Endoplasmic Reticulum-Localized Iridium(III) Complexes as Efficient Photodynamic Therapy Agents via Protein Modifications

Jung Seung Nam[1], Myeong-Gyun Kang[1], Juhye Kang[1], Sun-Young Park[2], Hyun-Tak Kim[1], Shin Jung C. Lee[1], Jeong Kon Seo[2], Oh-Hoon Kwon[1,2], Mi Hee Lim[1,*], Hyun-Woo Rhee[1,*] and Tae-Hyuk Kwon[1,*]

[1] Department of Chemistry, Ulsan National Institute of Science and Technology (UNIST), Ulsan 44919, Republic of Korea

[2]Center for Soft and Living Matter, Institute for Basic Science (IBS), Ulsan 44919, Republic of Korea

[3]UNIST Central Research Facility, Ulsan National Institute of Science and Technology (UNIST), Ulsan 44919, Republic of Korea

E-mail: j.s.nam@unist.ac.kr

Protein inactivation by reactive oxygen species (ROS) such as singlet oxygen ($^1O_2$) and superoxide radical ($O_2^{\bullet-}$) is considered to trigger cell death pathways associated with protein dysfunction[1-2]; however, the detailed mechanisms and direct involvement in photodynamic therapy (PDT) have not been revealed. Herein, we report Ir(III) complexes designed for ROS generation through a rational strategy to investigate protein modifications by ROS. The Ir(III) complexes are effective as PDT agents at low concentrations with low-energy irradiation ($\leq$ 1 J cm^{-2}) because of the relatively high $^1O_2$ quantum yield (> 0.78), even with two-photon activation. Furthermore, two types of protein modifications (protein oxidation and photo-cross-linking) involved in PDT were characterized by mass spectrometry. These modifications were generated primarily in the endoplasmic reticulum and mitochondria, producing a significant effect for cancer cell death. Consequently, we present a plausible biologically applicable PDT modality that utilizes rationally designed photoactivatable Ir(III) complexes.[3]

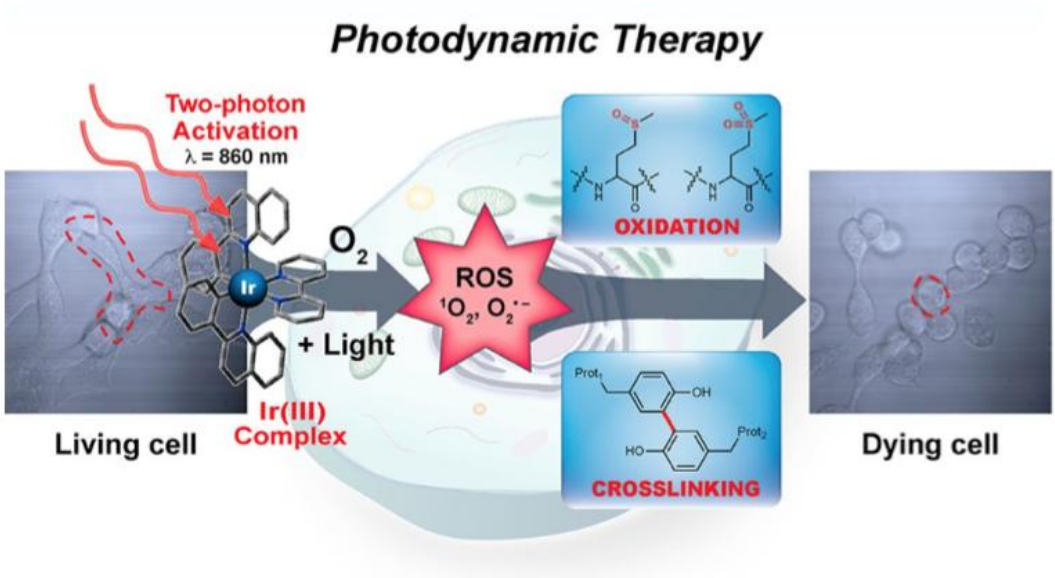

Figure 1. Schematic illustration of cancer cell death pathway by photo-activation of Ir(III) complex: oxidation and cross-linking

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