

FRAP AND CONFOCAL IMAGING STUDIES OF THE INFLUENCE OF DNA-BINDING DRUGS ON INTERACTIONS BETWEEN DNA AND HISTONES

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DNA-binding dyes are useful in contrasting cell nuclei and chromatin for live cell fluorescence microscopy; however, they may interfere with nuclear and DNA structure and function. We investigated the influence exerted by two DNA dyes on chromatin and nuclear structure, as well as histone–DNA interactions in live HeLa cells. A membrane permeant fluorescent DNA intercalator DRAQ5 (anthracycline derivative), at a concentration of 1 μM , caused microscopically detectable changes of nuclear architecture. Following DRAQ5 intercalation into DNA, chromatin aggregated into distinct areas and foci. The loss of 3D chromatin distribution was exerted via interference with a dynamic exchange of a linker histone (H1), which is a known chromatin stabilizing factor. At higher concentrations (3 and 7.5 μM), DRAQ5 interfered with binding of H2B core histones to DNA. Similar effects resulted from intercalation of chemotherapeutic drugs, adriamycin and daunomycin, but were not observed after binding to DNA of a minor groove binder, Syto17.