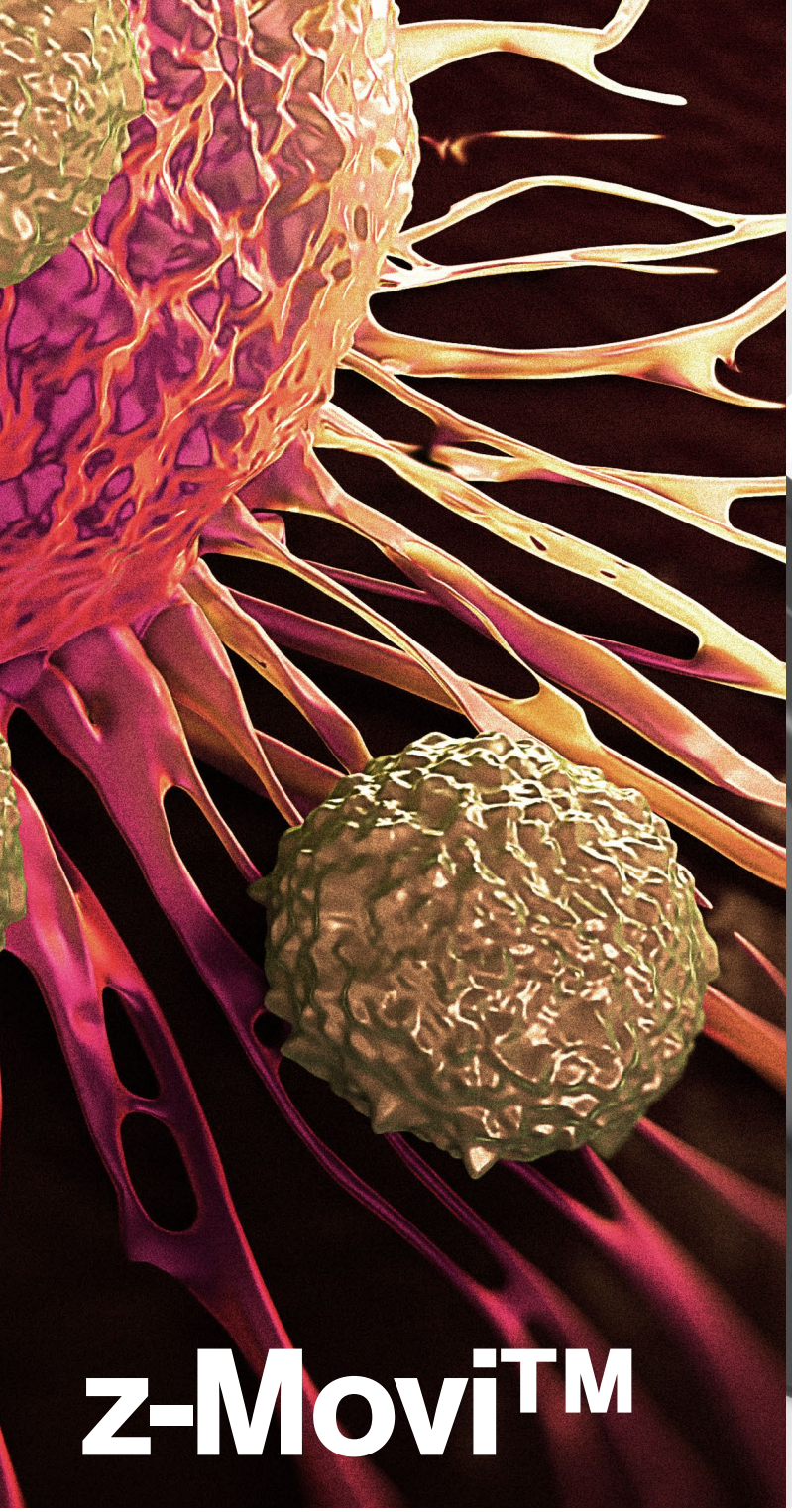
