

The therapeutic potential of regulatory T lymphocytes in periodontitis: A systematic review

Cafferata E.A.

Jerez A.

Vernal R.

Monasterio G.

Pandis N.

Faggion C.M.

Jr.

This systematic review aimed to: (a) generate a descriptive synthesis of preclinical studies assessing the therapeutic potential of regulatory T lymphocytes (Tregs) to arrest periodontitis, (b) evaluate the methodological heterogeneity of the reviewed animal studies and (c) assess the risk of bias (RoB) of the included studies. The electronic search for animal studies included the MEDLINE, EMBASE, Web of Science and LILACS databases. In addition, a manual search assessed the high-ranked scientific journals in ?periodontics/immunology? and the references listed in the included studies. There were no language, year or publication status restrictions. Two independent reviewers selected and extracted the data, and Cohen's Kappa coefficient was calculated to determine the inter-examiner agreement. The Systematic Review Center for Laboratory Animal Experimentation's (SYRCLE) tool was used to assess the RoB. A total of 21 of the 425 studies obtained from the database search were included. Treg function was mainly described in Porphyromonas gingivalis-induced periodontitis (57.1%) in mice (76.2%), where Treg suppression was strongly related to disease progression and Treg induction was strongly related to immuno-inflammatory response reduction. Of those 21 studies, eight included eight animal experiments using three distinct therapeutic approaches, including: P. gingivalis-driven immunization (n = 3), retinoic acid inoculation (n = 2) and anti-inflammatory molecules in polymeric carriers (n = 3), which could modulate the Treg activity through cytokine production (interleukin-10 and

transforming growth factor- β 1), CC-chemokine- and CC-chemokine receptor-mediated chemoattraction (CCL22 and CCR4) or Th17-associated receptor activator of nuclear factor κ B ligand (RANKL) downregulation. However, the studies with animal experiments did not specify the randomization sequences and housing conditions that were used, and therefore, 42.11% of the entries were rated as unclear RoB. Distinct therapeutic strategies involving Tregs could potentially suppress the immuno-inflammatory response and restore alveolar bone homeostasis during periodontitis. Nevertheless, important methodological variability, poor reporting of treatment effect estimates and unclear RoB suggest using caution when assessing the results of these studies. ©

2018 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd

animal experimentation

periodontitis

regulatory T lymphocytes

review

beta chemokine

cytokine

osteoclast differentiation factor

animal

Bacteroidaceae infection

bibliographic database

human

immunology

metabolism

microbiology

mouse

periodontitis

Porphyromonas gingivalis

regulatory T lymphocyte

Animals

Bacteroidaceae Infections

Chemokines, CC

Cytokines

Databases, Bibliographic

Humans

Mice

Periodontitis

Porphyromonas gingivalis

RANK Ligand

T-Lymphocytes, Regulatory