

5. OBJECTIVES OF THIS WORK

In this work, the response of colon carcinoma cell lines to UCN-01 or to CPT-11 was analysed. In particular, we wished to clarify the role of p53 or hMLH1 proteins in the response to these chemotherapeutic agents. This was accomplished by comparing isogenic or nearly isogenic colorectal cell lines differing in the presence/absence of the p53 or hMLH1 proteins.

Mainly two parameters were used to compare the effects of UCN-01 or CPT-11 in p53- or hMLH1-proficient cell lines *versus* p53- or hMLH1-deficient cell lines: Cell cycle arrest and apoptosis. They represent the most common cellular responses to chemotherapeutic treatment and influence the treatment outcome. Further, expression levels of proteins and activities of enzymes known to be involved in cell cycle arrest or apoptosis were systematically analysed. This allowed further elucidation of p53- or hMLH1-dependent response pathways to treatment with UCN-01 or CPT-11.