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**DEACTIVATION OF EEF2 IS ASSOCIATED WITH INTRACELLULAR CALCIUM HOMEOSTASIS IN RESPONSE TO SEVERE BURN INJURY**

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**Introduction:** The liver plays a central role during the post-burn response by mediating metabolism, immune function, and protein production. Liver integrity is required for recover post-burn, however severe burn leads to liver damage and dysfunction. We suggest that by improving liver dysfunction and damage recovery of severely burned patients can be enhanced. The aim of the present study was to determine the molecular signaling mechanism that lead to an altered hepatic protein synthesis post-burn.

**Methods:** Adult male Sprague-Dawley rats (250-300gram) were randomized to either control or burn and received a full thickness burn of 60% of their total body surface area. Rat primary hepatocytes (RPH) were isolated by liver perfusion 24 hours postburn and intracellular calcium homeostasis was evaluated by calcium imaging **in vitro**. Liver tissue was snap frozen in liquid nitrogen and processed for Western blotting to determine the hepatic response to burn injury **in vivo**.

**Results:** Fura-2 staining showed that RPH had markedly elevated cytosolic calcium concentrations in response to burn. Blocking of the ER calcium pump SERCA by thapsigargin revealed that thermal injury leads to severely depleted endoplasmic reticulum (ER) calcium stores in RPH. Burn-induced ER calcium depletion caused an compensatory elevation of  $Ca^{2+}$  / calmodulin-dependent protein kinase III, eEF2k phosphorylated at serine 366, which leads to eukaryotic translation elongation factor 2 (eEF2) deactivated by phosphorylation. The expression of hepatic-derived albumin decreased 24 hr postburn.

**Conclusion:** Severe burn injury leads to dramatic hepatic disturbances in calcium homeostasis and markedly altered hepatic protein synthesis via eEF2k / eEF2 pathway.