REFINING PRECLINICAL SCREENING: 3D CELL CULTURE MODELS AS A TOOL FOR ASSESSING TARGETED THERAPIES IN ENDOMETRIAL CANCER

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Endometrial cancer is one of the most common female cancers, with a high incidence in Europe, especially in Central and Eastern Europe [1]. The development of the disease is determined by a number of interrelated factors, including hormonal imbalances, metabolic disorders, genetic predisposition, higher body mass index and older age [2]. Despite the effectiveness of surgical treatment in the early stages of the disease, some patients require additional systemic treatment, the results of which are not always optimal.

Following surgical intervention, adjuvant chemotherapy or radiotherapy is administered to patients stratified with even a minimal risk of recurrence to improve oncological outcomes. Unfortunately, standard chemotherapy based on platinum compounds and taxanes often has limited selectivity and causes significant side effects. For these reasons, increasing attention is paid to targeted therapy strategies that affect specific molecular signaling pathways and provide the basis for more precise and personalized treatment [3]. The PI3K/AKT/mTOR pathway, receptor tyrosine kinases inhibitors, various cell cycle, proliferation and survival regulators, PARP polymerase and the nuclear transport system have been identified as potential targets for endometrial cancer therapy.

In order to evaluate the efficacy of such compounds, suitable preclinical models that can reflect the biological complexity of the tumor are necessary. For a long time, two-dimensional (2D) cell cultures have dominated cancer research, but they do not adequately reproduce the tumor microenvironment, cell-cell interactions, and spatial structure. In recent years, three-dimensional (3D) cell culture models, such as spheroids and aggregates, have become increasingly popular, which better mimic This *in vivo* conditions, including diffusion gradients, tumor heterogeneity, and extracellular matrix-dependent signaling pathways [4]. Due to these properties, 3D models are considered more suitable for studying drug response and tumor behavior.

In our previous studies the effects of targeted therapy compounds on 2D and 3D model systems of endometrial cancer cells were evaluated by analyzing the metabolic activity of the cells. In order to more fully characterize the biological effects of these compounds, this work was supplemented with fluorescence microscopy data, which allows us to distinguish between metabolic activity and cell death in 3D cultures. Additionally, quantitative PCR (qPCR) was employed to characterize 3D cultures by changes in the expression of endometrial cancer and stemness markers compared to 2D models. Such methodological expansion provides an opportunity for a more comprehensive assessment of the action of targeted therapies and a better understanding of the response of endometrial cancer cells to treatment.

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