A highly selective ratiometric two-photon fluorescent probe for human cytochrome P450 1A

With the support by the National Natural Science Foundation of China and National Science & Technology Major Projects of China, members in Prof. Yang Ling's (**杨凌**) group cooperated with Prof. Cui Jing-Nan (**崔京南**) from the State Key Laboratory of Fine Chemicals, Dalian University of Technology, have designed and developed a new highly selective fluorescent probe for human cytochrome P450 1A. The related results were recently published online as a full article entitled "A highly selective ratiometric two-photon fluorescent probe for human cytochrome P450 1A" in *Journal of the American Chemical Society* (2015, 137 (45): 14488—14495).

Cytochrome P450 1A (CYP1A), one of the most important phase I drug-metabolizing enzymes in humans, plays an important role in metabolism of therapeutic drugs and activation of environmental contaminants or other xenobiotics to their ultimate carcinogens. A highly selective and sensitive probe for real-time monitoring of CYP1A activity in biological systems will be very helpful to evaluating the individual variations in CYP1A-involved drug disposition and to identifying the potential abnormalities of this key enzyme. This probe (NCMN) was designed on the basis of 3D structural information and the key amino acids in active cavity of CYP1A. To achieve a highly sensitive and selective probe for CYP1A, a series of 1,8-naphthalimide derivatives were synthesized and used to explore the potential structure-selectivity relationship. NCMN has been successfully used for two-photon imaging of intracellular CYP1A in living cells and tissues, and showed high ratiometric imaging resolution and deep-tissue imaging depth. All results suggested that NCMN could serve as a promising tool for exploring the biological functions of CYP1A in xenobiotics metabolism and toxicological related fields. Furthermore, the strategies employed in the design and optimization of this probe shed new lights on the development of other specific probes for a given drug-metabolizing enzyme.

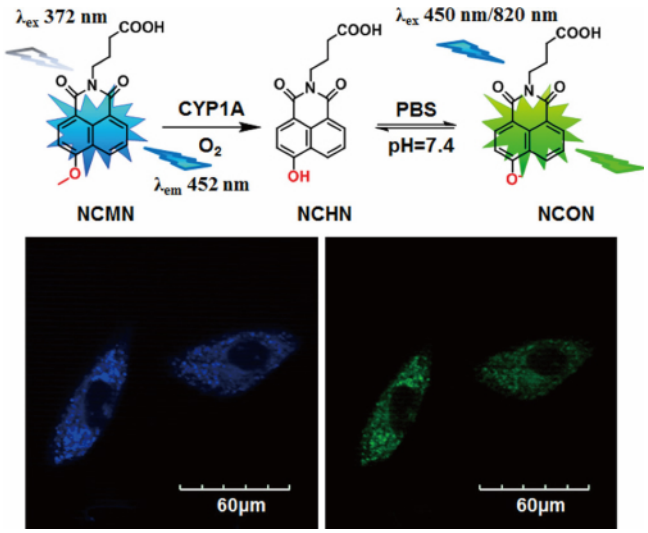

Figure NCMN and its fluorescence response towards CYP1A and fluorescence images of A549 cells.