Domande estratte n. 1, n. 2 , n. 4

AVVISO PUBBLICO, PER TITOLI E COLLOQUIO, PER L'ASSUNZIONE A TEMPO DETERMINATO DI N. 1 RISORSA NEL PROFILO DI RICERCATORE SANITARIO, CATEGORIA DS, CON LAUREA MAGISTRALE IN SCIENZE BIOTECNOLOGIE (LM8), LAUREA MAGISTRALE IN BIOTECNOLOGIE MEDICHE (LM-9). LAUREA MAGISTRALE IN SCIENZE BIOLOGICHE (LM-6), LAUREA MAGISTRALE IN GENETICA E BIOLOGIA MOLECOLARE (LM-6) O TITOLO EQUIPOLLENTE O EQUIPARATO AI SENSI DI LEGGE DA ASSEGNARE ALLA UOC GINECOLOGIA ONCOLOGIA DELL'ISTITUTO REGINA ELENA NELL'AMBITO DEL PROGETTO CODICE PNRR-MCNT1-2023-12378252 DAL TITOLO "ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING BASED RISK PREDICTION MODEL FOR IMPROVING ENDOMETRIAL CANCER CLINICAL MANAGEMENT: A COMPOSITE APPROACH INTEGRATING MULTIOMICS IMMUNE- ICONOGRAPHIC PATTERN (MOMIMIC SCORE) TOWARDS PRECISION ONCOLOGY AND SURGERY", FINANZIATO DAL MINISTERO DELLA SALUTE, CUP MASTER H53C24000300001, P.I. DR. ENRICO VIZZA

Prova Colloquio
5 FEBBRAIO 2025 ore 09:30

Prova tecnica

1. Ci descriva brevemente l'iter di stoccaggio di un campione tumorale. Dalla sala operatoria alla conservazione in biobanca;
2. Che cosa si intende per BioBanca di campioni biologici
3. Come si isolano i PBMC periferici?
4. Ci descriva brevemente cosa si studia con l'RNA-sequencing e cosa con il Whole Exome Sequencing. Qual è lo scopo dell'una e dell'altra tecnica?

Domande estratte n. 1, n. 2 , n. 4

AVVISO PUBBLICO, PER TITOLI E COLLOQUIO, PER L'ASSUNZIONE A TEMPO DETERMINATO DI N. 1 RISORSA NEL PROFILO DI RICERCATORE SANITARIO, CATEGORIA DS, CON LAUREA MAGISTRALE IN SCIENZE BIOTECNOLOGIE (LM8), LAUREA MAGISTRALE IN BIOTECNOLOGIE MEDICHE (LM-9). LAUREA MAGISTRALE IN SCIENZE BIOLOGICHE (LM-6), LAUREA MAGISTRALE IN GENETICA E BIOLOGIA MOLECOLARE (LM-6) O TITOLO EQUIPOLLENTE O EQUIPARATO AI SENSI DI LEGGE DA ASSEGNARE ALLA UOC GINECOLOGIA ONCOLOGIA DELL'ISTITUTO REGINA ELENA NELL'AMBITO DEL PROGETTO CODICE PNRR-MCNT1-2023-12378252 DAL TITOLO "ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING BASED RISK PREDICTION MODEL FOR IMPROVING ENDOMETRIAL CANCER CLINICAL MANAGEMENT: A COMPOSITE APPROACH INTEGRATING MULTIOMICS IMMUNE- ICONOGRAPHIC PATTERN (MOMIMIC SCORE) TOWARDS PRECISION ONCOLOGY AND SURGERY", FINANZIATO DAL MINISTERO DELLA SALUTE, CUP MASTER H53C24000300001, P.I. DR. ENRICO VIZZA

Prova Colloquio
5 FEBBRAIO 2025 ore 09:30

Domande di informatica

1. Cos'è Word
2. Cos'è Excel
3. Cos'è Power Point
4. Cos'è un Database

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Endometrial Cancer Immune Escape Mechanisms: Let Us Learn From the Fetal–Maternal Interface

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The immune escape mechanisms at the base of tumor progression in endometrial cancer mimic immune tolerance mechanisms occurring at the maternal–fetal interface. The biological and immunological processes behind the maternal–fetal interface are finely tuned in time and space during embryo implantation and subsequent pregnancy stages; conversely, those behind cancer progression are often aberrant. The environment composition at the maternal–fetal interface parallels the pro-tumor microenvironment identified in many cancers, pointing to the possibility for the use of the maternal–fetal interface as a model to depict immune therapeutic targets in cancer. [The framework of cancer environment signatures involved in immune adaptations, precisely timed in cancer progression, could reveal a specific "immune clock" in endometrial cancer, which might guide clinicians in patient risk class assessment, diagnostic workup, management, surgical and therapeutic approach, and surveillance strategies. Here, we review studies approaching this hypothesis, focusing on what is known so far about oncofetal similarities in immunity with the idea to individualize personalized immunotherapy targets, through the downregulation of the immune escape stage or the reactivation of the pro-inflammatory processes suppressed by the tumor.] 1

Keywords: cancer immune escape, fetal–maternal immune tolerance, immunotherapy potential targets, immunological parallelism in cancer and pregnancy, personalized medicine

INTRODUCTION

Innate and adaptive immune response affects development and progression of cancer through a process named immunoediting (1). Similar immune-mediated processes occur at the maternal–fetal interface (2–8). There is a parallelism between biological processes behind cancer progression and those behind the maternal–fetal interface such as proliferation, invasion, and angiogenesis (2). [While these processes are finely tuned during embryo implantation stages, they are conversely often aberrant in carcinogenesis. Interestingly, a recent study based on single-cell analysis 2

highlights that environment composition at the maternal–fetal interface parallels the pro-tumor microenvironment (TME) identified in many cancers (9), pointing to the possibility for the use of the maternal–fetal interface as a model to depict immune therapeutic targets in cancer.

