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CORRESPONDENCE

Expression of histidine decarboxylase in sweat glands of patients with atopic dermatitis

Sweat plays an important role in regulating skin homeostasis. Some patients with atopic dermatitis (AD) have difficultly sweating, and their sweat leaks into the skin, which exacerbates the skin condition.[1,2] Acetylcholine-induced sweating is suppressed by histamine.[3] The counterflow of a histamine solution from the sweat pores on the skin surface can reduce the mRNA expression of claudin 3—a component of the sweat duct-tight junctions.[4] Moreover, the claudin 3 expression is reduced in patients with AD.[4] With this background, it seemed that histamine is involved in sweat secretion and sweat leakage into the skin. In the skin, mast cells and keratinocytes produce histamine.[5] Histidine decarboxylase (HDC)—a key biosynthetic enzyme of histamine—is highly expressed throughout the epidermis in patients with AD.[6] Conversely, it is unknown whether the sweat glands produce histamine. Therefore, we investigated whether sweat glands possess HDC and whether their HDC increases in patients with AD.

(A)

Donor ID	Age	Gender	Diagnosis	SCORAD	Severity
1	22	Male	Healthy subject	0	—
2	40	Female	Healthy subject	0	—
3	18	Male	Healthy subject	0	—
4	34	Male	Patient with AD	56	Severe
5	40	Female	Patient with AD	50	Moderate
6	21	Male	Patient with AD	30	Moderate
7	35	Male	Patient with AD	60.4	Severe
8	40	Male	Patient with AD	81.5	Severe
9	34	Male	Patient with AD	77.6	Severe
10	20	Male	Patient with AD	80.5	Severe
11	40	Female	Patient with AD	51	Severe
12	39	Female	Patient with AD	53	Severe

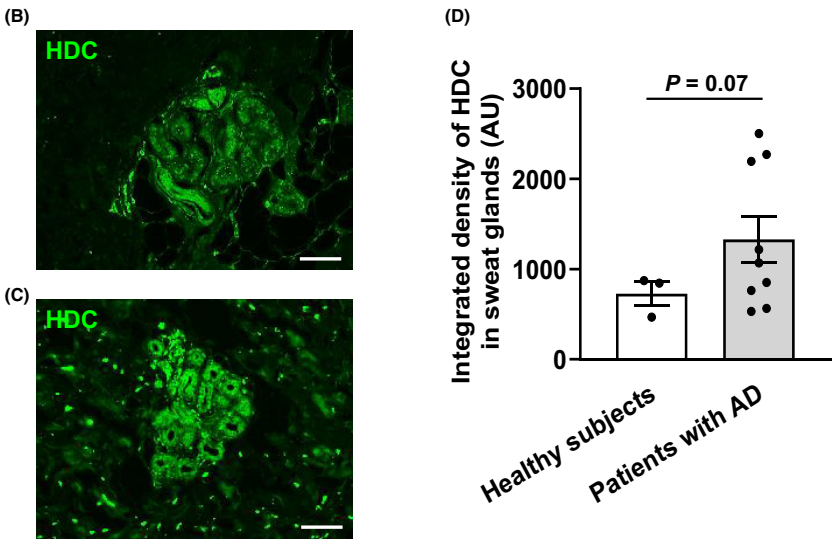

FIGURE 1 HDC immunoreactivity in the sweat glands of healthy subjects and patients with AD. (A) Subject information. The severity of AD was evaluated by SCORAD score as follows: mild (SCORAD score <25), moderate (25–50), or severe (>50). (B, C) Representative images of immunohistochemical staining for HDC (green) in the sweat glands of (B) a healthy subject and (C) a patient with AD (20× magnification). Scale bar = 100 μm. (D) 2–3 sections were collected for each subject, and 1–3 images (field size per image: 363 μm × 273 μm) were captured from each section. Data are presented as mean ± standard error of mean or scatter plot, with each circle representing one individual. Group means were compared by Welch's *t* test. The average integrated densities of HDC in the sweat glands were increased in patients with AD ($n = 9$) when compared with those in the healthy subjects ($n = 3$). AD, atopic dermatitis; HDC, histidine decarboxylase; SCORAD, Severity Scoring of Atopic Dermatitis

Pruritic skin samples from nine patients with AD and normal skin samples from three healthy subjects were obtained at Russian hospitals by Obio, LLC (El Segundo, CA, USA) (Figure 1A). All patients provided their informed consent before the study. The formalin-fixed paraffin-embedded skin sections (5-μm) were immunohistochemically evaluated. After dewaxing and antigen retrieval, the sections were incubated overnight at 4°C with a primary rabbit polyclonal anti-HDC antibody (1:100; PROGEN Biotechnik GmbH, Heidelberg, Germany). After washing, the obtained sections were incubated for 2 h at room temperature with the corresponding secondary antibody (1:500).

The HDC expression was observed in the sweat glands of healthy subjects and patients with AD (Figure 1B and C). The HDC expression level in the sweat glands of patients with AD was higher than that in the sweat glands of healthy subjects (Figure 1D).

The histamine levels in the sweat of patients with AD were much higher than those in the plasma of healthy subjects; however, the sweat histamine levels of patients with AD were similar to those of the healthy subjects.[7] A histamine release assay against sweat antigen using basophils from subjects revealed that the subjects without any common specific skin disorders, but with sweat allergies, have high levels of histamine in their sweat,[7] implying that the subjects experiencing sweat leakage have high levels of sweat histamine. Although the sample size in this study was small, we speculated that the HDC expression level increases in the sweat glands of patients with AD. Further studies are warranted to investigate why the sweat glands' HDC expression in patients with AD increases. If the sweat glands can synthesize histamine, they may be able to control the permeability of sweat gland-tight junctions by regulating histamine synthesis. The main source of sweat histamine is believed to be derived from mast cells around the sweat glands and ducts. In this study, we presumed that the sweat glands themselves can control sweat permeability. Further studies are needed to investigate the histamine-producing ability of sweat glands, activity of histamine-metabolizing enzymes, and trigger factors, such as bacterial toxins.

DECLARATION SECTION

Approval of the research protocol: HYM-17-001.
Informed Consent: N/A.
Registry and the Registration No. of the study/trial: N/A.
Animal Studies: N/A.

CONFLICTS OF INTEREST

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