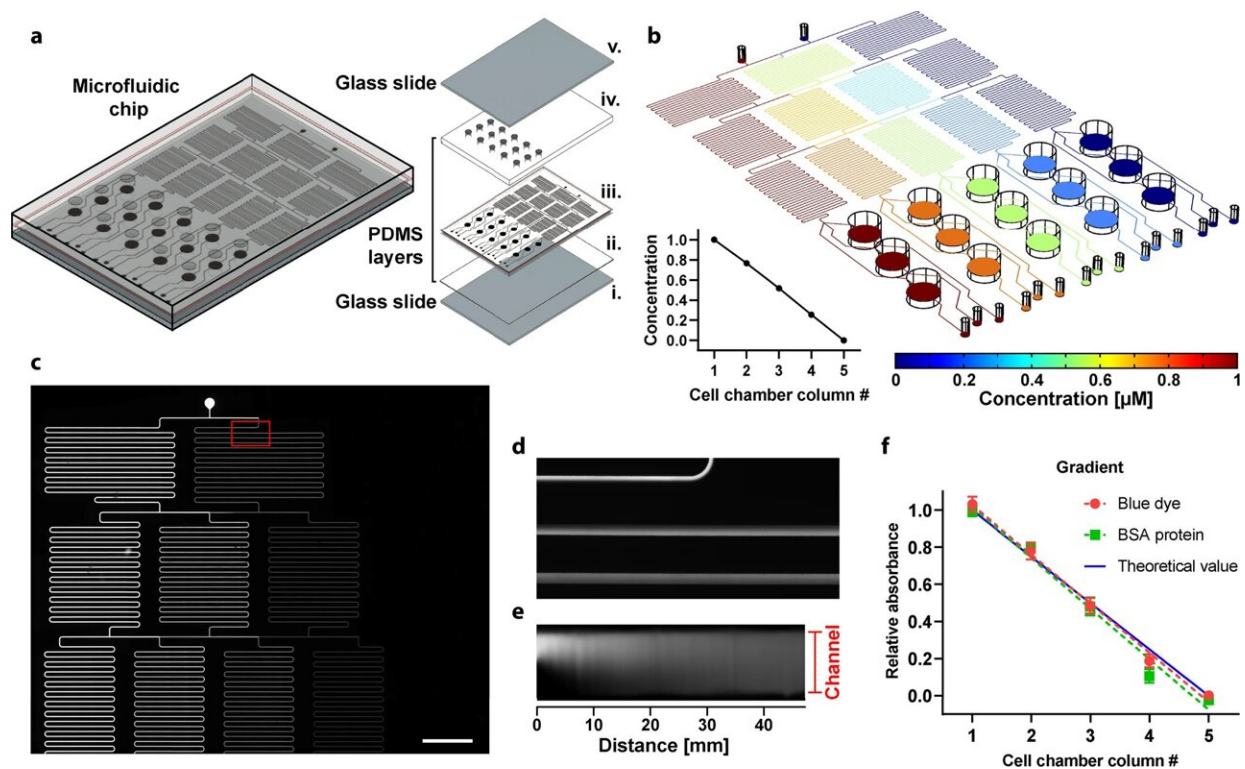


# Researchers design a microfluidics physics-based device to predict cancer therapy response

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Microfluidic dynamic BH3 profiling platform. **a** Schematic representation of the chip including exploded view of all the parts: (i) lower glass slide, (ii) thin PDMS layer, (iii) channels & chambers PDMS layer (1 mm thick), (iv), chambers PDMS layer (2 mm thick), and (v) upper glass slide. **b** Simulation of peptide concentration along with the whole microfluidic platform. The coordinate of the slice plot is selected at the middle of the microfluidic channels. Relative concentration as a function of the cell chamber (inset figure). **c** Fluorescence image of the network of microfluidic channels after injecting fluorescein in the

left inlet and distilled water in the right inlet at a pressure of 100 mbar. **d** Zoomed view of the region where both solutions are mixed. **e** Fluorescence intensity along with the first 47 mm of the mixer channel (total channel length is ~190 mm); Note that the image was processed in ImageJ to be plotted as a straight channel **f**. Colorimetric detection of BSA protein and relative absorbance of blue dye at the outlets of the chip measured at 562 and 640 nm, respectively, on a plate reader. Together with the blue dye, BSA protein was injected through one of the inlets, while MiliQ water was injected in the other (inlet pressure of 200 mbar). Data represent three independent experiments using different chips. Credit: *npj Precision Oncology* (2022). DOI: 10.1038/s41698-022-00333-0

One of the great challenges in the fight against cancer is to design new technologies for a personalized treatment for each patient. Depending on the molecular characteristics—DNA mutations for instance—of each tumor, precision medicine aims to make it easier for cancer patients, both adult and pediatric, to receive a personalized treatment that is appropriate to their pathology. But is it possible to know whether or not a patient can benefit from a treatment before starting therapy?

