CHIMERIC PROTEIN AND NANO-CONSTRUCT FOR TISSUE-RETAINED ENZYME TO LOCALLY SUPPRESS INFLAMMATION

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There is considerable need for new retention strategies of immunomodulatory biologics for localized suppression of inflammation. We developed a chimeric protein as a well as a self-assembled nano-construct incorporating novel approaches for both retention and suppression to induce potent, confined metabolic programming. Immunosuppressive indoleamine 2,3 dioxygenase (IDO), which depletes tryptophan through the kynurenine pathway, was fused to Galectin 3 (Gal3), which binds extracellular glycans and provides tissue anchoring. Using a luciferase-Gal3 fusion reporter, tissue retention was prolonged to ~6 d whereas native luciferase is not retained and undetectable by 24 h. IDO-Gal3 injected subcutaneously controlled local LPS-challenged tissue inflammation. Furthermore, subgingival injection suppressed periodontal disease (PD) in a polymicrobial challenged mouse model. Multiplex analysis of gingival tissue revealed decreased inflammatory (IL-1β, IL-12p70, KC, IP10, MCP1, MIP2) and increased anti-inflammatory (IL-10, TGFβ3) proteins, indicating a shift toward homeostasis. Animals treated with IDO-Gal3 also showed significant decrease in bone loss commonly associated with PD, as determined by μCT analysis.