Il minicorso si propone di stimolare i dottorandi alla conoscenza di ricerche recenti che vedono DNA ed RNA in conformazione di quadruplesso come potenziale target per agenti bioattivi di interesse farmaceutico sia in campo antineoplastico che antivirale.
DNA G-quadruplexes: moving toward a holistic view

The involvement of G-quadruplexes (G4s) in the epigenetic regulation of viral genomes has been recently established: in particular, G4s in the human immunodeficiency virus (HIV) and herpes simplex virus (HSV) have been thoroughly studied. The presence of G4s in these viral genomes, G4 function and interaction with proteins, G4 visualization in cells and targeting by small molecules have clearly emerged. All these data indicate the fine regulatory role of viral G4s and the possibility to target viral features currently unavailable to existing drugs.

In silico investigation of G-quadruplexes as non-canonical nucleic structures

In the last decade, it has been well demonstrated that, in addition to the familiar duplex, certain DNA sequences can fold into a four-stranded secondary structure called “G-quadruplex” (G4), localized at the telomeric ends of chromosomes and in other important areas of human genome, such as oncogenes. Stabilization of G4 architecture by small molecules is emerging as a potential anticancer approach. A remarkable effort in this sense has been given by experimental evidences, such as NMR and X-Ray G4 structures deposited in the Protein Data Bank, that have allowed the application of both traditional and enhanced in silico approaches in order to speed up the discovery of new more selective stabilizing agents.

Chemically Engineered Ligands and Probes Targeting Quadruplex Nucleic Acids.

The design, synthesis and performance of functional quadruplex ligands with a dual binding mode (non-covalent and covalent) and light up upon binding is described, compared, and related to the state of the art in the field. The covalent targeting is achievable in a fully controllable manner by external stimuli (i.e.: reduction, acid-base catalysis and irradiation). The fluorescent detection of quadruplex exhibiting different topologies by multi-chromophoric dyes is very effective and selective. Several potential useful applications, including quadruplex fluorescence tagging and “pull-down” are addressed.