mimics. However, regrettably many efforts have been primarily cost-driven and ignored much of the valuable lessons that evolutionary biology has to teach us if we look into details of glycan structure-activity-relationship and consider species-specific differences in milk oligosaccharide composition.

Glycom is committed to make human-identical milk oligosaccharides available for food applications, particularly infant formula. The technological challenges to achieve this are huge and dictate a step-wise approach, where the most significant individual components are developed and added to infant formula first. To date, this has been successfully achieved for two important HMOs where robust production technologies have been developed and first clinical results have become available.

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Novel extracellular matrix-derived peptides promote wound healing and tissue regeneration

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Recently, our work has revealed that Clostridial collagenase stimulates extracellular matrix remodeling along with epithelial and vascular cell injury responses while promoting impaired wound healing *in vivo*. Herein, we will review published findings and preliminary work yet to be published, which demonstrate that bacterial collagenase promotes wound healing responses by elaborating bioactive matrix fragments that stimulate epithelial, fibroblastic and angiogenic responses to injury. To these ends, we performed limited digestions of defined human dermal capillary-derived endothelial (HMVEC) and human fibroblast (HF)-derived extracellular matrices while MS/MS mass spectrometry was used to reveal several collagenase-generated matrix fragments derived from collagen and or collagen-associated proteins. Chemical synthesis and re-combination of some of these bioactive peptides were then used in several cells and animal-based wound healing assays to ascertain whether one or another peptide could activate cellular responses to injury *in vitro* and impaired wound healing *in vivo*. Results reveal that several peptides discovered significantly promote cell proliferation and angiogenesis *in vitro* and stimulate impaired wound healing *in vivo*. These findings indicate that collagenase indirectly possesses wound healing activity by the creation of bioactive peptides and that these wound healing peptides are able to convert non-healing wounds into those capable of closure.

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