# Hyperkalemic periodic paralysis M1592V mutation modifies activation in human skeletal muscle Na+ channel

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Mutations in the human skeletal muscle Na+ channel underlie the autosomal dominant disease hyperkalemic periodic paralysis (HPP). Muscle fibers from affected individuals exhibit sustained Na+ currents thought to depolarize the sarcolemma and thus inactivate normal Na+ channels. We expressed human wild-type or M1592V mutant ?-subunits with the ?- subunit in Xenopus laevis oocytes and recorded Na+ currents using two- electrode and cut-open oocyte voltage-clamp techniques. The most prominent functional difference between M1592V mutant and wild-type channels is a 5- to 10-mV shift in the hyperpolarized direction of the steady-state activation curve. The shift in the activation curve for the mutant results in a larger overlap with the inactivation curve than that observed for wild- type channels. Accordingly, the current through M1592V channels displays a larger noninactivating component than does that through wild-type channels at membrane potentials near -40 mV. The functional properties