**Training objectives**

To make students aware of the role in diseases of DNA damage and DNA damage response, altered RNA transcription and mRNA maturation and translation, altered post-translational modification and folding of proteins and altered structure/function of proteins.

The knowledge of diagnostic approaches and biotechnology applications at the molecular level are major objectives.

When approaching a disease model at the end of the course, students should be able to identify the above mentioned elements as well as the procedures needed to analyze at the molecular and cellular levels the structural and functional defects responsible for tissue and organ damage.

**Prerequisites**

Students should have basic knowledge and abilities in Biochemistry, Molecular Biology, Genetics and General Pathology to understand molecular mechanisms responsible for increased risk, onset and progression of diseases, and to learn about improved diagnosis and innovative therapeutic approaches.

**Course programme**

The course includes two theoretical blocks and seminar activities.

Theoretic modules:

1. Molecular characterization of diseases to understand physio-pathologic expression of RNA and proteins, and to identify elements for improved diagnosis and innovative therapeutic approaches.

***Lecture themes- 2016***

**Chromosome telomeres**\* and telomere- associated disease. Telomere structure and complexes. Telomere chromatin and chromatin modification – SIRT6- Telomere replication and protection- Telomere alteration and Cancer- Aging and telomere length. Mutations in telomere complex genes and disease. Telomerase therapy- models. Extra-telomere function of telomerase.

**Transposons** and Mobile Elements - L1 ORFs structure and function-Transposon Assays and Vectors- Transposon L1 and Cancer- Transposon Inhibition- methylation and chromatin modification. PiRNA pathway(s). Infertility and transposon inhibition.

**X chromosome Inactivation** - XIST structure and function, TSIX, XACT, lncRNAs, chromosome and chromatin structure and gene expression

**Oxygen sensing**- Hif, structure, function and degradation. Hypoxia responsive elements, HRE. Cancer related mutations in Hif 1alpha and Hif 2alpha. Proline hydroxylation, PHD. VHL and ubiquitination. CRISPR-Cas9 library. VHL inhibition and mitochondrial dysfunction. VHL ko, zebrafish. VHL loss and cancer. Treatment models, pharmacological VHL inhibition. Polycythemia, molecular bases. Epo, structure and function. Recombinant Epo and Epo mimetics, peptides and antibodies. Tissue protective peptides.

**Neonatal Fc receptor and protein half-life extension**- biology and biotechnology – extending protein half-life in plasma, fusion technology, fusion to albumin, improved half-life of IgG (Jan Terje Andersen)

**Pre-mRNA splicing** - biology and pathology. Spliceosome- Molecular bases of exon skipping –Splicing factors (Lectures given by Francisco Baralle)

**Hemorrhagic and thrombotic diseases**- **(Caterina Casari)** Molecular bases, cellular and animal models of Von Willebrand Disease

2. **Gender Medicine (Cristina Tarabbia):**

Epidemiology and disease gender differences

Biological bases of Differences, cellular differences, epigenetic components

**Didactic methods**

The theoretical parts are organized in frontal lessons (molecular bases and gender medicine for about 40 hours) and seminar activities (about 12 hours delivered by invited experts).

**Learning assessment procedures**

1. In general, evaluation of the capacity to integrate the information provided in the course (written). A few (3-4), ample questions, including experimental aspects, will be introduced and administered. Oral exams will be available on request.

**Reference texts**

* Slides provided during the course
* Internet sites (NCBI, KEGG…)
* Textbooks of Biochemistry/Molecular biology as well as Biology/Genetics/ /Molecular pathology