Fluorogenic Probe for Removal of Endoplasmic Reticulum Stress

Ardra M. S., Kaushik Pal and Apurba L. Koner*
Department of Chemistry, IISER Bhopal, Madhya Pradesh, INDIA
(E-mail: akoner@iiserb.ac.in)

Abstract:
Endoplasmic reticulum (ER), an organelle present in eukaryotic cells performs the important function of protein folding. All proteins that transit the secretory pathway first enter into ER where they fold and assemble into multi-subunit complexes before they are modified in Golgi apparatus and transported to their destined sites.[1] While performing the above-mentioned functions, certain environment and genetic factors disrupt ER function and causes accumulation of misfolded and unfolded proteins in the ER lumen.[2] This condition is termed ER stress. Stress can occur either due to the internally generated redox-active small molecules like Reactive Oxygen Species (ROS) or molecules that come in as an environmental pollutant like formaldehyde (FA). Under stressed condition ER could end up with some severe adverse effects on regulated cellular machinery.[3]

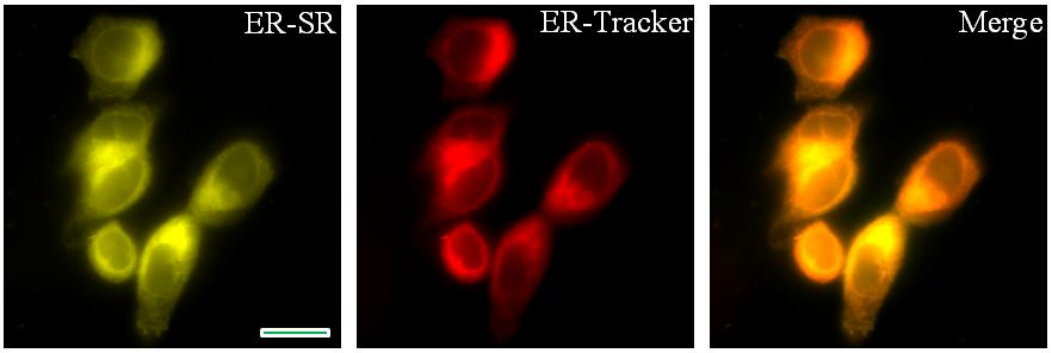

Figure 1: Showing selective accumulation of the probe inside ER confirmed by colocalization with ER-Tracker dye (scale bar-20 μm).

We have synthesized a napthalamide-based fluorescent probe that can selectively target ER and remove the stress from it. The probe is synthesized with a reactive functionality to consume the stress inducing agents like FA and ROS thereby curtailing the stress caused to the ER. The probe contains three segments, fluorogenic reporter, directing moiety and reaction site. The fluorogenic behaviour appears due to the possibility of photo-induced electron transfer which disappears after reaction with FA and ROS like OH, *tert*-butoxyl radical. We have validated the selectivity of the probe towards ER using fluorescence colocalization microscopy. Further, the stress removing ability was investigated against FA and *tert*-butoxyl radical in three different types of cancer cell lines *e.g.*, HeLa, MCF7 and HEK293.

References:

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3. Oslowski C. M.. and Urano F., *Methods Enzymol.*, **2011**, 490, 71–92.