

Iridium(III) Complexes as Efficient Photodynamic Therapy Agents via Protein Modifications

Jung Seung Nam¹, Myeong-Gyun Kang¹, Juhye Kang¹, 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

E-mail: kwon90@unist.ac.kr

Iridium complexes have a great attention in biosensors, bioimaging and photodynamic reagents because of their several advantages, such as easy color tuning, photostability, long lifetime (μs), and efficient singlet oxygen generation in hypoxia condition. Protein inactivation by reactive oxygen species (ROS) is considered to trigger cell death pathways associated with protein dysfunction; however, the detailed mechanisms and direct involvement in photodynamic therapy (PDT) have not been revealed. Thereby, we report herein Ir(III) complexes designed for ROS generation through a rational strategy to investigate protein modifications by ROS. The Ir(III) complexes were effective as PDT agents with low-energy irradiation because of the relatively high $^1\text{O}_2$ quantum yield, even with two-photon activation. In addition, two types of protein modifications (protein oxidation and photo-crosslinking) involved in PDT were characterized by mass spectrometry. Consequently, we present a plausible PDT modality that utilizes photo-activation of rationally designed Ir(III) complexes, indicating the feasibility of a better optimized Ir(III) complex for PDT^[1].

Furthermore, we report an Ir(III) complex, Ir-1, as a chemical tool for oxidation of amyloidogenic peptides which are related with Alzheimer's disease, upon photoactivation and subsequently modulation of their aggregation pathways. Our studies of Ir-1 demonstrate the next-generation of chemical tools for understanding their fundamental characteristics at a molecular level.^[2]

Funding: This research was supported by the Ulsan National Institute of Science and Technology research fund (1.150117.01 to T.-H.K. and H.-W.R and 1.140101.01 and 1.160001.01 to T.-H.K., H.-W.R., and M.H.L.).

Acknowledgement: I would like to appreciate my group members and collaborators.

References:

- [1] J. S. Nam, M.-G. Kang, J. Kang, S.-Y. Park, S. J. C. Lee, H.-T. Kim, J. K. Seo, O.-H. Kwon, M. H. Lim, H.-W. Rhee, T.-H. Kwon, *J. Am. Chem. Soc.* **2016**, *138*, 10968-10977.
- [2] J. Kang, S. J. C. Lee, J. S. Nam, H. J. Lee, M. G. Kang, K. J. Korshavn, H. T. Kim, J. Cho, A. Ramamoorthy, H. W. Rhee, T.-H. Kwon, M. H. Lim, *Chem. Eur. J.* **2017**, *23*, 1645 -1653.

