Oral Delivery and Immunomodulatory Effects of Oligodeoxynucleotides from Lactic Acid Bacteria

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Research into the action of probiotics against infectious and inflammatory diseases and allergies has recently attracted considerable attention in both the medical and food sciences. Bacterial DNA contains CpG motifs that stimulate Toll-like receptor 9 expressing cells to mount a protective innate immune response. Studies have also revealed that DNA derived from probiotics can ameliorate ulcerative colitis, suggesting that immunomodulatory probiotic DNA may contribute to the prevention or suppression of various diseases. Our research group has identified immunomodulatory DNA sequences from immunoregulatory probiotics (immunobiotics) and confirmed that several synthetic oligodeoxynucleotides (ODNs) derived from these sequences maintain the immunomodulatory properties [1]. To increase the *in vivo* half-life and stability of ODNs against enzymatic degradation, ODNs are typically thiolated by the introduction of phosphorothioate (PS) bonds into the phosphate backbone. PS-ODN was shown to have high immunological functionality when administered intraperitoneally, intranasally, or intravenously via the caudal vein in various animal models. However, because ODNs are rapidly degraded by gastric acids and digestive enzymes, few efficacy studies involving oral administration have been performed. Therefore, to develop ODNs that retain functionality after oral administration, our research group attempted to produce acid-resistant ODN nanoparticles by encapsulating ODNs in calcium-based nanocapsules (“DNanocaps”) using a cell transfection method with carbonate apatite particles [2]. As ODNs are composed of negatively charged nucleotides, they readily adsorb onto positively charged calcium ions and grow to form 50-200 nm nanoparticles that contain approximately 1 % DNA by weight. These "edible" ODNs retained their immunomodulatory activity when taken up by intestinal mucosal cells. The ability to produce nanocapsules containing immunomodulatory ODNs opens the possibility of using DNanocaps in studies involving mouse disease models. If the therapeutic efficacy of DNanocaps can be achieved without parenteral injection, the cost, complexity and inconvenience of immunomodulatory therapy could be dramatically reduced [3]. In addition, this approach may lead to the development of novel immunobiotic foods and feeds that will contribute to the prevention or suppression of many types of infectious, allergic, inflammatory, and autoimmune diseases.

References

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