INTRODUCTION: Current medications to relieve acute or chronic pain have a narrow spectrum of action and a multitude of adverse effects. Transient Receptor Potential Vanilloid 1, a voltage-gated ion channel, is a principle detector of noxious heat and inflammatory pain. Oxidized Linoleic Acid Metabolites (OLAMs) are specific TRPV1 agonists, released in response to heat injury and inflammation. The current study involves identifying enzymes, namely the Cytochrome P450s, responsible for OLAM synthesis in burn pain.

METHODS: Lipid extracts from human burned and normal skin were subjected to HPLC/Mass Spec analysis to estimate 9-HODE, 9-oxoHODE, 13-HODE and 13-oxoHODE levels. The Glue Grant Trauma-Related Database (TRDB) was used to determine changes in expression pattern of transcripts in 87 patients after cutaneous burn as compared to 41 control skin biopsies. The Affymetrix HG-U133_Plus_2 human microarray was used to analyze a total of 102 genes, including 86 genes known to oxidize poly unsaturated fatty acids (the general class of lipids that includes linoleic acid). A total of 87 burn patients had associated 238 Affymetrix microarrays and 253 burn patients had 602 blood leukocyte Affymetrix microarrays conducted up to 1 year after injury. This was compared to a control human data set of 41 skin samples and 95 blood leukocyte samples. A total of 187 trauma patients had 785 blood leukocyte Affymetrix microarrays. Data were analyzed by log2 expression differences from control with adjustment of alpha levels for multiple comparisons.

RESULTS: HPLC/Mass spec results revealed a significant increase in OLAM levels in burned human skin compared to control human skin. As compared to control samples, burn injury in humans triggered significant upregulation of specific gene transcripts in circulating blood leukocytes and a separate subset of gene transcripts in skin tissue biopsies. Trauma injury in humans also triggered a significant upregulation of specific gene transcripts in circulating blood leukocytes up to 30 days from injury.

CONCLUSION(S): Thermal injury in humans triggers a massive, selective and sustained alteration in the expression pattern of enzymes capable of forming OLAMs in both skin and blood. The Cytochrome P450 family appears to play a critical role in OLAM formation and inhibition of the CYPs may play a role in increasing thermal thresholds. Identification and targeting specific enzymes responsible for OLAM synthesis after burns could provide a novel approach in controlling burn pain.