ATOPIC ECZEMA/DERMATITIS

CUTANEOUS DEGRADATION OF HYALURONAN INDUCES SUPPRESSIVE EFFECT TO CHRONIC ALLERGIC DERMATITIS

J Muto [1] - D Watanabe [2] - R Gallo [3] - K Sayama [1]

Ehime University Graduate School Of Medicine, Department Of Dermatology, Toon, Japan [1] - Aichi Medical University, Department Of Dermatology, Nagakute, Japan [2] - University Of California, San Diego, Department Of Dermatology, La Jolla, United States [3]

Introduction: Hyaluronan (HA) has been implicated in wound healing and inflammation, and its biological properties are thought to be dependent on its breakdown and molecular size.

Objective: In this study we investigated if cutaneous HA degradation could influence inflammation of chronic allergic dermatitits.

Materials and Methods: The function of a tetramer form of HA (oligo-HA) was examined in a chronic dermatitis model induced by repeated DNFB application. This dermatitis model produces Atopic Dermatitis (AD)-like skin inflammation in an IL-4 dependent manner. Wild-type (WT) mice were painted with either DNFB or vehicle on both ears once a week over 29 days. Oligo-HA cream (1 %) or vehicle alone was applied topically daily from day 15 for 2 weeks.

Results: Topical application of oligo-HA significantly suppressed the increase in ear thickness after the fifth DNFB painting ($p<0.001$). Histological evaluation of skin tissues by hematoxylin and eosin staining confirmed that AD-like skin lesions were significantly alleviated. and the number of polymorphonuclear leukocytes (PMNs) in the ears of DNFB treated mice was significantly decreased by oligo-HA application ($p<0.01$). Furthermore, we found the mRNA expression of IL-4 ($p<0.05$) and MIP-2 ($p<0.001$) in ears of DNFB treated mice were significantly suppressed by oligo-HA application when measured by quantitative real-time PCR. The elevation of serum IgE levels in DNFB treated mice were also attenuated ($p<0.01$). To test if the dynamic breakdown of HA acts as an endogenous signal of injury we generated transgenic mice that conditionally overexpressed Hyaluronidase 1 (HYAL1). We evaluated the chronic dermatitis model in the tamoxifen-inducible K14-dependent Cre system and the increase in ear thickness after the fifth DNFB paintingwas was significantly suppressed in K14CreERT/HYAL1 ($p<0.01$).

Conclusions: These data show that cutaneous degradation of HA induces the suppressive effect to AD-like dermatitis by affecting the inflammatory status in skin and can influence

clinical outcome.