Histone Deacetylase And Acetyltransferase Inhibitors Decrease Organic Dust-Mediated Activation Of Proinflammatory Gene Expression

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RATIONALE: Post-translational modification of histone proteins are major mechanisms that modify chromatin structure and regulate gene expression in eukaryotes. Activation of histone acetyltransferase (HAT) or inhibition of histone deacetylases (HDAC) is generally believed to allow chromatin to assume a more open state, permitting transcriptional activity.
METHODS: Organic dust was obtained from settled surface dust from swine confinement facilities and extracted in Hanks' balanced salt solution. Bronchial epithelial cells, BEAS-2B cell line, were pretreated for 30-120 min with trichostatin A (1-10 ug/ml) and anacardic acid (0.1 to 1 uM), then stimulated with organic dust for 4 hours. Cell-free supernatants were harvested and assayed for IL-6 and IL-8 by ELISA.
RESULTS: We report here the surprising observation that treatment of a human bronchial epithelial cell line, BEAS-2B cells, with the inhibitor histone deacetylase, trichostatin A, or the histone acetyltransferase inhibitor, anacardic acid, strongly inhibited induction of both IL-6 and IL-8 protein upon stimulation with organic dust.
CONCLUSION: These data suggest that chromatin remodeling regulates organic dust-induced IL-6 and IL-8 protein production. The mechanism (s) of this regulation will be an area of future investigation.

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