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Design and synthesis of 8-hydroxyquinoline derivatives for the diagnosis and treatment of cancer

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8-Hydroxyquinoline (8HQ or oxine) and its derivatives are potent metal chelating agents and often used as fluorescence sensors of Zn^{2+} and other metal cations. Recently, 8HQ have also been proposed as potential candidates for enzyme inhibitors and drugs to treat cancer, HIV, neurodegenerative diseases, and so on. In this paper, we present (i) the design and synthesis of 8HQ-based radioprotective agents for radiation therapy and (ii) the application of the photochemical cleavage reaction of 8-quinolinyl sulfonates (8QS) to the isolation of intact ligand-receptor complexes or living target cells. (i) In radiation therapy, adverse side effects are often induced due to the apoptosis that occurs in radiosensitive normal cell mainly caused by apoptosis-induction by the p53 protein. Therefore, radioprotective drugs that can protect normal cells from radiation by temporary inhibition of p53 functions are highly desirable. We have screened some zinc (II) chelators for the inhibition of radiation-induced p53-dependent apoptosis in MOLT-4 cells and found that *N,N'*-bis(2-pyridylmethyl)-1,2-ethanediamine and some 8HQ derivatives have the potent radioprotective activity, accompanied by a low cytotoxicity. (ii) We previously discovered the photochemical S-O bond cleavage reactions of 8QS in aqueous solution at neutral pH. Its application to QS-based photocleavable biotin-linkers for the isolation and recovery of the intact ligand-receptor complexes or living cells such as specific tumor cells will be presented.

Biography

Shin Aoki graduated from the University of Tokyo and received PhD from the same University in 1992. After working as an Assistant Professor at the University of Tokyo, a Postdoc at the Scripps Research Institute, USA and an Assistant Professor in Hiroshima University, he became a Professor at the Faculty of Pharmaceutical Sciences, Tokyo University of Science in 2003. He is a recipient of several awards including the Pharmaceutical Society of Japan Award for Young Scientists (2002). His research interests include bioorganic chemistry, supramolecular chemistry, photochemistry, and medicinal chemistry.

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