The Editor's Choice

Abe R

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Acetylcholine-induced whealing in cholinergic urticaria – what does it tell us?

Cholinergic urticaria (CholU) is characterized by the occurrence of itchy wheals induced by sweating. Intradermal injections of acetylcholine (ACh) have been proposed to help with diagnosing. Altrichter S et al compared the rates of positive ACh test results in well characterized CholU patients and to identify clinical features of CholU linked to ACh reactivity. At 15 minutes after intradermal injections of ACh, wheal and flare responses were significantly more frequent in CholU patients than healthy controls, wheals. Also, wheals were 168% and flares 52% larger and of longer duration in CholU patients than in healthy controls. CholU patients with ACh-induced wheals (ACh+) had larger flare but not wheal responses in response to histamine than those without (ACh-). Also, ACh-induced wheal responses were significantly correlated with sweating. Finally, wheal responses lasted longer in ACh+ than in ACh- patients. ACh-induced wheals, in patients with CholU, is linked to sweating and longer lasting symptoms. Intradermal ACh testing is an interesting tool for mechanistic studies in CholU.

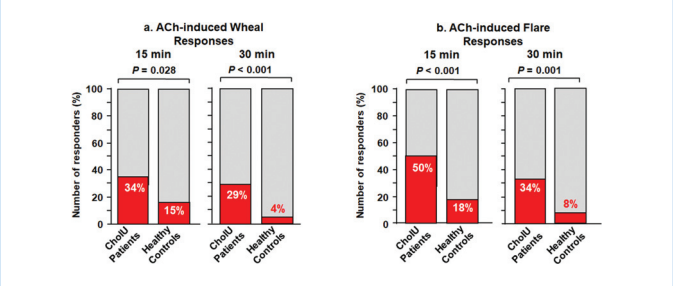

Fig.1. The number of cholinergic urticaria (CholU) patients (n = 38) and healthy controls (n = 73) who showed positive (a) wheal and (b) flare response (red shading) 15 and 30 min after an intradermal injection of 50 µL of 100 µL/mL acetylcholine. None of the patients displayed a wheal and flare type skin response after saline intradermal injection. Significance was calculated using Fisher's Exact Test.

Mucopolysaccharide polysulfate promotes microvascular stabilization and barrier integrity of dermal microvascular endothelial cells via activation of the angiopoietin-1/Tie2 pathway

Mucopolysaccharide polysulfate (MPS) is a heparinoid and MPS containing formulations are widely used as moisturizers for dry skin and to treat peripheral vascular insufficiency. Although MPS has therapeutic effects in skin diseases with microvascular abnormalities, the effects of MPS on microvascular function remain incompletely understood. Fujiwara S et al evaluated the functional activities of MPS on human pericytes (HPC) and human dermal endothelial cells (HDMEC), and on microvascular permeability of the skin. MPS dose-dependently enhanced Ang-1 secretion, which activated Tie2 in HDMEC. In HDMEC, MPS significantly increased the production of PDGF-BB, which recruits HPC to the vascular endothelium, and the phosphorylation of Tie2, as results of the Ang-1/Tie2 signaling pathway activation. MPS increased the expression of tight junction protein claudin-5 and TEER in the HDMEC. Moreover, the intradermal injection of MPS prevented VEGF-induced increase in vascular permeability in mouse skin. The authors found that MPS promoted microvascular stabilization and barrier integrity in HDMEC via Ang-1/Tie2 activation. These results suggest that MPS might improve microvascular abnormalities in various diseases accompanied by disturbances in Ang-1/Tie2 signaling.

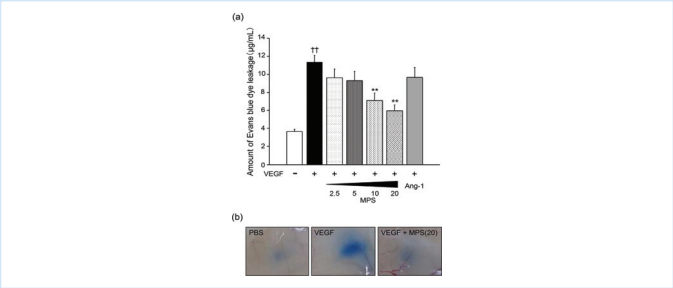

Fig. 5. Inhibitory effect of MPS on VEGF-induced vascular permeability *in vivo*. Effect of MPS on vascular permeability was assessed using the Miles assay. Mice were treated with an intravenous injection of 100 µL 1% Evans blue solution into the tail vein 30 min prior to the intradermal injection of PBS control, VEGF alone (50 ng/site), VEGF (50 ng/site) + MPS (2.5, 5, 10, or 20 µg/site), or VEGF (50 ng/site) + Ang-1 (500 ng/site). (a) Evans blue dye extravasation to the adjacent tissue was quantified (n = 16 per group, 2 tissues were sampled from 8 mice; 1 sample per administration site). Each column represents the mean ± S.E. (b) The images show the back of mice under each condition. **: $P < 0.01$ by Dunnett's multiple comparison test compared with VEGF (50 ng/site) (VEGF+, MPS-), ††: $P < 0.01$ by F-test followed by Aspin-Welch's *t*-test, compared with PBS (VEGF-, MPS-).

Intracellular oxidative stress induced by calcium influx initiates the activation of phagocytosis in keratinocytes accumulating at S-phase of the cell cycle after UVB irradiation

In the epidermis, the phagocytosis of melanosomes into keratinocytes is important to protect their DNA against damage from UVB radiation. Furthermore, it is considered that UVB activates the phagocytosis by keratinocytes but the detailed mechanism involved is not fully understood. Katsuyama Y et al clarify the mechanism of UVB-enhanced phagocytosis in keratinocytes, and investigated the relationship between the phagocytic ability of keratinocytes and the cell cycle stage of keratinocytes. The phagocytosis of fluorescent beads into keratinocytes was enhanced by UVB and also by oxidative stress. Keratinocytes exposed to UVB or oxidative stress were at S-phase of the cell cycle. Furthermore, keratinocytes synchronized to S-phase showed a higher phagocytic ability according to the increased intracellular ROS level. Keratinocytes synchronized to S-phase and exposed to UVB or oxidative stress had increased levels of intracellular calcium and their enhanced phagocytic abilities were diminished by the calcium ion chelator. Taken together, intracellular oxidative stress induced by intracellular calcium influx mediates the UVB-enhanced phagocytic ability of keratinocytes accumulating at S-phase of the cell cycle.

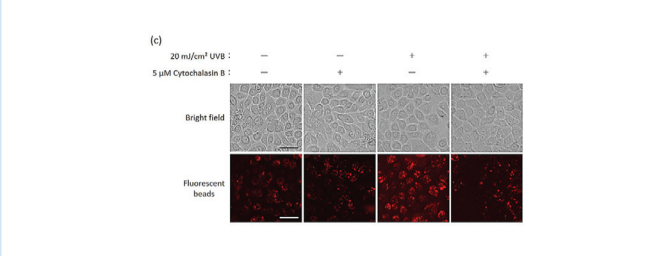

Fig. 1. Influence of UVB, H_2O_2 and BSO on the incorporation of fluorescent beads in NHEKs. (c) Effect of UVB and/or cytochalasin B on fluorescent bead uptake by NHEKs; fluorescence images were observed using a Floid® Cell Imaging Station. Scale bar: 50 µm.