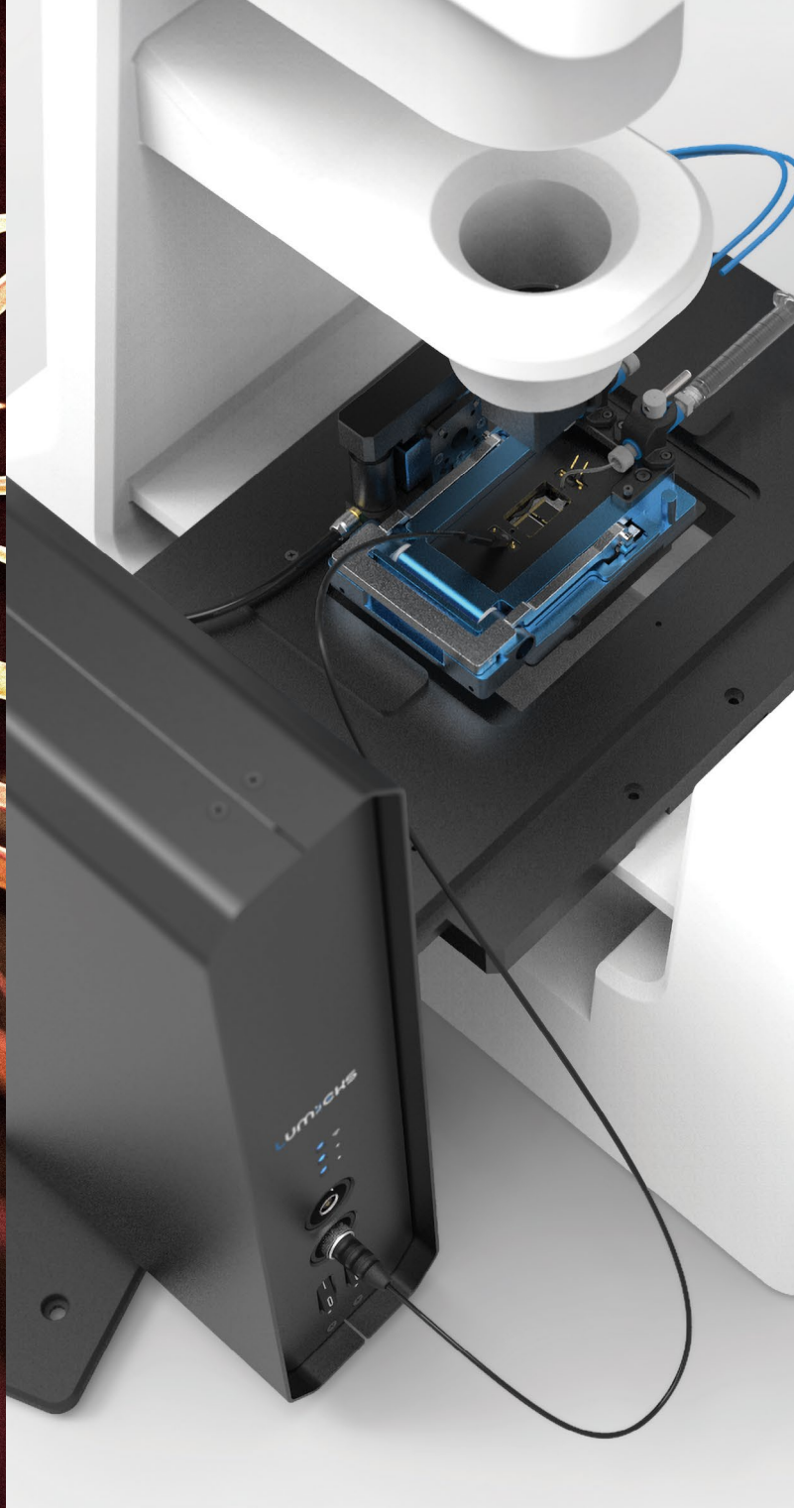


