Lidocaine Suppresses TRPM7 Channel Activity: Implications for the Use of Anesthetics as Post-Operative Anti-Tumor Therapeutics

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Transient receptor potential (TRP) channels constitute a superfamily of ubiquitously expressed voltage and ligand-gated, non-selective cation channels involved in diverse biological processes including sensory transduction and vasoregulation. Specifically, transient receptor potential melastatin 7 (TRPM7) channels are critical for the maintenance of Ca2+ and Mg2+ homeostasis, cell cycle progression, and cellular growth and survival. Previous studies have demonstrated TRPM7 overexpression facilitates the progression of various human carcinomas, neurodegenerative disorders, and ischemic conditions. Consequently, the goal of this work was to assess the inhibitory potential of the widely used local anesthetic lidocaine on TRPM7 channel activity. Whole-cell patch-clamp recordings on human embryonic kidney (HEK-293) cells overexpressing TRPM7 revealed lidocaine significantly decreased TRPM7 currents and its effects were reversible upon extracellular solution washout. Furthermore, biochemical assays indicated both decreased cell viability and migration of non-small cell lung cancer (A549) cells exposed to lidocaine. In clinical settings, these results implicate lidocaine may be efficacious as a therapeutic postoperative agent targeting TRPM7, thus reducing metastatic potential resulting from immunosuppressive regimens following tumor resection. Ultimately, this work suggests a new approach of utilizing anesthetics for the development of supplemental anti-cancer therapies.

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