heptad positions a, d, e, and g are crucial in stabilizing keratin structure, positions a and d might be more critical than positions e and g for stabilizing keratin structure. In addition, the acidity/polarity of the substituted amino acid is also related to keratin structure and the phenotypic severity of EHK.

References

[1] Smith F. The molecular genetics of keratin disorders. Am J Clin Dermatol 2003;4:347–64.
[2] Muller FB, Kuster W, Wodecki K, Almeida Jr H, Bruckner-Tuderman L, Krieg T, et al. Novel and recurrent mutations in keratin KRT5 and KRT14 genes in epidermolysis bullosa simplex: implications for disease phenotype and keratin filament assembly. Hum Mutat 2006;27:719–20.
[3] Osawa R, Akiyama M, Izumi K, Ujiie H, Sakai K, Nemoto-Hasebe I, et al. Extremely severe palmoplantar hyperkeratosis in a generalized epidermolytic hyperkeratosis patient with a keratin 1 gene mutation. J Am Acad Dermatol 2011;64:991–3.
[4] Oh SW, Lee JS, Kim MY, Kim SC. Novel keratin 5 mutations in epidermolysis bullosa simplex: cases with unusual genotype–phenotype correlation. J Dermatol Sci 2007;48:229–32.
[5] Tsubota A, Akiyama M, Sakai K, Yanagi T, McMillan JR, Higashi A, et al. Congenital ichthyosiform erythroderma mimicking ichthyosis bullosa of Siemens. Br J Dermatol 2008;158:191–4.
[6] Yang JM, Nam K, Kim HC, Lee JH, Park JK, Wu K, et al. A novel glutamic acid to aspartic acid mutation near the end of the 2B rod domain in the keratin 1 chain in epidermolytic hyperkeratosis. J Invest Dermatol 1999;112:376–9.
[7] Quinlan R, Hutchison C, Lane B. Intermediate filament proteins. Protein Profile 1994;1:779–911.
[8] Sybert VP, Francis JS, Corden LD, Smith LT, Weaver M, Stephens K, et al. Cyclic ichthyosis with epidermolytic hyperkeratosis: a phenotype conferred by mutations in the 2B domain of keratin K1. Am J Hum Genet 1999;64:732–8.
[9] Liu J, Zheng Q, Deng Y, Cheng CS, Kallenbach NR, Lu M. A seven-helix coiled coil. Proc Natl Acad Sci U S A 2006;103:15457–62.
[10] Arin MJ, Oji V, Emmert S, Hausser I, Traupe H, Krieg T, et al. Expanding the keratin mutation database: novel and recurrent mutations and genotype-phenotype correlations in 28 patients with epidermolytic ichthyosis. The British journal of dermatology 2011;164:442–7.
[11] Sun XK, Ma LL, Xie YQ, Zhu XJ. Keratin 1 and keratin 10 mutations causing epidermolytic hyperkeratosis in Chinese patients. Journal of dermatological science 2002;29:195–200.
[12] Michael EJ, Schneiderman P, Grossman ME, Christiano AM. Epidermolytic hyperkeratosis with polycyclic psoriasiform plaques resulting from a mutation in the keratin 1 gene. Experimental dermatology 1999;8:501–3.
[13] Muramatsu S, Suga Y, Mizuno Y, Hasegawa T, Tsuchihashi H, Matsuba S, et al. A novel threonine to proline mutation in the helix termination motif of keratin 1 in epidermolytic hyperkeratosis with severe palmoplantar hyperkeratosis and contractures of the digits. The British journal of dermatology 2005;152:1087–9.
[14] Syder AJ, Yu QC, Paller AS, Giudice G, Pearson R, Fuchs E. Genetic mutations in the K1 and K10 genes of patients with epidermolytic hyperkeratosis. Correlation between location and disease severity. The Journal of clinical investigation 1994;93:1533–42.
[15] Lee DY, Ahn KS, Lee CH, Rho NK, Lee JH, Lee ES, et al. Two novel mutations in the keratin 1 gene in epidermolytic hyperkeratosis. The Journal of investigative dermatology 2002;119:976–7.
[16] Chassaing N, Kanitakis J, Sportich S, Cordier-Alex MP, Titeux M, Calvas P, et al. Generalized epidermolytic hyperkeratosis in two unrelated children from parents with localized linear form, and prenatal diagnosis. The Journal of investigative dermatology 2006;126:2715–7.
[17] Rothnagel JA, Dominey AM, Dempsey LD, Longley MA, Greenhalgh DA, Gagne TA, et al. Mutations in the rod domains of keratins 1 and 10 in epidermolytic hyperkeratosis. Science 1992;257:1128–30.
[18] Shimomura Y, Sato N, Tomiyama K, Takahashi A, Ito M. A sporadic case of epidermolytic hyperkeratosis caused by a novel point mutation in the keratin 1 gene. Clinical and experimental dermatology 2006;31:286–7.

