Matrix Metalloproteinase-responsive Iridium(III)-based Hydrogels for Tumor Cell-specific Imaging, Anti-metastasis, and Lysosome-targeted Photodynamic Therapy

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Many cancer cells have elevated matrix metalloproteinases (MMPs) levels, which are closely implicated in tumor growth and invasion. The most common MMP-related anticancer approach was the development of MMP-sensitive materials for stimuli-responsive drug release. Herein, we report the synthesis and characterization of MMP-sensitive iridium(III)-based PEG-peptide hydrogels through the inverse electron-demand Diels–Alder (IEDDA) reaction of a PEG polymer bearing four tetrazine units with an MMP-sensitive peptide containing two bicyclo[6.1.0]nonyne units in both ends and an iridium(III) *bis*-tetrazine complex [Ir(dptz)$_2$(Ph$_2$-phen)](Cl) (Hdptz = 3,6-diphenyl-1,2,4,5-tetrazine, Ph$_2$-phen = 4,7-diphenyl-1,10-phenanthroline). Upon degradation of the hydrogels by the MMPs excreted from the cancer cells, the iridium(III) complex fragments were subsequently released. Their (photo)cytotoxic effect on cancer cells and inhibition effects on cell migration and invasion were studied using laser-scanning confocal microscopy.

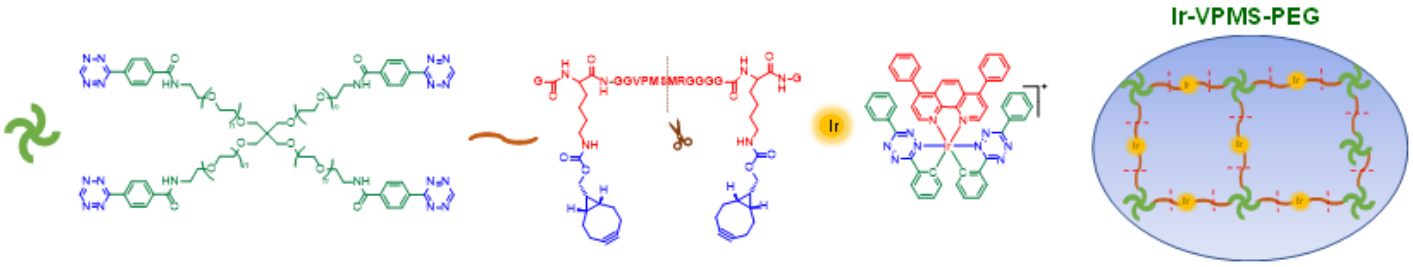

Figure 1. Structure of the hydrogels Ir-VPMS-PEG.

We thank the Hong Kong Research Grants Council (CityU 11302820) for financial support. We also thank the funding support from “Laboratory for Synthetic Chemistry and Chemical Biology” under the Health@innoHK Program launched by Innovation and Technology Commission, The Government of Hong Kong S.A.R, P.R. China.

References

[1] A. M.-H. Yip, C. K.-H. Lai, K. S.-M. Yiu, K. K.-W. Lo, *Angew. Chem. Int. Ed.* **2022**, *61* (16), e202116078, DOI: 10.1002/anie.202116078