z-Movi™



High-throughput Label-free Cell Interaction Studies

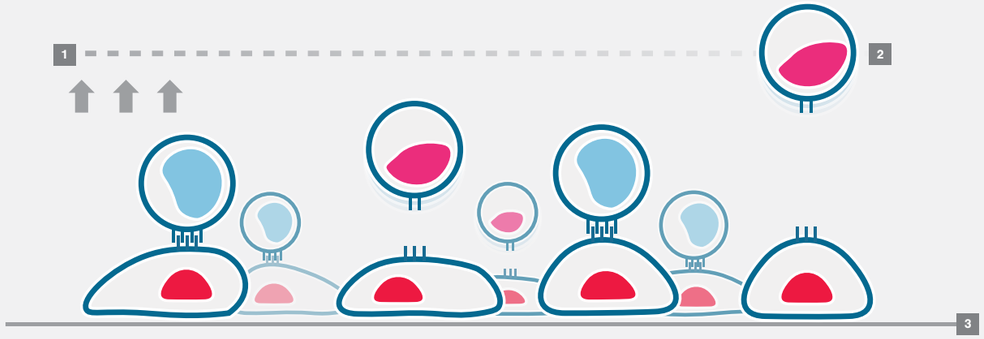
z-Movi™ I Application & Product Brochure

Avidity based screening & sorting: z-Movi™ enables direct and label-free screening and sorting of thousands of cells based on their interaction to cell or protein targets.

High-throughput label-free cell interaction studies.

Biological and pathological phenomena are heavily dependend on cells interacting with specific targets including ligands, proteins or other cells. To this date, there is no method that can directly measure these interactions and screen cells thereon, which are critical hurdles for the development of many novel therapies.

Cell–cell Interactions



Cell–Ligand Interactions

1 Planar acoustic node generated by a standing wave.

2 Cell pulled towards the acoustic node.

3 Adherent cells cultured on the functionalized glass surface.

4 Glass surface coated with ligand.

Introducing z-Movi™

z-Movi™ is a breakthrough technology for research and development of personalized therapies, including immunotherapy. It is the first platform able to directly measure the strength of interaction, or avidity, between cells with specific targets and sort cells of interest, in a high-throughput and label-free manner.