A team of experts from the Faculty of Medicine and Health Sciences of the University of Barcelona and the Institute for Bioengineering of Catalonia (IBEC) has designed a microfluidic device called microfluidic dynamic BH3 profiling ( $\mu$ DBP) that predicts the effectiveness of cancer treatment quickly and automatically, using a small number of cells from biopsies and without requiring specialized technical staff.

The study, published in the journal *npj Precision Oncology*, was led by Joan Montero, professor at the UB Department of Biomedicine and IBEC, and Javier Ramón-Azcón, ICREA research professor at IBEC.

The paper—whose first author is Albert Manzano (UB-IBEC), who

received his Ph.D. from the UB in 2022 with a thesis on [precision medicine](#) in the fight against cancer—involves experts from the UB Faculty of Physics, the Vall d'Hebron Institute of Oncology (VHIO) and the Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN).

## **Precision medicine in the fight against cancer**

Personalized medicine has revolutionized the way we design effective cancer treatments. Considering that each tumor is unique and has its own characteristics, having predictive indicators of each patient's response to treatment is a major step forward in oncology. The dynamic BH3 profiling (DBP) was initially developed in the laboratory of Professor Anthony Letai—Professor Montero was a co-inventor in this study—and patented in 2015 by the Dana-Farber Cancer Institute (United States).

It was one of the first functional assays successfully tested to predict treatment in various types of cancer. This system brings cancer cells into contact with different therapeutic options to quickly identify *ex vivo* the ones that might be most effective in removing the tumor. Conceptually, it is very similar to the antibiograms used to identify antibiotics to treat bacterial infections.

"DBP has been used to identify the efficacy of treatments on a preclinical and clinical scale in many different cancers, both solid and liquid. These studies have used [cell lines](#), animal models and primary samples with high predictive ability in all cases. However, this assay has not yet been widely applied in hospitals," says lecturer Joan Montero.

"So far," he adds, "several studies have found a good correlation between DBP results and clinical response in primary leukemia samples. There are currently several [clinical trials](#) underway, and we would like this technology to be implemented in hospitals in the coming years to

improve cancer therapies."

## **Predicting the therapeutic response with few cancer cells**

Now, the new DBP microfluidic device—known as  $\mu$ DBP—solves several functional assay challenges: it reduces the number of [cancer cells](#) needed to test potential ex vivo therapies and automates the process to facilitate [clinical application](#) without specialized technical staff.

"One of the main limitations of the DBP is the number of cells needed to perform the assay. When a biopsy is performed on a patient, the number of tumor cells we obtain is very limited, which does not allow a study with many different treatments and limits the ability to identify one that is effective," notes Albert Manzano.

When a biopsy is received, the sample is dissociated to obtain [individual cells](#) using mechanical and enzymatic treatments. Once processed, the sample is filtered to obtain individual cells which are then subjected to the desired treatments and seeded in the [microfluidic device](#).

"Thanks to our  $\mu$ DBP microfluidic platform, which is equipped with small wells for seeding cells, we can reduce the number of cells required to test a treatment. This is a decisive innovation to increase the number of drugs that can be tested," adds Manzano.

### **A fast and fully automated system**

The paper published in the journal *npj Precision Oncology* is the first to apply microfluidics to perform the functional assay of the DBP. Unlike other versions developed so far, such as the high-throughput DBP (Bhola et al., *Science Signaling*, 2020) with automated plates and dispensers to

test hundreds of treatments, the new  $\mu$ DBP device is aimed at testing treatments in situ in a very fast, simple and automated way, without needing expensive machinery or specialized staff.

"The biggest advantage of the  $\mu$ DBP device is also the automation of the whole process, which would help to implement this functional methodology on a clinical scale. All these advantages would ease the adoption of DBP in hospitals as a routine trial," the experts add.

"We have developed this new tool with the idea of making it available to oncologists. This [automated system](#) allows us to obtain personalized patient and treatment information," says Javier Ramón-Azcón (IBEC).

## **Nanotechnologies: A revolution in biomedicine**

Nanotechnology—especially the application of microfluidics to different processes—is driving several improvements in the design of these devices to reduce the amount of reagents, lower economic costs, automate processes or to increase the analytical capacity of certain methodologies, such as the DBP.

The team is currently working on the design of a new prototype with further technical improvements to facilitate the DBP analysis and to obtain more experimental evidence with primary samples to show its clinical utility in improving the treatment of different cancers, both pediatric and adult.

As the team details, "We will continue to work with our clinical collaborators to analyze patient samples and adapt this methodology to improve personalized treatment of multiple cancers for the benefit of all [cancer patients](#)."

**More information:** Albert Manzano-Muñoz et al, Microfluidic-based

dynamic BH3 profiling predicts anticancer treatment efficacy, *npj Precision Oncology* (2022). [DOI: 10.1038/s41698-022-00333-0](https://doi.org/10.1038/s41698-022-00333-0)

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