Anterograde traffic of the Kv7.1/KCNE1 complex

P04-04

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The voltage-gated potassium channel Kv7.1 associates with the KCNE1 β-subunit to form the slowly activating delayed rectifying potassium current, IKs, which modulates the repolarization of cardiac action potential. Mutations in both subunits lead to severe cardiac channelopathies, such as long QT syndrome. Despite the functional effect of KCNE1 onto Kv7.1 and the subsequent specific interaction domains have been widely described, there is still an intense debate about where the assembly of the complex takes place. We demonstrate that Kv7.1-KCNE1 complex is not yet built within the initial stages of the secretory pathway, at the endoplasmic reticulum. Our results prove that both channel subunits can use different routes to reach the cell surface. While KCNE1 relays on COPII-dependent forward trafficking machinery, Kv7.1 can alternatively use a non-conventional secretory pathway that skips the Golgi apparatus. Once associated, Kv7.1 redirects KCNE1 to a COPII-independent route to the membrane surface. Finally, studies in plasma membrane lawn preparations demonstrate that the functional complex is fully assembled at the membrane surface, suggesting that Kv7.1-KCNE1 association takes place in an alternative route late in the secretory pathway.

Supported by MINECO (Spain) and FEDER (BFU2014-54928-R and BFU2015-70067-REDC)