One of the most puzzling questions surrounding the long QT syndrome (LQTS) concerns the reasons underlying the impressive phenotypic heterogeneity in the presence of the same genotype. Individuals who carry the same mutation often have strikingly different clinical manifestations, ranging between sudden death, syncope, and no events whatsoever. This difference is regarded as due to “modifier genes”, relatively common genetic variants able to interact either with the disease-causing mutation or with the substrate (e.g. action potential duration, autonomic nervous system, etc). Founder populations are ideal for the study of modifier genes because large numbers of carriers of the same mutation allow a powerful analysis aimed at the identification of “modifiers” capable of either increasing or decreasing risk. Probably, the LQTS founder population better characterized so far is the South African group of LQT1 families carriers of A341V mutation, which includes 26 families with over 500 members of whom over 200 are mutation carriers. All these individuals are descendants of a Dutchman, curiously by the name of Pieter Swart, who left the Netherlands for South Africa in 1690 and settled in the region around Cape Town. Studies in this population have already allowed the identification of common polymorphisms associated with a significantly higher risk for sudden cardiac death and, consequently, the establishment of a more aggressive preventive strategy.

Keywords: Long QT syndrome, genetics, founder population