Jae Yong Sung[a],
Se-Woong Oh[b],
Song Ee Kim[a],
Soo-Chan Kim[a,*]
[a]*Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea*;
[b]*Hus' hu Dermatology Clinic, Seoul, Republic of Korea*

*Corresponding author at: Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, Gangnam Severance Hospital, Eonjuro 211, Gangnam-gu, Seoul 135-720, Republic of Korea. Tel.: +82 2 2019 3360; fax: +82 2 3463 6136
E-mail address: kimsc@yuhs.ac (S.-C. Kim)

21 June 2012

http://dx.doi.org/10.1016/j.jdermsci.2013.03.001

Letter to the Editor

Histamine, TNF, C5a, IL-6, -9, -18, -31, -33, TSLP, Neopterin, and VEGF are not elevated in chronic spontaneous urticaria

Spontaneous urticaria is a common skin disorder which is classified as acute or chronic depending upon disease duration (less or more than 6 weeks, respectively). At any one time, 0.5–1% of the population is thought to be suffering from chronic spontaneous urticaria (CSU). CSU is debilitating and results in a large socio-economic burden due to a reduction in performance of 20–30% [1]. The underlying cause of CSU is rarely identified, therefore, symptomatic treatment is the most frequently used form of management [1,2]. Treatment aims to ameliorate or suppress symptoms by inhibiting the release and/or the effect of mast cell mediators [2]. There are only a few differential diagnoses to CSU, including Schnitzler syndrome, urticaria vasculitis and Muckle Wells syndrome in patients with wheals, and ACE-inhibitor-induced or hereditary angioedema in patients

Table 1
Previously reported markers in chronic spontaneous urticaria.

Measured marker	Number of patients vs. controls	Number of centers	Correlation with disease activity	Ref.
IL-9	~50 vs. 48	1	No	[6]
IL-18	55 vs. 20	1	No	[7]
	73 vs. 40	1	No	[8]
IL-31	46 vs. 28	1	Not analyzed	[9]
MMP-9	29 vs. 18	1	No	[10]
	52 vs. 30	1	Yes	[11]
Neopterin	28 vs. 96	1	No	[12]
TNF, IL-6, IL-13, IL-12p70, IL-10	29 vs. 33	1	Not analyzed	[4]
VEGF	80 vs. 53	2	Yes	[13]

