Vanilloid receptor agonists and antagonists are mitochondrial inhibitors: how vanilloids cause non-vanilloid receptor mediated cell death.


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Abstract

Time-lapse photomicroscopy of human H460 lung cancer cells demonstrated of the transient receptor potential V1 (TRPV1) channel agonists, (E)-capsaicin and resiniferatoxin, and the TRPV1 antagonists, capsazepine, and SB366791, were able to bring about morphological changes characteristic of apoptosis and/or necrosis. Immunoblot analysis identified immunoreactivity for the transient receptor potential V1 (TRPV1) channel in rat brain samples, but not in rat heart mitochondria or in H460 cells. In isolated rat heart mitochondria, all four ligands caused concentration-dependent decreases in oxygen consumption and mitochondrial membrane potential. (E)-Capsaicin and capsazepine evoked concentration-dependent increases and decreases, respectively, in mitochondrial hydrogen peroxide production, whilst resiniferatoxin and SB366791 were without significant effect. These data support the hypothesis that (E)-capsaicin, resiniferatoxin, capsazepine, and SB366791 are all mitochondrial inhibitors, able to activate apoptosis and/or necrosis via non-receptor mediated mechanisms, and also support the use of TRPV1 ligands as anti-cancer agents.

PMID: 17214968 [PubMed - indexed for MEDLINE]