A genetically encoded bioluminescent copper sensor for imaging the intracellular dynamics

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Copper is an essential micronutrient acting as a co-factor for enzymes in many cellular processes. Due to the high exposure of copper ions (Cu^{2+}) associated with the formation of reactive oxygen species (ROS) and leads to several diseases such as kidney failure, gastrointestinal disease, Menkes syndrome, Wilson's disease, amyotrophic lateral sclerosis (ALS), Parkinson's and Alzheimer's disease. In addition, it is reported that the free copper absents inside cells, a network of proteins has evolved to labile of the intracellular copper pool.[1] The dynamics and distribution of copper ions in cells can be studied with an appropriate detection system. Although, the analytical analysis based techniques such as plasma mass spectrometry (ICP-MS) and atomic absorption spectrometry (AAS) have been developed for Cu^{2+} detection.[1-2] Those techniques are complicated and required sophisticated skills for operation. Fluorescent protein-based indicators have proven an essential part of the molecular biology toolbox. This technique requires an external illumination that allows photobleaching, phototoxicity and auto-fluorescence from the specimen in cellular imaging. On the other hand, bioluminescent protein, such as luciferase don't require excitation light that offers minimal phototoxicity and allowing high signal detection with better depths in tissues. Herein, we report a genetically encoded bioluminescent Cu^{2+} sensor which is only sensitive to the concentration changes of Cu^{2+} and enable to visualize the uptake of Cu^{2+} in cells with a nanomolar affinity (K_d = 786nM). Our indicator shows acid tolerance properties which contribute the Cu^{2+} imaging in acidic cellular compartments.

Reference

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