CDDO-Me Attenuates Inflammation in Healthy and Systemic Sclerosis Macrophages

Saemi Han1,2, Rajan Bhandari2, and Dr. Patricia A. Pioli2 (Advisor)

1 Department of Biology, Dartmouth College, Hanover, New Hampshire, United States of America,
2 Department of Microbiology and Immunology, Dartmouth Medical School, Lebanon, New Hampshire, United States of America

BACKGROUND

- Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by fibrosis, inflammation, autoantibody formation, and vascular abnormalities.
- There are approximately 180,000 SSc patients in the US. The incidence and prevalence rates are much higher in females than males.
- There are currently no validated diagnostic markers, disease altering FDA-approved treatments or cures for this disease.
- Mechanism of disease pathogenesis is poorly understood.

MATERIALS & METHODS

- Healthy human peripheral blood derived monocytes were isolated by cold aggregation. Monocyte purity was >90%.
- Cells were differentiated in healthy or control plasma and treated with 15µg/ml of MCP and 30nM CDDO-Me or vehicle control as indicated.
- Total RNA was extracted using miRNeasy Mini Kit. cDNA was synthesized with random hexamers and analyzed by qRT-PCR.
- Flow cytometry was performed using an 8-color MACSQuant 10 with three laser sources (405 nm, 488 nm, 635 nm) and FlowLogic 501.2A software.

RESULTS

CDDO-Me attenuates CCL2 levels in both healthy and systemic sclerosis macrophages

- CDDO-Me inhibits expression of CCL2 in both healthy and SSc macrophages.
- CDDO-Me induces Nrf2 activation in SSc macrophages, increasing expression of KEAP1 and HO-1.
- CDDO-Me treatment decreases the number of healthy and SSc macrophages that express CCL2.
- CDDO-Me also decreases the percent of CDF16-expressing healthy control macrophages, but does not mediate changes in SSc cells.

CONCLUSIONS

CDDO-Me attenuates expression of pro-fibrotic CCL2 and induces Nrf2 activation in SSc macrophages, suggesting it may be useful as a therapeutic for SSc patients.

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