

DOCTORAL THESIS

Luminescent bioprobes for imaging and inhibition of EBV associated cancers

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ABSTRACT

The high incidence rate of Nasopharyngeal Carcinoma (NPC) in southern China, including Hong Kong, has attracted worldwide attention. According to the Center for Health Protection in Hong Kong, there were 841 new cases of NPC, with 655 cases of males and 186 cases of females in 2013. The development of NPC is highly associated with the infection of one human herpes virus, the Epstein-Barr virus (EBV). Given that the homodimerization of one of the EBV endogenous protein-Epstein-Barr Nuclear Antigen 1 (EBNA1) is essential for both viral genome maintenance and infected-cell survival, thus the interference of EBNA1 homodimerization would be a novel strategy for the inhibition of EBV-positive tumours. In this thesis we devote to conjugate several kinds of organic fluorophores with various EBV-specific peptides in order to achieve the highly responsive and selective imaging, as well as the effective inhibition of EBV-positive tumours *in vitro* and *in vivo*. The first research focused on the conjugation of a styrene pyridine fluorophore with two EBNA1-specific peptides, aiming to develop a dual-probe for the imaging and inhibition of EBV-positive tumour cells. Then we tried to introduce a Nuclear Localization Sequence into the EBNA1-specific peptide, and used an Intra-molecular Charge Transfer characterized fluorophore for the following second research, it showed an impressively responsive signal when the probe binds with EBNA1 both *in vitro* and *in vivo*, more importantly, only 4 μg probe can inhibit 92.8% of growth inhibition of an EBV-positive tumour. Along this line, our last research centred on the further improvement of the imaging by taking advantage of lanthanide.

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