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Synopsis

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WOMEN'S CANCER: FROM PREVENTION TO NEW TREATMENTS

Every year, three and a half million women around the world die of cancer, six thousands of them in Catalonia. Some of these tumors are only found in women, like ovarian and cervical cancer. Others are most common in women, like breast, and other present unique characteristics, such as lung cancer, which is on the rise among women, who started smoking later.

In the fight to limit its impact and mortality, **several factors are key** and must be paid special attention. On one hand, **studying the biology of cancer** is essential to understanding its mechanisms, weaknesses and ways of presenting, as well as for designing more effective **treatments**. On the other, knowledge allows doctors to more precisely establish each woman's susceptibility to the disease and develop better **prevention and early detection** tools. Moreover, **patients' associations** are playing an increasingly active and important role in the fight for their rights and improving quality of life.

To debate the current situation, as well as the challenges and advances in women's cancer, several top international experts met for a session organized by [B-Debate](#), [Women's Cancer](#), an initiative of [Biocat](#) and the ["la Caixa" Foundation](#) to promote scientific debate.

CONCLUSIONS

- Studies of the **biology of cancer** are leading to **new treatment ideas**, whether through precision medicine, immunotherapy or attacking telomeres, to name just a few.
- Scientists are looking for **new gene signatures and models to calculate women's susceptibility to cancer**, which would improve early detection and treatment outcomes.
- One of the preventative treatments that is expected to become widespread is the **vaccine for human papilloma virus**, which is highly effective in protecting against cervical cancer.

- **The doctor-patient relationship and access to information** are two of the most important aspects of increasingly participative medicine.

1. FROM BIOLOGY TO NEW TREATMENTS

Although it is not an exclusively female tumor (far from it), **the history of lung cancer is in good part a history of how our approach to cancer has evolved in recent years**. This history was summed up in the inaugural speech by [Silvia Novello](#), professor of medical oncology at the University of Turin, and is about small, increasingly specific and unique, steps in the fight against the enemy with a thousand faces.

“In 2005, therapies weren’t very effective and barely had an average survival rate of one year,” explained Novello. But then came new approaches. In 2008, doctors started using new drugs that target the blood vessels and subtypes of tumors began being treated differently. And, **in 2010, the concept of precision medicine was truly introduced**, with drugs targeting specific mutations (like those in the EGFR gene). Since then, new drugs, targets and markets have appeared and, at the same time, we have seen that, although the steps forward have been substantial, it isn’t enough. **Tumors generally end up becoming resistant**, so studies and new drugs are launched to overcome the resistance. In addition, in the midst of this escalation, **immunotherapy** has appeared, opening a new door (still in the early days) for hope.

Lung cancer is increasingly common among women; as they started smoking later, the cases have started increasing at an alarming rate in recent years. **Breast cancer**, on the other hand, is overwhelmingly a female cancer (although not exclusively), and there are several parallels to the approach to lung cancer, with subtypes treated in different ways.

In some cases, the treatments are quite successful thanks in large part to precision medicine. In others, however, the options don’t have the desired results. This is the case of what are known as “**triple negative**” tumors, a definition that alludes to the lack of targets for treatment that others do have.

“**When people ask me if we’re making headway with this type of tumor, my answer is yes. But we still have a long road ahead,**” said [Carey Anders](#), professor of Medicine at the University of North Carolina. Through extensive genetic analysis, scientists are working to find specific gene signatures to guide treatment. For example, by inhibiting androgen receptors or proteins that repair DNA. And, in the end, “**whether we like it or not, all oncologists are turning into immunologists,**”

confessed Anders, alluding to the new forms of immunotherapy. “The results aren’t great yet, but we’re starting to see that, the sooner we start treatment the more effective it is.”

Biological knowledge is allowing researchers to conduct trials with breast cancer therapies that weren’t originally designed for this disease. **“Some patients could benefit from a drug that is currently being prescribed for osteoporosis,”** explained [Eva González Suárez](#), researcher at IDIBELL Barcelona and co-leader of this B-Debate. They are [RANK](#) pathway inhibitors, which curb bone degeneration and seem to also play a role in developing mammary tissue. Clinical trials are already scheduled to discover their true value.