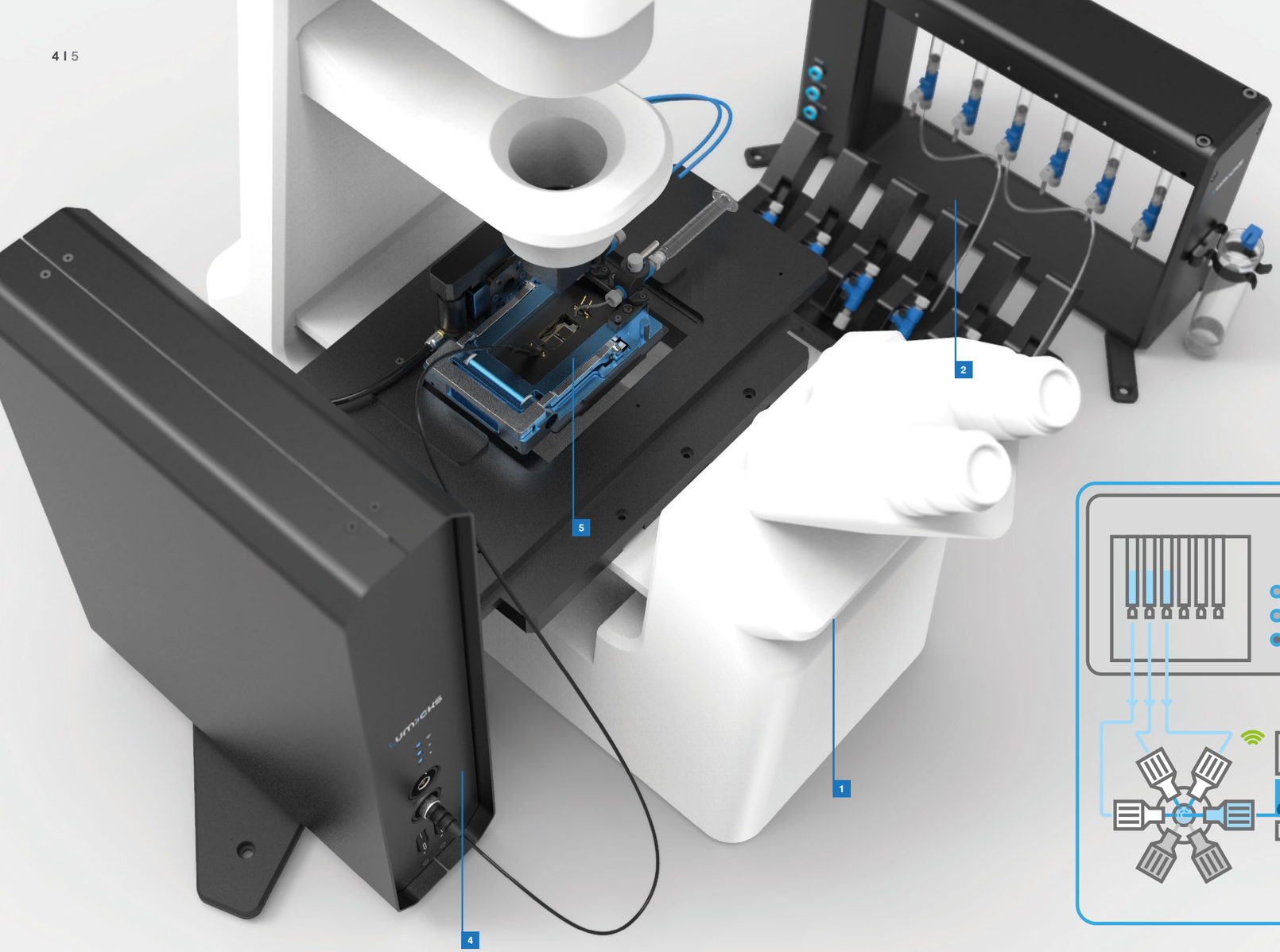
Working principle

The illustration above shows multiple cells interacting with targets. These targets can be adherent cells — such as tumor cells — or ligands coated to the surface of a chip.

Quantification of the cell-target interaction strength is possible by exerting forces on thousands of cells in parallel and measuring the rupture force at the single-cell level.

Cells interacting with the targets require a certain amount of force to detach from their partners. The higher the interaction strength between the cells and their targets, the higher the force one needs to apply in order to separate them.

Avidity-based sorting of cells can be achieved by gradually increasing the force, while flushing out and collecting the consequently detaching cells. In this way, it is possible to sort sub-populations of cells based on their interaction strength with the specific target.



1 z-Movi: the z-Movi platform can be combined with a large range of inverted microscopes.

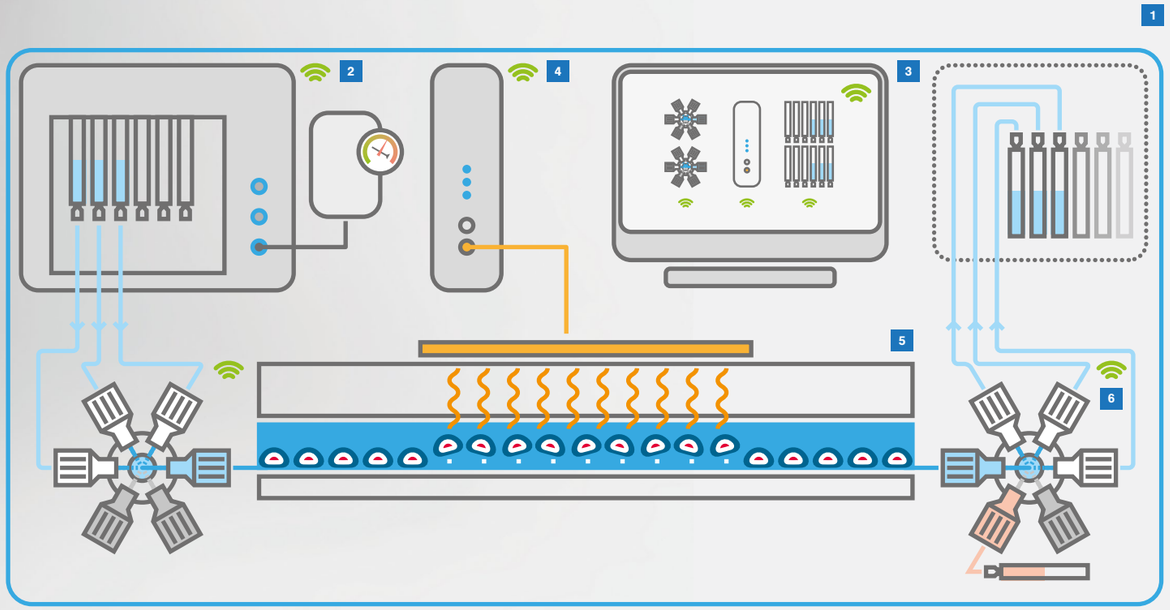
2 Microfluidics: custom-designed, up to 10 different channels that can be individually controlled to create different gradients for effective cell incubation and experimentation.

