# Regulation of Cardiac Electrical Activity by Lysine Deacetylation

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The voltage gated cardiac $Na^+$ channel ($Na_v1.5$), encoded by the *SCN5A* gene, conducts the inward depolarizing cardiac $Na^+$ current ($I_{Na}$) and is vital for cardiac electrical activity. Inherited loss of function mutations in *SCN5A* are associated with cardiac conduction disorders. Here we show that the SIRTUIN1 lysine deacetylase (SIRT1) stimulates $I_{Na}$ and trafficking of $Na_v1.5$ to the plasma membrane via deacetylation of $Na_v1.5$ on lysine 1479 (K1479). Deficiency of cardiac SIRT1 in mice induces K1479 hyperacetylation on $Na_v1.5$, precipitates conduction abnormalities, phenocopies human cardiac arrhythmias associated with loss of function of $Na_v1.5$, and leads to premature death. Therefore, SIRT1-dependent dynamic lysine acetylation of $Na_v1.5$ governs $I_{Na}$, cardiac electrical activity, and cardiac rhythm.