San Antonio Breast Cancer Symposium (SABCS)

Young women and breast cancer: research in focus

At the San Antonio Breast Cancer Symposium (SABCS) in December, three experts presented new approaches and study results for the treatment of breast cancer in young women.

In her lecture, Camila dos Santos explained that the development of the mammary glands is strongly controlled by hormones that promote cell growth and cell division. 'During pregnancy, there are significant structural and functional changes in the breast, such as the expansion of cells and the production of new proteins to prepare for milk production,' said the Associate Professor at Cold Spring Harbor Laboratory, New York.

'These hormonal influences not only change the growth pattern of epithelial cells but also affect the collagen structure of the breast and its alignment, as shown by microscopic techniques such as collagen staining.' She emphasized that pregnancies leave epigenetic changes that permanently affect the gene expression of breast cells. 'Early pregnancies can reduce the risk of breast cancer by 30–40%, depending on the subtype and genetic mutations. This protective effect often lasts into postmenopausal age,' explained dos Santos. Using mouse models, it was shown that pregnancies promote cell aging, which inhibits tumour development. It was also discovered that pregnancy affects the immune system by infiltrating certain types of T cells that can alter the tissue environment of the breast and inhibit tumour growth.

Urinary tract infections promote tumour growth

The systemic effects of urinary tract infections (UTIs) on the breast are still relatively unknown. They lead to a systemic inflammatory reaction and increased collagen deposition in the breast. In mouse models, it was found that UTIs cause hyperplasia of the mammary gland ducts and changes in cell behaviour. These changes can accelerate tumour growth in genetically susceptible models. 'Pregnancy and systemic factors such as infections can influence breast development and breast cancer risk in multiple ways. These findings could lead to the development of preventive therapies that modulate the immune system or influence epigenetic changes to reduce breast cancer risks,' summarized the expert.

Suppression of ovarian function

In her presentation, Prudence Francis looked at various approaches to suppressing ovarian function in premenopausal women with early breast cancer. The medical oncologist breast cancer clinician-researcher at Peter MacCallum Cancer, Melbourne, Australia, pointed out that ovarian function can be reversibly suppressed by GnRH agonists, which is particularly suitable for young women to avoid permanent menopause. 'Alternatively, surgical menopause is an option for women close to the natural menopausal age,' said the expert.

Monitoring estradiol levels is also important to ensuring effective suppression of ovarian function. 'In clinical practice, this is often not done routinely unless specific symptoms indicate that suppression is inadequate. However, studies show that younger women, women without chemotherapy, and those with higher BMI are at increased risk of not achieving persistent suppression,' Francis explained. Ovarian suppression is particularly indicated in premenopausal women with a high risk of recurrence, for example in very young women or those who are to be treated with an aromatase inhibitor. For premenopausal women with estrogen receptor-negative breast cancer, ovarian suppression is increasingly being discussed as a means of reducing the risk of premature menopause. 'Although there is no oncological benefit in this group, the quality of life and health of women could be improved by avoiding premature menopause,' the expert made clear.

Aftercare and treatment: a multidisciplinary approach

Dr Jenni Sheng addressed the various aspects of follow-up care and treatment for young women with breast cancer in her presentation. The Assistant Professor in the Department of Oncology at the Johns Hopkins University School of Medicine, Baltimore, emphasized that a multidisciplinary approach is necessary to optimize survival and quality of life, as this patient group is often underrepresented in studies. 'There is a particular focus on fertility and family planning, including the importance of early fertility preservation discussions. Studies show that pregnancy after breast cancer does not worsen disease-free survival or overall survival,' said Sheng. Another key point of her presentation was psychosocial health: 'Younger patients often suffer from higher levels of psychological stress. The fear of relapse is widespread, but can be reduced through cognitive interventions,' the expert made clear, emphasizing the importance of couples therapy to improve coping strategies. Problems such as insomnia could be successfully treated with a combination of cognitive behavioural therapy and light therapy.

