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Authors	Malray, Jordan L
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Synthesis of Near-infrared Heptamethine Cyanine Dyes as Biological Imaging Agents

Jordan L. Malray², Eric Owens¹, Phong Nguyen¹, Quoc Bao Nguyen¹, La'Tranese Sapp², Maged Henary*¹

¹Georgia State University, Department of Chemistry, Petit Science Center, 100 Piedmont Ave., Atlanta, GA 30303, USA

²Georgia State University, Department of Biology, Petit Science Center, 100 Piedmont Ave., Atlanta, GA 30303, USA

Abstract

NIR polymethine cyanine dyes exhibit long wavelengths that cannot be detected by the naked eye, whereas normal biological tissues fluoresce in the visible region of the electromagnetic spectrum. Using FLARE (Fluorescence-Assisted Resection and Exploration) imaging technology, both visible and NIR light can now be superimposed and visualized simultaneously. This technology has increased research in the field of biological contrast imaging agents. Polymethine cyanine dyes have shown specificity for certain cell types, while leaving the cells of neighboring tissues unaffected. The NIR properties of these dyes allow surgeons to differentiate cell types, thus the surgeon can avoid or target such tissues. The number of carbons and functional groups on the polymethine cyanine dye can alter its λ_{MAX} and distribution coefficient, manipulating the fluorescence of the dye and where it will bind in the body. In this experiment four near-infrared (NIR) heptamethine cyanine dyes were synthesized using a multi-step synthetic approach. *In vivo* testing at Harvard Medical College revealed these four dyes exhibited interesting binding in the vasculature of the brain, with dye JM-1 displaying the most intensity. Synthesis, purification, characterization, and *in vivo* test results of the four dyes will be discussed.