Synthesis of novel probes based on GSK7975A to study SOCE

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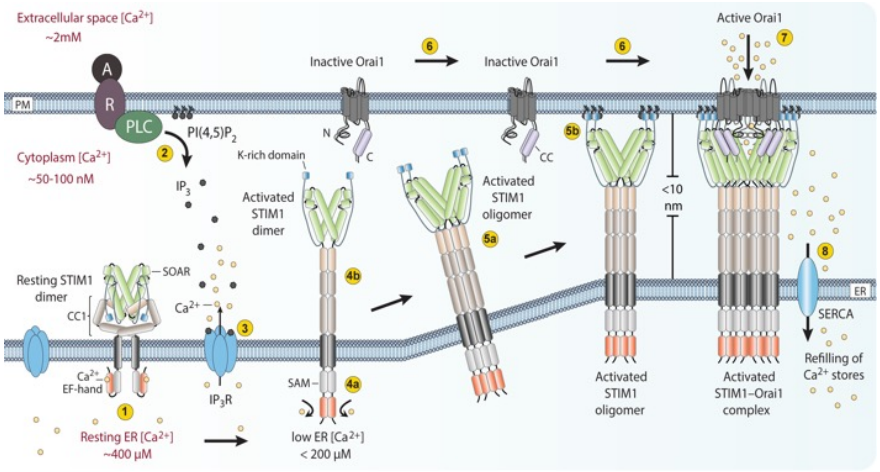
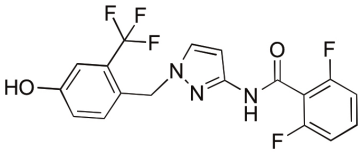
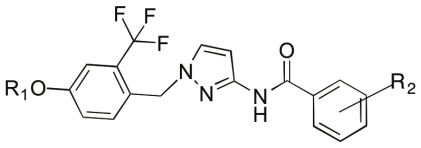
A wide array of physiological functions including cell differentiation, proliferation, muscle contraction, neurotransmission and fertilization are regulated by calcium cations. Ca^{2+} signaling pathways that induce endoplasmic reticulum store depletion trigger a refilling process known as store operated Ca^{2+} entry (SOCE). Enhanced SOCE has been associated with severe diseases such as several types of cancer (e.g. breast, prostate). Deficiency of SOCE has been related to immunodeficiency and autoimmune diseases.



To provide a better understanding of the process of SOCE and the proteins involved (i.e. Orai, STIM), we synthesized novel probes based on the known SOCE-inhibitor GSK7975A. This class of inhibitors feature two functionalities: a photo-crosslinking moiety for covalent target modification as well as a handle for bioorthogonal chemical modifications. Herein, we present the synthesis of these novel probes and their preliminary biological assessment.

GSK7975A



Novel probes featuring additional functionalities