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Mechanisms of intracellular calcium elevation in human airway epithelial cells by an airway disease-relevant extract of hog-barn dust

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A subset of workers in swine confinement facilities develop chronic inflammatory lung disease, and an aqueous hog-barn dust extract (HDE) induces diverse inflammation-related responses in cultured BEAS-2B human airway epithelial cells, including release of inflammatory cytokines. These responses require the calcium (Ca)-dependent protein kinase C-alpha isozyme, and we showed previously that HDE stimulates Ca elevation in these cells. Two distinct fractions of HDE stimulate Ca responses, so we hypothesized that two different Ca regulatory pathways would be involved. BEAS-2B cells were loaded with Fluo-4 and treated with agents to alter various Ca signaling pathways, and the effects of these agents on HDE modulation of intracellular Ca were then assessed by Flex Station assays. Pretreatment with pertussis toxin, the phospholipase C (PLC) inhibitor U73122 but not its inactive analog U73343, and the IP3 receptor Ca channel inhibitors 2-APB and xestospongin C all markedly reduced the HDE Ca response. TrpV1 receptor Ca channels mediate some responses to inhaled pollutants, and the TrpV1 inhibitor capsazepine and TrpV1 inactivation by pretreatment with resiniferatoxin both markedly reduced HDE Ca responses also. These data suggest that a Gi/o-mediated PLC pathway to IP3 receptor activation and TrpV1 channel activation both contribute to HDE Ca responses. *Supported by NIOSH 2R01-OH008539*.