Structural Studies on Acridine Derivatives Binding to Telomeric DNA

Shirley Miles[a,b], Susana Teixeira[a,b], Yu Gan[c], William Denny[d], Chris Cardin[c], Trevor Forsyth[a,b], *[a]I.L.L., Grenoble, France. [b]Keele University, UK. [c]School of Chemistry, Reading, UK. [d]Aukland Cancer Society Research Center, Aukland, New Zealand.* E-mail: miles@ill.fr

Acridine derivatives are known to inhibit a variety of nuclear enzymes, such as topoisomerases and telomerases, by binding or intercalating to DNA. This class of compounds is of great interest in the development of novel anticancer agents, some of which are currently under clinical trial [1, 2].

Despite the obvious pharmaceutical interest and recent successes in determining the crystal structure of some of the compounds complexed with DNA [1,2,3], a lot is still unknown about the mechanisms of action, binding preferences and biological targets.

In this study a variety of techniques is employed to investigate the binding behaviour of a selection of drugs to DNA. Fiber diffraction is used to obtain information about sequence preferences and to analyze structural changes in the DNA upon drug binding using a continuous polymer. Data is usually obtained at lower resolution and complements crystal diffraction studies. Crystal diffraction is then used to analyze DNA-drug complexes in oligonucleotides at high resolution. With the information gained, neutron diffraction studies are planned to analyze the hydrogen bonding patterns of the DNA-drug complexes.

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