Calcium transport by sarcoplasmic reticulum Ca2+-ATPase: stimulatory and inhibitory effects investigated on a solid supported membrane

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The sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA) belongs to the P-type ATPase family of membrane transporters. In muscle cells SERCA couples ATP hydrolysis to the transport of two Ca^{2+} ions against their electrochemical gradient from the cytoplasm into the lumen of the sarcoplasmic reticulum (SR), thus promoting muscle cell relaxation. SERCA maintains a low cytoplasmic Ca^{2+} concentration and contributes to intracellular calcium homeostasis which is essential for cell signaling and survival. SERCA dysfunction has been related to several pathologies, such as cardiovascular diseases, diabetes and cancer. Thus, SERCA represents an important target for the development of novel therapeutic compounds. A bioelectrochemical approach based on a solid supported membrane (SSM), which consists of a gold-supported hybrid alkanethiol/phospholipid bilayer, was used to investigate the transport activity of SERCA. SR vesicles containing SERCA were adsorbed on the SSM and were activated by an ATP concentration jump. Following SERCA activation, an electrical current was detected which was attributed to movement of Ca^{2+} ions across the vesicular membrane. We used the SSM method to characterize the effects of different compounds, e.g. natural products or compounds of synthetic origin, on SERCA activity. Our results indicated that such compounds affect Ca^{2+} transport by SERCA and behave like activators or inhibitors of the SERCA enzyme. In particular, we examined the effect of a novel photoactivable ruthenium complex, which can be used as a molecular photosensitizer in photodynamic therapy. We found that photoactivation of the ruthenium complex induced the synthesis of the potent singlet oxygen which markedly affected SERCA transport activity with an inhibitory effect dependent on the duration of light exposure.

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