The hereditary Long QT Syndrome (LQTS) is a familial disorder in which most affected family members have delayed ventricular repolarization manifest on the ECG as QT prolongation. Since 1995 when the first two genes responsible for LQTS were identified, molecular genetic studies have revealed a total of 12 genetic forms of congenital LQTS caused by mutations in genes involving potassium-channel proteins, sodium-channel proteins calcium-related channel factors, and a membrane-adapter protein. LQTS variant 3 (LQT3) is caused by mutations in SCN5A, the gene coding for the alpha subunit of the primary voltage-gated sodium channel in the heart, NaV1.5. SCN5A mutations that cause LQT3 in general disrupt Na+ channel inactivation thereby promoting a component of Na+ channel activity that persists during the plateau phase of the ventricular action potential, the cellular correlate to the QT interval of the ECG. LQT3 mutations confer distinct pharmacological properties on mutant Na+ channels which enables a mutation-specific approach to therapeutics. Here, in addition to discussing the biophysical consequences and pharmacological impact of specific LQT3 mutations, for the first time contributions of unique patient-specific complex genetics on therapeutic strategies will be discussed using cardiac myocytes derived from inducible pluripotent stem cells (iPS cells) derived from an LQT3 family.

**Keyword:** frontiers of channelopathy