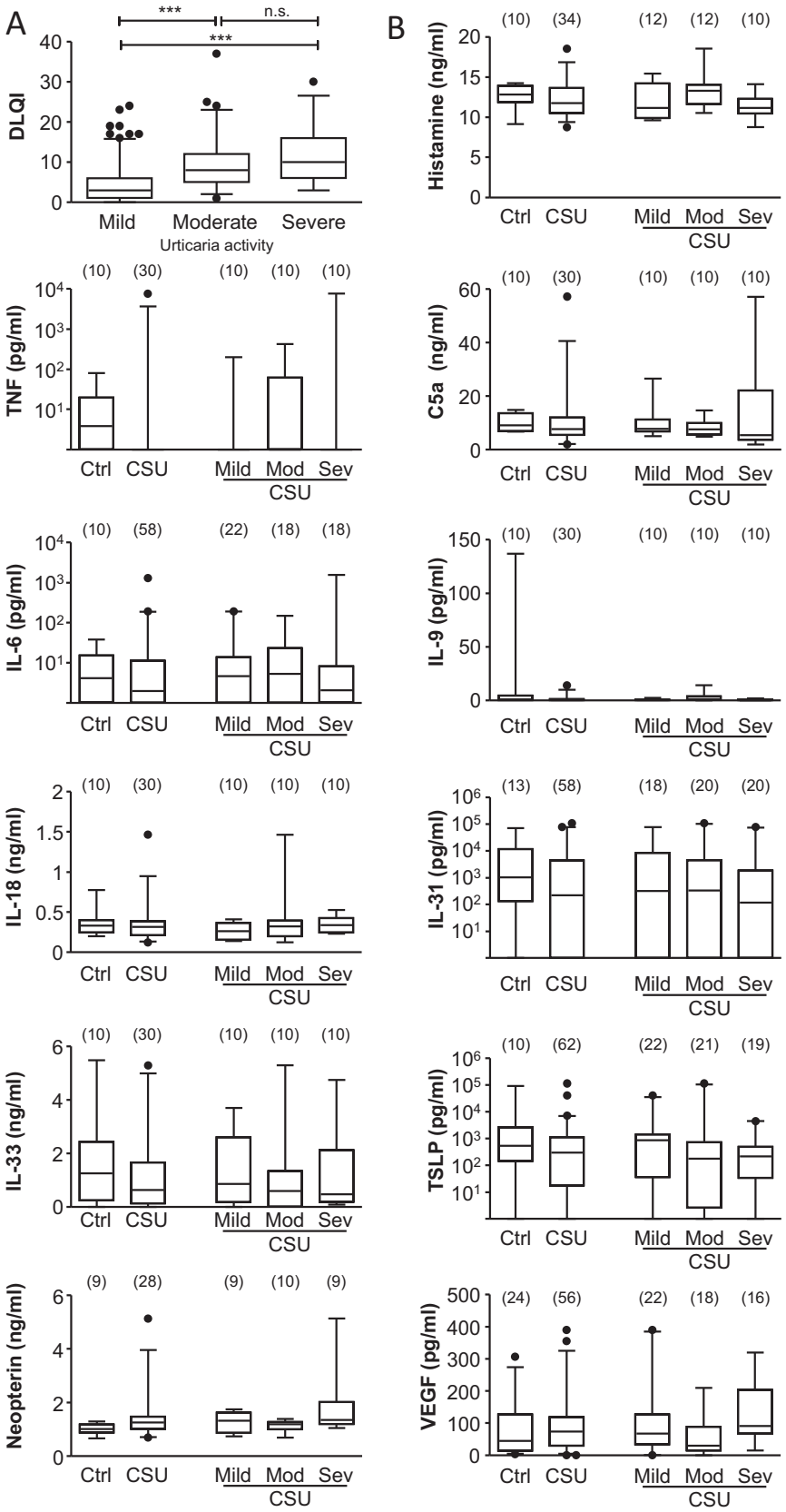

Fig. 1. (A) Differences in Dermatology Life Quality Index (DLQI) in different diesease severity subgroups as defined by urticaria activity score (UAS): mild (n = 164) = UAS 1–15, moderate (n = 131) = UAS 16–29, severe (n = 33) = 30–42 and (B) sera concentrations of different possible disease mediators in healthy controls (Ctrl) and patients with chronic spontaneous urticaria (CSU). Different numbers of samples were analysed, number of patients per group is given in parentheses. All data are shown with median and lower and upper quartile, whiskers represent the 5th and the 95th percentile.