Insights: Publications

Specific HDAC6 inhibition by ACY-738 reduces SLE pathogenesis in NZB/W mice

Clinical Immunology

January 1, 2016

"Specific HDAC6 inhibition by ACY-738 reduces SLE pathogenesis in NZB/W mice," Co-Author, *Clinical Immunology*

Abstract

We sought to determine if a selective HDAC6 inhibitor (ACY-738) decreases disease in NZB/W mice. From 22 to 38 weeks-of-age, mice were injected intraperitoneally with 5 or 20mg/kg of ACY-738, or vehicle control. Body weight and proteinuria were measured every 2 weeks, while sera anti-dsDNA, Ig isotypes, and cytokine levels were measured every 4 weeks. Kidney disease was determined by evaluation of sera, urine, immune complex deposition, and renal pathology. Flow cytometric analysis assessed thymic, splenic, bone marrow, and peripheral lymphocyte differentiation patterns. Our results showed HDAC6 inhibition decreased SLE disease by inhibiting immune complex-mediated glomerulonephritis, sera anti-dsDNA levels, and inflammatory cytokine production and increasing splenic Treg cells. Inhibition of HDAC6 increased the percentage of cells in the early-stage developmental fractions of both pro- and pre-B cells. These results suggest that specific HDAC6 inhibition may be able to decrease SLE disease by altering aberrant T and B cell differentiation.