

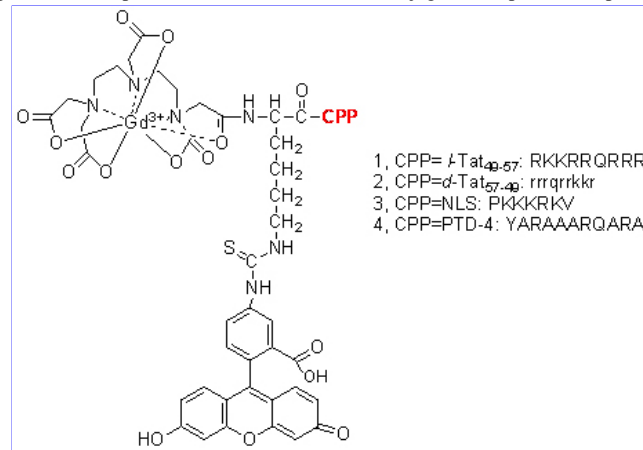
Preparation, Characterization and Visualization of CPP-Mediated MR Contrast Agents

Category: Multifunctional probes

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Recent developments in MR imaging have enabled in vivo imaging at near microscopic resolution. In order to visualize and track cells by MR imaging, it is necessary to tag cells magnetically. Cell-penetrating peptides (CPPs) have been used as an efficient way of internalizing a number of marker proteins into cells. Here we describe the synthesis and testing of a series of bi-labeled (magnetic and fluorescent) Gd(III)-based MR contrast agents conjugated to fluorescent dye and CPPs, including *l*-Tat₄₉₋₅₇, *d*-Tat₅₇₋₄₉, PTD-4 and NLS (Fig. 1). The CPP fragments were synthesized by solid phase with the Fmoc (9-fluorenylmethoxycarbonyl) mediated scheme. FITC (fluorescein isothiocyanate) was coupled to Fmoc-lysine at first. Then FITC-Fmoc-lysine and diethylenetriaminepenta-acetic dianhydride (DTPA dianhydride) were coupled to CPPs, respectively. Finally the conjugates were chelated with Gd³⁺. The products were purified by reversed-phase HPLC and characterized by ESI-MS. Cellular uptake of these agents were confirmed by fluorescent microscopy and spectroscopy, as well as by T1 and T2 MR analysis of the Gd(III) agents in NIH 3T3 fibroblasts. Further optical and MR evaluation is under progress. The comparison of these different CPP conjugates can provide helpful



data for the design of new intracellular MR contrast agents for in vivo tracking of cells.