3 Software: fully optimized and integrated for fluidics control, acoustic forces and sorting of cells.

4 Acoustic force field generator: for the controlled application of highly-precise pulling forces.

5 Chip: lab-on-chip with microfluidic channel, piezo elements and integrated temperature-control.

6 Sorting: fast switching between different collection tubes for the isolation of cell fractions.



The z-Movi™ set-up

The z-Movi is an automated, standardized platform to deliver effective screening and sorting of cells based on their interaction with other cells or ligands.

Explained

The core of the z-Movi platform is the microfluidic glass chip with integrated piezo transducers that create an acoustic force field. This acoustic field effectively applies forces on the cells of interest without the need for any labeling or alteration of those cells.

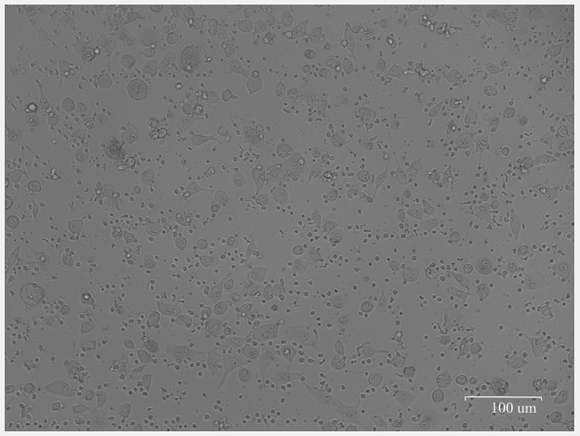
z-Movi includes an automated fluidic delivery system that enables an easy workflow for sample preparation and experimentation. Cell culture and incubation inside the chip is possible in a highly-controlled fluid- and temperature environment, including the option for gas-conditioned fluidics. This enables culturing of target cells in the chip or coating the chip surface with a target biomolecule, under controlled conditions.

By facilitating the use of multiple types of fluids and by creating a gradient from one microfluidic channel to another, it is possible to test different environmental conditions and introduce multiple cells and/or components within one experiment.

The constant fluid flow, together with simultaneous application of acoustic forces, enables sorting of cells based on their target-specific avidity. Because of the non-invasiveness of the z-Movi platform and the use of unlabeled cells, scientists can isolate and collect cells of interest for further experimental use.

APPLICATION EXAMPLE

Screening & sorting of potent T-cells

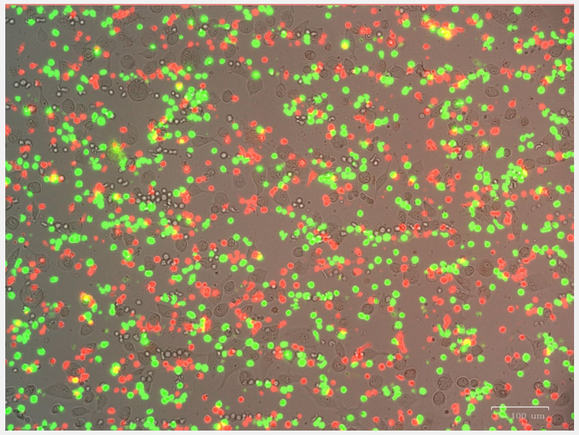


1 Cell culturing

An example of the z-Movi workflow is featured in this data set acquired in collaboration with the Molecular Oncology and Immunology Division of the Netherlands Cancer Institute (NKI, prof.dr. T. Schumacher and dr. W. Scheper) in Amsterdam.

A patient-derived melanoma cell line was cultured inside the chip.

