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**Blockade of the HERG Human Cardiac K<sup>+</sup> Channel by the Antidepressant Drug Amitriptyline**

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Amitriptyline has been known to induce QT prolongation and ventricular arrhythmias such as torsades de pointes which causes sudden death. We studied the effects of amitriptyline on the human *ether-a-go-go*-related gene (*HERG*) channel expressed in *Xenopus* oocytes. Amitriptyline blocked HERG channels dose-dependently (IC<sub>50</sub> value of 5.51 mM). Block of HERG channel by amitriptyline was voltage and use dependent: exhibiting a higher degree of block at more positive voltages and much faster block at higher activation frequency. We concluded that amitriptyline is a potent blocker of HERG channels. This effect may account for the clinical occurrence of QT prolongation and ventricular arrhythmias observed with amitriptyline.