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Effect of High-Salt and Low-Salt Conditions on Differentiation of Regulatory T cells

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Summary

Autoimmune inflammatory diseases, such as rheumatoid arthritis (RA), have been previously thought to be mediated by the proinflammatory cytokine interleukin 17 (IL-17). The population of IL-17 producing $CD4^+$ helper T cells (Th17 cells) plays a pivotal role in autoimmune inflammatory diseases. A second $CD4^+$ T lymphocyte subset, termed regulatory T (Treg) cells, is essential for dominant immunologic tolerance. Treg cells have been shown to suppress immune effector cells by a variety of cell contact dependent and independent mechanisms. These include the production of cytokines such as an anti-inflammatory cytokine IL-10, sequestration of cytokines essential for cell growth such and IL-2, surface expression of the immunosuppressive molecule cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), and utilization of the perforin-granzyme pathway to kill activated targets or tumor cells. However, little is known regarding the dietary factors that directly influence Th17 cells or Treg cells. Kleinweietfeld M. *et al*. reported that increased salt (sodium chloride; NaCl) concentrations found locally under physiological conditions in vivo dramatically boost the induction of murine and human Th17 cells (Kleinweietfeld M. *et al*., Nature 2013). In the present study, we examined the effect of increased salt concentrations on the Treg cell differentiation and the function. Furthermore, we investigated the effect of high salt condition on Th17 and Treg cells in collagen induced arthritis (CIA) mice, an experimental model animal of rheumatoid arthritis.

Healthy DBA/1J or C57BL/6j female mice were fed the standard diet (AIN93G) or the high salt diet (AIN93G containing 4% NaCl, HSD) from Day 0 until Day 50. HSD did not affect the frequency of Treg cells and Th17 cells in mice. The IL-10 production from Treg cells in mice with HSD also did not changed. However, the production of IL-17 from Th17 cells in mice with HSD increased. Furthermore, HSD results in the acceleration of the severity of experimental arthritis model (CIA). The frequency of Th17 cells and the IL-17 production also increased in CIA mice with HSD. On the other hand, HSD did not affect the Treg cells frequency and the function in CIA mice.

Here we show that increased diet salt concentrations found under physiological conditions in vivo dramatically boost the induction of Th17 cells but not Treg cells in experimental rheumatoid arthritis model animal.