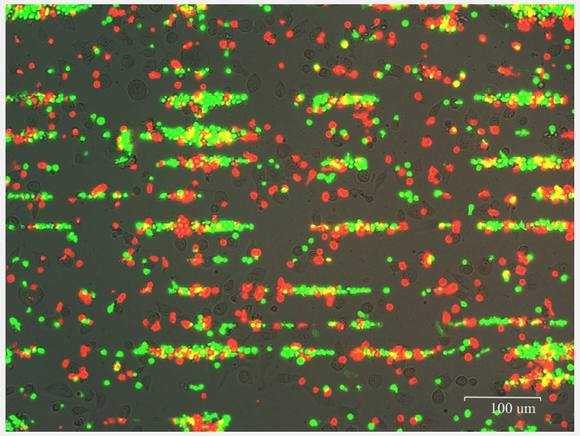
Next, a mix of two different T-cell populations was flushed into the chip.



2 T-cell incubation

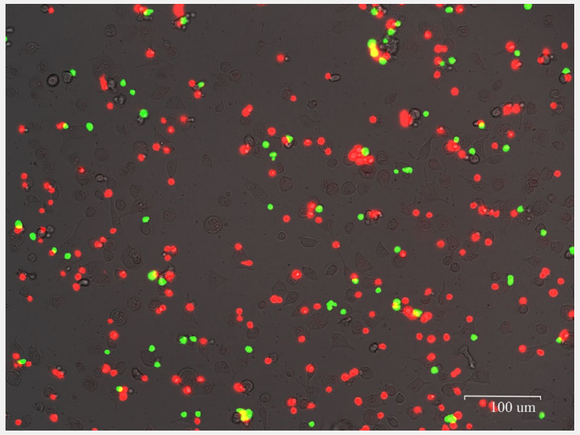
One population of non-tumor specific T-cells (fluorescently stained in green) and a second population of T-cells (fluorescently stained in red) engineered to express a tumor specific T-cell receptor recognizing an antigen presented by the tumor cell line, were infused.

The chip was incubated for 30 minutes at 37 °C to allow tumor cell recognition to occur.



3 Avidity-based sorting

To subsequently select and isolate specifically bound T-cells, an acoustic force was generated and applied on the T-cell sample. Weakly or non-specifically bound T-cells were acoustically levitated upwards forming green horizontal bands.



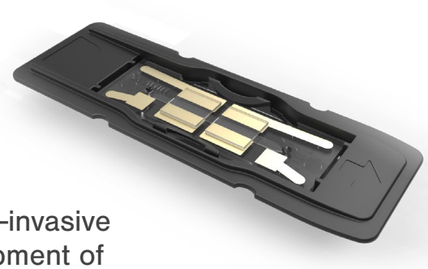
4 T-cell collection

Gentle flushing of the chip allowed the collection of the unbound cells, resulting in an enriched specific T-cell population in the chip. By repeating the experiment at increasing applied acoustic forces it was possible to screen and sort T-cells based on their tumor cell avidity. Subsequently, the tumor-specific T-cells can be collected.

Simultaneously, accurate characterization of adhesion strength can be monitored over time, using dynamic or constant forces.

Discover the power of acoustic sorting

The essence of the z-Movi technology lies in a glass microfluidic chip with a piezo element that generates resonant acoustic waves (ultrasound). These resonant acoustic waves are used to exert forces on cells.

