Expression Suppression and Activity Inhibition of TRPM7 Regulate Cytokine Production and Multiple Organ Dysfunction Syndrome During Endotoxemia: a New Target for Sepsis

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BACKGROUND: Main pathological features detected during sepsis and endotoxemia include over-secretion of pro-inflammatory cytokines and multiorgan dysfunction syndrome (MODS). Unfortunately, current clinical efforts to treat sepsis are unsatisfactory, and mortality remains high. Interestingly, transient receptor potential (TRP) melastatin 7 (TRPM7) ion channel controlling Ca2+ and Mg2+ permeability is involved in cytokine production and inflammatory response. Furthermore, TRPM7 downregulation has been shown to alleviate local symptoms in some models of sepsis, but its effects at a systemic level remain to be explored. OBJECTIVE: To test whether TRPM7 mediates cytokine production and MODS during endotoxemia. METHODS: Endotoxemic and sham-endotoxemic rats were subjected to pharmacological inhibition of TRPM7 using carvacrol, or to expression suppression by adenovirus delivery of shRNA (AdVshTRP