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Characterization of molecular pattern in sensory pain signaling following mustard exposure on mouse ear vesicant model

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Characterization of molecular pattern in sensory pain signaling following mustard exposure on mouse ear vesicant model

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Abstract

Boyer Category: discovery

Background: Sulfur mustard (SM, bis(2-chloroethyl sulfide) is a warfare chemical that causes inflammation, epidermal blistering, fibrosis and delayed skin pain. However, the underlying mechanisms mediating sensory pain following mustard exposure remain unclear. We have previously demonstrated activation of cannabinoid signaling following exposure of skin to mustards on inflammation. Herein, we determine that downstream signaling following activation of cannabinoid receptors by mustards may modulate the sensory pain following mustard exposure in skin delay in pain. In this study, we investigated if reprogramming of dermal sensory pain receptors alters by chemokines or neurotransmitters following mustard exposure.

Design/Methods: Utilizing mouse ear vesicant skin models (MEVM) and mouse keratinocyte pam212 cells, we examined if blistering chemical exposure to sensory pain with regard to cell proliferation and cellular responses in delayed skin pain which reflect exhibited distinct redox patterns. we measured differences in the expression of opioid receptors compared with cell proliferation, various neurotransmitter and its metabolic determinants compared to keratinocytes following mustard exposure using real-time PCR quantitation.

Results: We found the cell tropism as keratinocyte cell resisted longer compared to cell proliferation biomarkers in mouse ear tissue. Cell tropism of pain receptors in mouse skin was distinctly altered by suppression of kappa opioid receptor (OPRK) and mu-opioid receptor (OPRM) was completely suppressed compared to the delta-opioid receptor (OPRD) in a time-dependent manner. However, OPRM mRNA was detected in mouse keratinocytes. we also found that NGF mRNA may play a role in the early phase responses in contrast to other neurotransmitters. Interestingly, SM triggered transient receptors by TRPV1 mRNA or TRPV3 mRNA activated by a biphasic response in a time-sensitive manner. in particular, two chemokines like CXCl1 and CCL20 were down-regulated following by SM exposure in the MEVM model. Our results indicate that sensitivity to cannabinoid receptors in mouse skin was diminished in later time periods when compared to early responses. Furthermore, we observed the FAAH, downstream catalytic enzymes in Cannabinoid signaling was altered by induction.

Conclusions: We speculate that those alteration of opioid receptors may implement cannabinoid signaling by promoting TRPV1 signaling a process effected by mustard exposure in the dermal lesion.

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