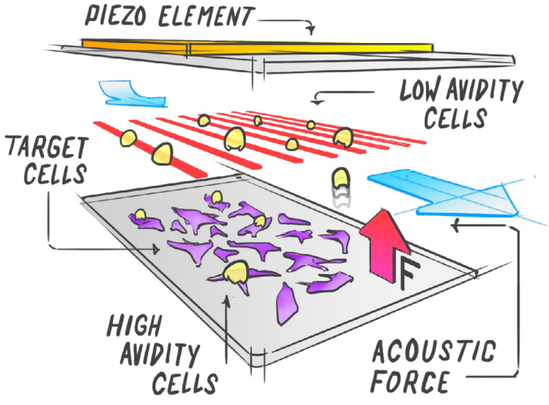


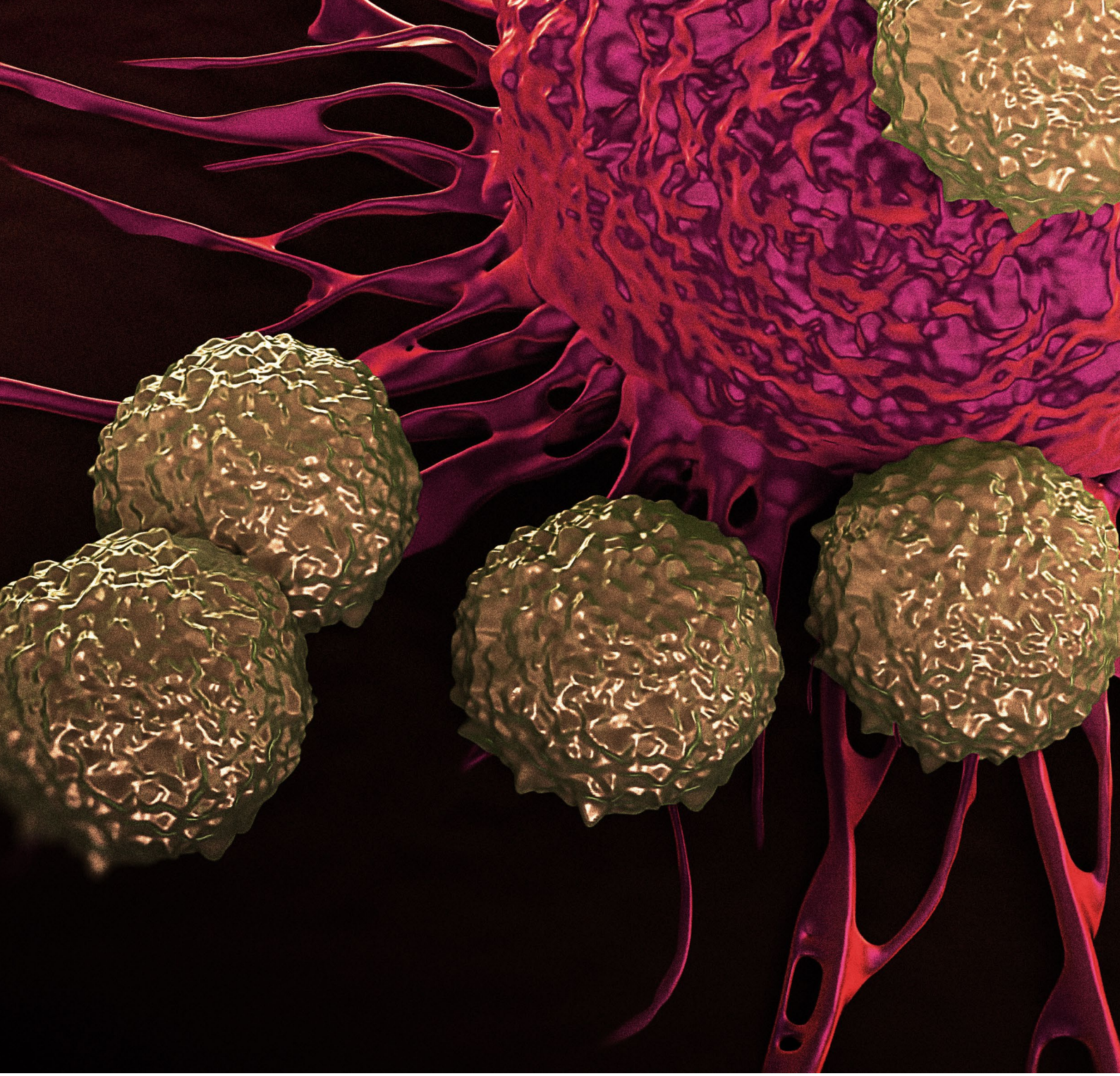
By screening and sorting cells in a label-free and non-invasive manner the z-Movi™ is the perfect tool for the development of personalized immunotherapy approaches.

Illustrative schematic

Target-cells are immobilized on the surface of the chip and cells of interest are flushed into the chip via the microfluidic channel.

The applied acoustic force pulls low avidity cells upwards, detaching them from their targets after which they are flushed out and collected. Higher avidity cells remain bound. Repeating this process with an increasing force allows screening and sorting cells based on their avidity.





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