Development of Near-infrared Fluorescent Probes for *In Vivo* Imaging

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The number of reports on new techniques in molecular imaging has been recently increasing because of their usefulness in biological, medical, and clinical research. Fluorescence imaging methods are generally superior in terms of sensitivity, selectivity and ease of use. Cyanine dyes have been employed as fluorescent labels in fluorescence imaging studies of biological mechanisms. In particular, tricarbocyanines have the advantage that light at their emission and absorption maxima in the near-infrared (NIR) region around 650-900 nm is relatively poorly absorbed by biomolecules, and so can penetrate deeply into tissues. There is also less autofluorescence in this region. In addition to cyanine dyes for straightforward fluorescence labeling, we successfully developed cyanine dyes whose fluorescence intensity changes upon specific reaction with nitric oxide, which is an important signaling molecule involved in the regulation of a wide range of physiological and pathophysiological mechanisms, and many disorders.

Then, we synthesized dipicolylcyanine (DIPCY), consisting of tricarbocyanine as a fluorophore and dipicolylethylenediamine as a heavy metal chelator, and investigated its response to various heavy metal ions. Upon addition of zinc ion, a red shift of the absorbance maximum was observed. Namely, DIPCY can work as a ratiometric fluorescent sensor for zinc ion in the NIR region.

Moreover, we have recently developed several pH probes based on the amine-substituted tricarbocyanine fluorophore. We could measure pH with these fluorescent probes by a ratiometric monitoring method.