Electric fields impact cellular functions by activation of ion channels or by interfering with cell membrane integrity. Ion channels can regulate cell cycle and play a role in tumorigenesis. While the cell cycle may be directly altered by ion fluxes, exposure to direct electric current of sufficient intensity may decrease tumor burden by generating chemical products, including cytotoxic molecules or heat. We report that in the absence of thermal influences, low-frequency, low-intensity, alternating current (AC) directly affects cell proliferation without a significant deleterious contribution to cell survival. These effects were observed in normal human cells and in brain and prostate neoplasms, but not in lung cancer. The effects of AC stimulation required a permissive role for GIRK2 (or K(IR)3.2) potassium channels and were mimicked by raising extracellular potassium concentrations. Cell death could be achieved at higher AC frequencies (>75 Hz) or intensities (>8.5 microA); at lower frequencies/intensities, AC stimulation did not cause apoptotic cellular changes. Our findings implicate a role for transmembrane potassium fluxes via inward rectifier channels in the regulation of cell cycle. Brain stimulators currently used for the treatment of neurological disorders may thus also be used for the treatment of brain (or other) tumors.

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