**Immagine che contiene testo

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**Dottorato di ricerca in**

**Medicina Molecolare e Biotecnologie Mediche**

**Advanced courses**

***“Innovative approaches to integrate disease diagnosis”***

**Overview of the course**

Diagnosis of different diseases is usually made by the integrated evaluation of clinical, biochemical, and genetic data. For inherited diseases the genetic screening is essential for diagnosis confirmation and to extend the diagnosis to the other family members. Genetic analyses can integrate the diagnosis also of non-inherited diseases, but research activity is essential to improve interpretation of genetic data. Besides the diagnosis, several innovative laboratory investigations can provide additional data for prognostic evaluations useful for patient management.

The course will cover three examples in which innovative molecular approaches can improve disease diagnosis and/or prognostic evaluation of different diseases.

**Schedule (~6 hours)**

The course will include three lessons (2 hours each), as follows.

**Program**

**Lesson one (*prof.* *Giulia Frisso*): 13, November 2023, 14:30.**

Seminar room 4th floor Torre Biologica

Title: *Digenic inheritances in rare diseases: a possible non-Mendelian disease transmission*

Digenic inheritance (DI) is a mechanism that occurs when the interaction of two genes is required for the expression of a phenotype. Mutations in at least one copy of each gene are required for the expression of a phenotype and may be the cause of the onset of a rare disease. The lesson will address the possibility of digenic transmission in some hereditary metabolic diseases and try to elucidate the mechanisms that can justify the DI.

1. Schäffer AA. Digenic inheritance in medical genetics. J Med Genet. 2013 Oct;50(10):641-52. doi: 10.1136/jmedgenet-2013-101713. Epub 2013 Jun 19.
2. Okazaki A, Ott J. Machine learning approaches to explore digenic inheritance. Trends Genet. 2022 Oct;38(10):1013-1018. doi: 10.1016/j.tig.2022.04.009. Epub 2022 May 14.
3. Deltas C. Digenic inheritance and genetic modifiers. Clin Genet. 2018 Mar;93(3):429-438. doi: 10.1111/cge.13150. Epub 2018 Jan 25.

**Lesson two (*prof. Carmela Nardelli*): 15, November 2023, 14:30.**

Seminar room 4th floor Torre Biologica

Title: *Human microbiome analysis: a possible integrative tool in clinical investigation*

Human microbiome refers to the collection of genomes from all the microorganisms inhabiting several niches of our body. The advance of research technologies allows us to examinate how microbiota maintain human health and contribute to pathogenesis.

The lesson will initially be focused on the microbiome analysis by using 16S rRNA sequencing and then some results obtained by the study of the microbiome in obese patients with colorectal cancer will be discussed.

**References**

1. Hou K, Wu ZX, Chen XY, Wang JQ, Zhang D, Xiao C, Zhu D, Koya JB, Wei L, Li J, Chen ZS. Microbiota in health and diseases. Signal Transduct Target Ther. 2022 Apr 23;7(1):135. doi: 10.1038/s41392-022-00974-4.
2. Wensel CR, Pluznick JL, Salzberg SL, Sears CL. Next-generation sequencing: insights to advance clinical investigations of the microbiome. J Clin Invest. 2022 Apr 1;132(7):e154944. doi: 10.1172/JCI154944.
3. Nardelli C, Granata I, Nunziato M, Setaro M, Carbone F, Zulli C, Pilone V, Capoluongo ED, De Palma GD, Corcione F, Matarese G, Salvatore F, Sacchetti L. 16S rRNA of Mucosal Colon Microbiome and CCL2 Circulating Levels Are Potential Biomarkers in Colorectal Cancer. Int J Mol Sci. 2021 Oct 4;22(19):10747. doi: 10.3390/ijms221910747.

**Lesson three (*Maria Donata Di Taranto*): 16, November 2023, 14:30.**

Seminar room 4th floor Torre Biologica

Title: *Molecular diagnosis of inherited dyslipidemias: from functional characterization of genetic variants to prognostic evaluation*

Functional characterization is often mandatory to define the pathogenicity of variants identified during genetic screening of patients. The lesson will focus on different dyslipidemias illustrating the advantages and limitations of the experimental procedures, together with the precautions that should be considered for functional assays. Different molecular approaches useful for a prognostic evaluation of patients will be also discussed.

**References**

1. Pfisterer, S. G. *et al.* Multiparametric platform for profiling lipid trafficking in human leukocytes. *Cell Rep Methods* 2, 100166 (2022).

2. Di Taranto, MD. Et al. Identification and in vitro characterization of two new PCSK9 Gain of Function variants found in patients with Familial Hypercholesterolemia. Sci Rep. 2017 Nov 10;7(1):15282.

3. Benito-Vicente, A. *et al.* Leu22\_Leu23 Duplication at the Signal Peptide of PCSK9 Promotes Intracellular Degradation of LDLr and Autosomal Dominant Hypercholesterolemia. *Arterioscler Thromb Vasc Biol* 42, e203–e216 (2022).

4. Han, P. *et al.* Identification and functional characterization of mutations in LPL gene causing severe hypertriglyceridaemia and acute pancreatitis. *J Cell Mol Med* 24, 1286–1299 (2020).

5. Péterfy, M. *et al.* Characterization of two novel pathogenic variants at compound heterozygous status in lipase maturation factor 1 gene causing severe hypertriglyceridemia. *J Clin Lipidol* 12, 1253–1259 (2018).