Finally, Sheng discussed support programmes for young adults. These should cover a broad spectrum, from psychosocial support and fertility counselling to the treatment of menopausal symptoms. 'However, the implementation of such programmes is hampered by limited financial and human resources,' she criticized. ■

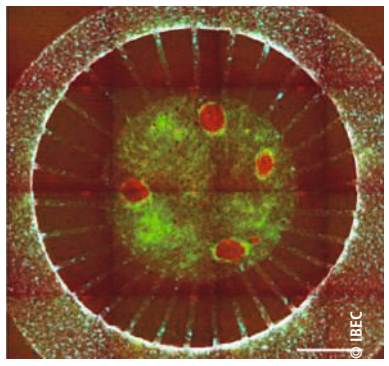
Report: Sonja Buske

Replicating tumours to assess cancer immunotherapy efficacy

The Micro Immune Response On chip (MIRO) allows tumours and their environment to be replicated in order to understand their response to immunotherapy-based treatments.

The device, which has already been successfully tested on breast cancer samples, could be key to developing new treatments and determining the most appropriate therapy for each patient in a personalized way. The work, published in Nature Communications, is the result of a collaboration between the Institute for Bioengineering of Catalonia and the Research Institute of the Hospital del Mar.

The MIRO device makes it possible to fill a gap in the creation of treatments against cancer cells. Many developments offer promising results in the laboratory, in vitro and in mouse models, but they do not work as well when transferred to humans. "MIRO enables to recreate not only the tumour, but its environment and the interaction they have with the cells of the immune system. This relationship is vital for the success of immunotherapy-based treatments which, despite their curative potential, currently only work in between 20 and 40% of patients" explains Dr Anna Labernadie, who designed the microfluidic system during at IBEC and now leads the Cell Behavior and Tissue Bioengineering laboratory at the Príncipe Felipe Research Center (CIPF) in Valencia.



Representative image of MIRO co-culture on day 10

The researchers who have developed this technology have already tested it with breast cancer samples known as HER2-positive. This type of cancer cell has very high levels of the HER2 protein, which promotes rapid tumour growth, but at the same time, can be treated with therapies that specifically target this protein.

The tests carried out have made it possible to verify the importance of the environment surrounding breast tumours in protecting them from the most common treatment in this type of cancer, the monoclonal antibody trastuzumab. "Thanks to MIRO, we have been able to track the immune cells, see how they lose speed, movement, as they approach the tumour, which makes the treatment not work. They encounter a barrier formed by the tumour environment and become blocked", explains Dr Alexandre Calon, head of the Translational Research Laboratory in Tumour Microenvironment at the Hospital del Mar Research Institute.

The MIRO device, which has already been tested with other types of solid tumours, such as lung or colon tumours, is manufactured using microfluidic techniques. These techniques allow fluids and cells to be manipulated on a very small scale. MIRO includes cell cultures of different types, separated into compartments in order to direct and observe their evolution. This model, the first of its kind created with these techniques, makes it possible to recreate and study in detail the interaction between cancer cells, their connective tissue and immune responses. "This model allows us to directly test the treatments that would be used with patients," explains Dr Xavier Trepat, ICREA research professor at IBEC, where he leads the Integrative Cell and Tissue Dynamics group, and member of the University of Barcelona (UB).

The device's ability to analyse the functioning of different treatments, the emergence of possible resistance and even identify new biomarkers individually for each patient, represents a great advance in the design and personalisation of immunotherapy treatments in oncology. In this sense, Dr Joan Albanell, head of the Medical Oncology Service at Hospital del Mar and director of the Cancer Research Program at his research institute, pointed out that "MIRO is an innovative preclinical model that can help improve the success rate and efficacy of new strategies with immunotherapy once we transfer them to clinical trials".

As for future work, IBEC, ICREA and Hospital del Mar Research Institute have already filed a joint patent application for MIRO's technology. "Our goal is to transfer this technology to the pharmaceutical industry and hospitals to be able to apply it to patients," explains Dr Anna Labernadie.

The study described is part of Alice Perucca's PhD thesis at IBEC. Her work focuses on investigating the role of the immunocompetent ecosystem in cancer progression.

The work also included the collaboration of the Institute for Research in Biomedicine (IRB Barcelona), the University of Barcelona (UB), the Bioengineering, Biomaterials and Nanomedicine Networking Biomedical Research Centre (CIBER-BBN), Pompeu Fabra University and the Oncology Networking Biomedical Research Centre (CIBERONC-ISCIII); and has received partial funding from the "la Caixa" Foundation. ■

Source: Institute for Bioengineering of Catalonia