Inflammation and immune tolerance are key mechanisms which ensure the proper establishment of pregnancy. The early stage of pregnancy is characterized by an inflammatory process responsible for proper implantation. This inflammatory stage should switch, in a second step, to a down-modulation of the immune response, ensuring the "non-rejection" of the semi-allogenic fetus. In pregnancy, the decidualized stromal cells, involved in the implantation process, are the gatekeepers of this key immune switching mechanism at the fetal–maternal interface, involving different immune cells, such as regulatory macrophages, natural killer (NK) cells, and T cells. In the last stage of pregnancy, and especially in activating labor, an inflammation process is required again; therefore, a new switching process is needed (10–18) (**Figure 1A**, left panel).

Several groups in the last years have shown that immunological properties acquired by both maternal–fetal interface and TME share the same molecular patterns related to the modulation of the inflammatory response involving innate and adaptive immune response (19). Tumor progression exploiting immune tuning mimics the immune maternal–fetal interface processes. In the early stage of carcinogenesis, the immune system recognizes cancer cells as non-self, inducing the proper pro-inflammatory environment to lead them to apoptosis. In a second step, the cancer cells are able to induce the switching of the immune system to an anti-inflammatory response, through different immune-editing mechanisms (20), thus leading to cancer immune escape. The fetal–maternal immune properties required to evade the immune system are limited in time and space; when labor starts, the immune system goes back to the initial steps. Conversely, the immune escape process in cancer goes on uncontrolled, and it does not revert to a pro-inflammatory feature (20) (**Figure 1A**, right panel). Therefore, the switching from immune suppression to immune activation occurring during pregnancy is lacking in carcinogenesis.

The existence of parallel situations between pregnancy and cancer gave rise to the term "oncofetal" and is common to many events. To take advantage of the knowledge of the similarities among immune regulation in pregnancy and tumor growth could lead to identification of new potential targets for cancer immunotherapy (2). Aberrations in placentation process, particularly in the modulation and tuning of the immune system, can lead to pregnancy complications; research has helped to develop the proper models to investigate immune tolerance in aberrant processes in pregnancy and to translate them to cancer investigations. Here, we summarize what is known so far about oncofetal similarities in immunity and which are the most recent and promising developments in this research area. A focus will be devoted to endometrial cancer (EC).

Therefore, this review is intended to focus on what is already known about the immune parallelisms between fetal–maternal interface immune tolerance and immune escape mechanisms during EC progression (**Figure 1B**).

FOCUS ON EC

EC is a relevant gynecological malignancy which occurs in fertile and postmenopausal women. The mean age of women affected by this tumor is decreasing; thus, the incidence in worldwide women under 40 years of age is on the rise (21). EC is linked to obesity (21), and the pandemic of obesity is a global threat. Patients with EC have a good prognosis at early-stage incidence, while the prognosis for recurrent or metastatic EC remains poor (22). It is therefore mandatory to understand the mechanisms fueling EC progression and ways to inhibiting them, to improve therapeutic chances (23). A deep knowledge of the interplay between positive and negative immunological molecular players and its timing in EC development and progression is still missing; several findings so far indicate that the immune escape mechanisms are at the base of EC progression and could be due to similar immune tolerance modulations occurring at the maternal–fetal interface (24). The EC is an ideal tumor model to study these mechanisms; EC tissue remains similar to the endometrial tissue of origin, and its related tumor progression develops in different steps, from endometrial hyperplasia to endometrioid carcinoma type 1 (grading: G1, G2, and G3), depending on its histological similarity to the physiological endometrial tissue (23). The immune escape pathways underlying the progression from physiological endometrium to carcinoma could represent new targets for personalized immunotherapy by the reactivation of the pro-inflammatory response processes suppressed by the tumor. A contribution to the immune escape in EC is also provided by the immunosuppressive interplay between regulatory T and regulatory B lymphocytes, regulatory NK, and tolerant dendritic cells, also traceable at the decidualized endometrial tissue in the fetal–maternal interface during implantation processes (24, 25).

The maternal–fetal interface and EC represent a "new" complex network where many immune cells of innate (dendritic cells, macrophages, and NK cells) and adaptive immune system cells (regulatory T and regulatory B lymphocytes) play a synergistic role in immune tolerance and immune escape mechanisms. The following part summarizes the similarities observed to date in the different cell lineages involved in the immunological processes underlying pregnancy and EC.

EC Traditional Classification and Biomolecular Classification

EC was historically classified into two different clinicopathological and molecular types: type I is the much more common endometrioid adenocarcinoma (80–90%), and type II comprises non-endometrioid subtypes such as serous, clear-cell, and undifferentiated carcinomas, as well as carcinosarcoma/malignant-mixed Müllerian tumor (10–20%) (26). Molecular data are now considered as an important part of pathologic evaluation, since type I carcinomas are associated with PTEN, KRAS, CTNNB1, and PIK3CA genetic