Other studies are working to untangle the **role obesity plays in cancer**, specifically in breast cancer. “We know that not only does the risk increase but also the prognosis is worse. Specifically, the risk of metastasis is higher,” said [Daniela Quail](#), professor at the Goodman Cancer Research Centre in Montreal, Canada. Her studies have found it is tied to greater inflammation, more immunosuppressive white blood cells and molecular messengers like those known as GM-CSF or interleukin IL-5. This opens the door to not only personalizing dietary interventions, but also trying to cut off some of those messengers using specific antibodies.

María Blasco, director of the Spanish National Cancer Research Center (CNIO) in Madrid, presented her latest results in the fight against multiform glioblastoma, a particularly serious brain tumor. It is not found only in women, but her work is world renowned and “she is a benchmark as a woman in research,” explained Eva González Suárez. For years, her group has **studied the role of telomeres in cancer, as the structures that act as an “expiration date” for cells** and that many tumors manage to regenerate in order to effectively become immortal. They previously tried with drugs that had failed, “surely because they selected cells with the longest telomeres, as with cancer stem cells.” This meant that part of the tumor could hang on and grow back.

Now they have tried a different approach, **“attacking the action of telomeres, more than their length.”** [The results have been spectacular](#) in lab mice and they are already designing drugs to be used in clinical trials. At the same time, they are also studying “the biology of stem cells and the role of resistances, which will surely appear,” says Blasco.

Another, less known, part of research focuses on the **tumor environment, where it develops**. The group led by [Frances Balkwill](#), professor of Cancer Biology at the University of London, has found a [signature of 22 genes](#) expressed in this environment that predicts a better or worse prognosis for ovarian cancer, “a tumor whose survival rate

hasn't changed much in recent years," recognized the researchers. Plus, the genes in the signature "could also be shared by other types of cancer."

On the role of the environment and the structure in which cells grow, particularly emphatic and provocative were the words of [Mina Bissell](#), an extremely prestigious researcher at the Lawrence Berkeley National Laboratory, in the United States. "**We accumulate mutations, but the cancer doesn't appear until the architecture is damaged,**" she explained. Bissell says, "**We know almost everything about the genome, but we know nothing about the language of shapes,**" which is why so many studies sequencing DNA haven't come up with hardly any **treatments.** "Text books are important, but they can be corrupted because they seem to want to be written in stone," she warned. And she concluded with a final suggestion: "Don't get arrogant. The most famous scientists are arrogant. Why? It kills the passion."

2. FROM PREDISPOSITION TO PREVENTION

Mutations of certain genes predispose people to developing certain types of cancer. This is what happens, for example, with certain alterations in the **BRCA1 and BRCA2 genes**, which increase the chances of developing breast or ovarian cancer and tend to accumulate in some families (which is why **Angeline Jolie** chose to have these organs removed). The scenario, however, is complex: depending on which mutation a woman has, the risk is higher or lower, there can be interactions with other variants, or lifestyle or hormonal factors, and there are many mutations in other genes that are also being studied to determine their role.

Understanding the markers and risks in depth would help choose the best measures: surgery in some cases or, in many others, personalized periodic monitoring like mammograms for breast cancer. For this type, "**in theory, combining everything, we could go from 5% prediction to 45%, but we don't have those models yet,**" explained [Antonis Antoniou](#), a professor at the University of Cambridge who has participated in [several international consortia](#) on susceptibility to cancer.

According to [Nicoline Hoogerbrugge](#), professor of Hereditary Cancer at Radboud University Medical Center, in the Netherlands, **up to 40% of these patients have a family history of cancer** but, in most cases, we do not know which genes are responsible. One that could be behind some cases is NTHL1, a gene that when mutated comes with a higher risk of colon cancer. Her group has also shown it increases the risk of breast cancer as well.

