

Inhibition of Alveolar Bone Loss in Periodontitis Using Adenosine

Harrison Edward Mackler

Over-activation of the Th1-type immune response can result in inflammatory periodontal bone resorption due production of receptor activator of NF- κ B ligand (RANKL), a potent inducer of osteoclastogenesis. Therapeutic approaches aimed to control this immune-mediated pathogenesis in periodontitis, however, are not available. Extracellular adenosine generated by FoxP3+ T-regulatory lymphocytes (Tregs) is implicated as a down-regulatory factor for inflammatory and immune responses. Given this, we evaluated the osteoimmunological responses of the adenosine receptor agonist 5'-(N-ethylcarboxamido)adenosine (NECA) using our periodontitis mouse model, which is triggered by a hyper-immune reaction to oral bacteria after immunization with cross-reactive *Aggregatibacter actinomycetemcomitans* (Aa). 8-week-old female mice were placed into four groups: 1) untreated negative controls (n=7), 2) positive controls receiving Aa-immunization alone (n=7), and 3) Aa + 0.01mg/kg/day NECA (n=7). After 30 days, mice were sacrificed and alveolar bone loss was measured. Gingival tissue inflammatory cytokine expression and serum antibody response to Aa were profiled using ELISA. Administration of NECA significantly suppressed the bone loss induced by Aa-immunization ($p < 0.001$). Elevated levels of TNF α , soluble RANKL, and IL-1 β in Aa-only mice were suppressed to the levels of negative controls in mice receiving NECA ($p < 0.001$). Aa immunization of mice significantly increased anti-Aa antibodies; however, NECA treatment suppressed the levels of anti-Aa IgG2b antibody ($p < 0.05$), suggesting a down-modulation of Th1 response. Systemic NECA administration resulted in suppression of immune-mediated periodontal bone destruction through suppression of Th1 responses, indicating that strategies aimed to increase extracellular adenosine may lead to the development of novel therapeutic regimens for periodontitis.