



RESEARCH TOPIC MEM5

Unraveling genomic and epigenomic changes in ovarian cancer precursors lesion

Curriculum MEM standard

Research Area

Onco

Laboratory name

Laboratory of Cancer Pharmacology/Translational Genomic Unit

Research Supervisor

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Abstract

A significant proportion of high-grade serous epithelial ovarian cancer (HGS-EOC) does not originate within the ovary but from a malignant precursor lesion situated in the fallopian tubes, known as STIC (serous tubal intraepithelial carcinoma). Enhancing the curative potential of HGS-EOC, which stands as one of the most lethal gynecological malignancies, requires the adoption of a molecular test for the identification of STIC.

The candidate will delve into genomic and epigenetic defects related to the STIC, with the objective of optimize the accuracy of the screening test devised by the research group. Additionally, the project seeks to enhance our understanding of the evolutionary trajectory from normal tubal epithelium to an in situ malignant carcinoma, and ultimately in HGS-EOC. This research will aim to validate and refine the test for the early diagnosis and contribute to in-depth study on the molecular dynamics involved in the pathogenesis of HGS-EOC.

Main technical approaches

The applicant should have:

1. the ability to prepare genomic libraries from both liquid and solid tumor biopsies.
2. soft skills to interact with clinicians and pathologists.
3. interest in translational research.

Scientific references

1. Paracchini L, Mannarino L, Romualdi C, Zadro R, Beltrame L, Fuso Nerini I, Zola P, Laudani ME, Pagano E, Giordano L, Fruscio R, Landoni F, Franceschi S, Dalessandro ML, Canzonieri V, Bocciolone L, Lorusso D, Bosetti C, Raspagliesi F, Garassino IMG; TOWARDS group; D'Incalci M, Marchini S. Genomic instability analysis in DNA from Papanicolaou test provides proof-of-principle early diagnosis of high-grade serous ovarian cancer. *Sci Transl Med.* 2023 Dec 6;15(725):eadi2556.

2. Paracchini L, Mannarino L, Beltrame L, Landoni F, Fruscio R, Grassi T, Dalessandro ML, D'Incalci M, Marchini S. Targeted Mutational Analysis of Circulating Tumor DNA to Decipher Temporal Heterogeneity of High-Grade Serous Ovarian Cancer. *Cancers (Basel)*. 2022 Jul 29;14(15):3697.

3. Capoluongo ED, Pellegrino B, Arenare L, Califano D, Scambia G, Beltrame L, Serra V, Scaglione GL, Spina A, Cecere SC, De Cecio R, Normanno N, Colombo N, Lorusso D, Russo D, Nardelli C, D'Incalci M, Llop-Guevara A, Pisano C, Baldassarre G, Mezzanzanica D, Artioli G, Setaro M, Tasca G, Roma C, Campanini N, Cinieri S, Sergi A, Musolino A, Perrone F, Chiodini P, Marchini S, Pignata S. Alternative academic approaches for testing homologous recombination deficiency in ovarian cancer in the MITO16A/MaNGO-OV2 trial. *ESMO Open*. 2022 Oct;7(5):100585.

4. Pesenti C, Beltrame L, Velle A, Fruscio R, Jaconi M, Borella F, Cribiù FM, Calura E, Venturini LV, Lenoci D, Agostinis F, Katsaros D, Panini N, Bianchi T, Landoni F, Miozzo M, D'Incalci M, Brenton JD, Romualdi C, Marchini S. Copy number alterations in stage I epithelial ovarian cancer highlight three genomic patterns associated with prognosis. *Eur J Cancer*. 2022 Aug;171:85-95.

5. Paracchini L, Pesenti C, Delle Marchette M, Beltrame L, Bianchi T, Grassi T, Buda A, Landoni F, Ceppi L, Bosetti C, Paderno M, Adorni M, Vicini D, Perego P, Leone BE, D'Incalci M, Marchini S, Fruscio R. Detection of TP53 Clonal Variants in Papanicolaou Test Samples Collected up to 6 Years Prior to High-Grade Serous Epithelial Ovarian Cancer Diagnosis. *JAMA Netw Open*. 2020 Jul 1;3(7):e207566.

Type of contract

PhD scholarship of € 21.000 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 21.000 annui lordi erogata da Humanitas University. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.