Some of these genes can also be found in a panel Hospital Vall d'Hebron has studied in more than 1,200 patients in recent years. The study, which will be published soon, was presented by Judith Balmaña, of the Vall d'Hebron Institute of Oncology. According to the results, **adding a panel of 19 genes on top of those already commonly studied could help improve risk detection.**

Preventative treatment would also be related. Really, the end goal, according to [Jack Cuzick](#), director of the Wolfson Institute of Preventive Medicine in London, is **to do what cardiologists did years ago: “starting to use risk factors (cholesterol, high blood pressure) as a treatable disease.”** Something like this has been achieved with estrogen inhibitors, which are sometimes used to treat or prevent breast cancer. But work is underway to improve them and to find preventative therapies for tumors that these drugs don't work on.

Cervical cancer deserves a chapter of its own. Mainly caused by infection with one of the different types of human papilloma virus (although infection does not necessarily mean it will develop), there is now a **vaccine that is “extraordinarily effective for prevention,”** said [Francesc Xavier Bosch](#), senior researcher at IDIBELL Barcelona. Plus, there is a very powerful screening tool for the virus, “which is here to stay and will soon be widespread,” added Bosch.

Regular pap smears are currently used, although they are not that sensitive and cannot always identify lesions, which means they must be repeated often. Bosch is one of the promoters of the [HPV-Faster program, which aims to extend the use of the vaccine beyond pre-adolescent girls:](#) the idea is to give it to women under 30, or even 50 in some cases, along with a personalized screening program to consider giving it to men as well.

3. PANEL DISCUSSION: TOWARDS PARTICIPATIVE, PERSONALIZED MEDICINE

In a session open to the public, representatives from patients' associations, the media, bioethics and oncology, as well as individual patients, debated the current and future states of medicine, its problems, strengths and weaknesses. Most of the debate focused on the **doctor-patient relationship and access to information.**

“The first oncologist I saw was a good doctor, I'm not saying he wasn't,” explained [Laura Sancho](#), Catalan actress diagnosed with breast cancer in 2008, “but **he hardly looked**

at me, and gave me monosyllabic answers to many of my questions. The people who really helped me were the nurses.” Sancho was diagnosed after undergoing some tests to try to get pregnant, something she had to give up on: the increased estrogen levels that come with pregnancy increase the risk of relapsing.

“That wasn’t my case,” explained Rosa Gasa, IDIBAPS Barcelona researcher and breast cancer patient. “Surely, **being a researcher, communication is better**, but I felt it was very open.”

“**One of the most common concerns is communication,**” highlighted [Clara Rosàs](#), head of the Catalan Federation of Organizations Against Cancer (FECEC). “We know some do a very good job, but that isn’t always the case.”

[Joan Brunet](#), medical oncologist at the Catalan Institute of Oncology (ICO), said, “When I was studying for my degree, there wasn’t any sort of training in this regard, but now they have included it and you can see the improvement in recent years.” In addition to this, better communication does not take much more time: some studies show that **“generating empathy doesn’t add more than a minute or two to visit times.”**

“In my opinion, **we’re still in a client-like doctor-patient relationship**, more suitable to providing services than based on trust. However, things have improved a lot in terms of recognizing that patients are an active part of the process and want to make decisions,” said professor of Moral Philosophy [Victoria Camps](#). “Part of the problem is surely that there isn’t enough time to develop the relationship.”

“The part about participation is true,” recognized Brunet. “**But there are also people who turn it down, who don’t want it, and there are times over the course of the disease when doctors have to be more like executives.**”

Another key aspect is access to information, mainly on the Internet. Sancho admitted to having spent “hours at the computer. I would look for cases similar to mine and I found loads of nonsense.” For science communicator [Pere Estupinyà](#), “It’s definitely getting worse. On one hand, **there’s very good information. Those who complain there isn’t, aren’t looking for it. But the problem is that there’s also a lot of bad information that reaches us via social media without any sort of filter.** I think we should design a strategy to rank information sites, to have a benchmark for credibility.” In reality, “when people ask me how to improve science communication, I think what we have to do is eliminate the worst of it.”