Maga research activity

Enzymology of DNA replication
We are interested in understanding the complex relationships between the DNA synthetic machinery (replisome) and other aspects of cell metabolism such as DNA repair, DNA damage tolerance and cell cycle regulation. We focus our attention on the specialized human DNA polymerases beta, lambda, Tdt and eta, characterizing how they cope with DNA lesions such as abasic sites and 8-oxo-dG. More recently we are addressing how these specialized DNA polymerases influence the accumulation of ribonucleotides in the genome and their subsequent removal.

Novel antiviral strategies against HCV/HIV/Influenza infections. We are studying the replication machinery of the HCV virus with the aim of finding novel valuable targets for chemotherapy. We have already identified a potent non-nucleosidic inhibitor of the helicase activity of the viral protein NS3. We are also interested in exploiting the host-virus relationships in the case of HIV infection, in order to find alternative strategies for antiviral treatment. We are currently focusing on the cellular protein DDX3, an RNA helicase, and we have shown that its inhibition blocks the replication of several RNA viruses. We are also characterizing the cellular interactors of the protein NS1 of the avian and human influenza A virus.

HIV drug resistance. Current anti-HIV drugs targeted to the reverse transcriptase are severly limited by the development of drug resistance. We are currently undertaking a sytematic evaluation of the impact of drug resistance mutations in the viral RT on the viral fitness and drug sensitivity. We clone multi-resistant HIV-1 RTs from clinical isolates coming from AIDS patients failing therapy, express and purify the recombinant enzymes and evaluate their enzymological parameters. With this approach we already identified uncommon inter-class drug resistance patterns for mutations such as Y181I/C, Q145M, G190S, T215Y.

Novel targets for anticancer chemotherapy. We are exploiting a number of enzymes as targets for cancer therapy. We are currently focusing on the human terminal transferases TDT and DNA polymerase λ as poential targets for treating leukemias and on tyrosine kinases such as FAK, Src-family and Abl, as targets for treatment of different type of tumors. We have already identified a number of active compounds targeting each of these enzymes