Miniaturized FISH

Tethis has automated its microFIND™ technology by adapting a Freedom EVO® liquid handling platform with accessories to accommodate the characteristics of this microfluidic device. The resulting system, known as autoFIND-F75, provides an affordable way of performing large scale FISH screening of cytological specimens.

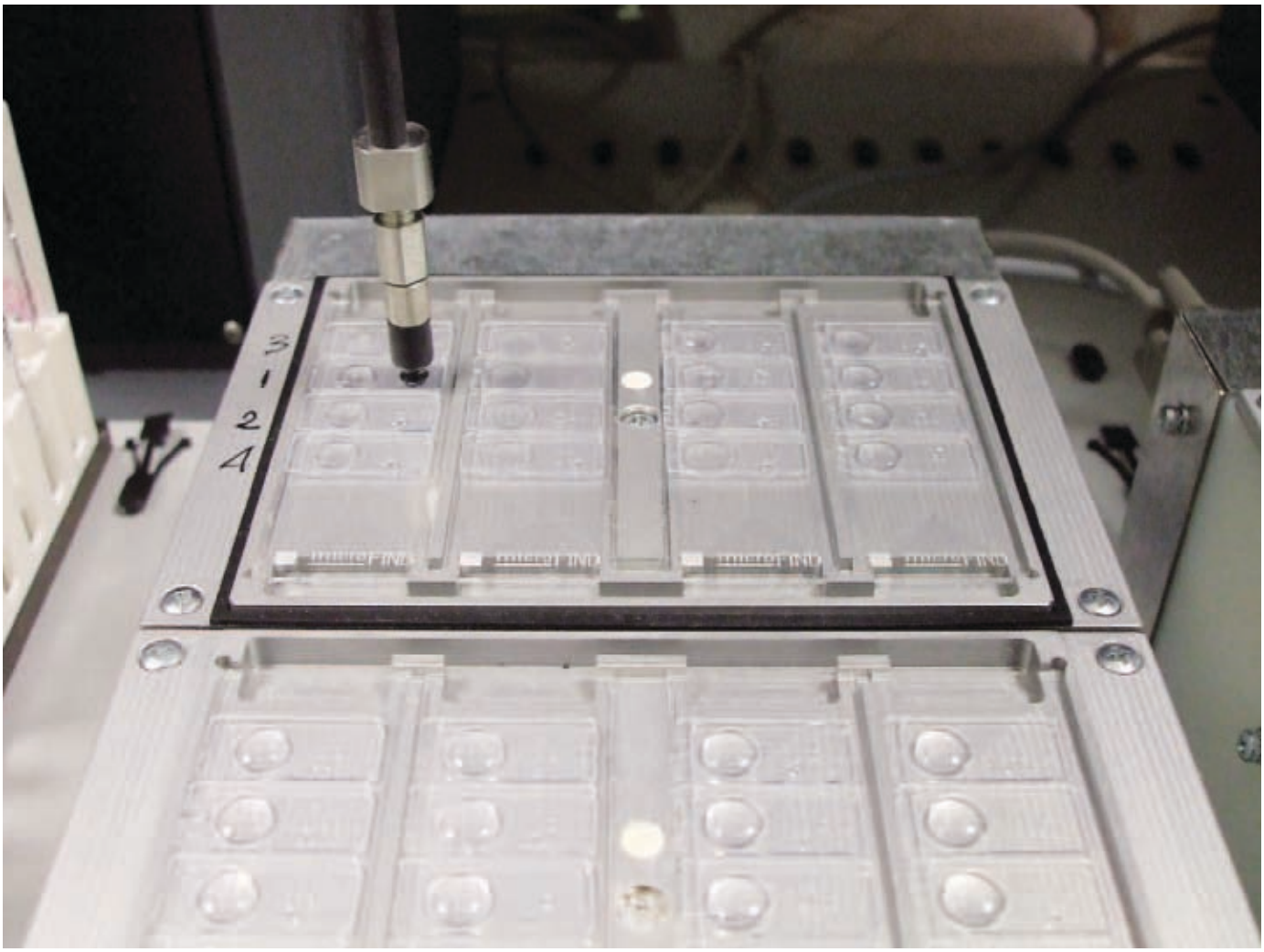
Tethis SpA, part of Genextra Group, is based in Milan, Italy, and specializes in developing new applications for the biotechnology and drug discovery fields using nanomaterials. The Company has recently automated its microfluidic fluorescence *in situ* hybridization (FISH) assay, by customizing a Freedom EVO 75 liquid handling platform to meet the specifications of the microFIND chip. microFIND is a novel miniaturized device for handling cytological specimens, based on state-of-the-art, patented nanocoating technology, which performs miniaturized FISH protocols for the identification of chromosomal aberrations.

Massimo Gatelli, General Manager at Tethis, explained: "The microFIND project evolved from the idea of developing a new technique for FISH, by performing the assay inside a disposable microfluidic device. An important issue to consider when designing a microfluidic assay for cells is the flow of liquid inside the microfluidic channels. The cells need to remain inside the device, but a strong liquid flow tends to detach non-adherent cells unless they have been very well fixed. To overcome this problem, a nanomaterial coating with the capability to firmly attach cells was developed for the inside of the microfluidic device. We use a patented method known as PMCS (pulse microplasma cluster source), which can directly apply nanomaterials to any kind of surface. With microFIND, the film is deposited over a glass microscope slide, allowing us to attach the cells to the slide very tightly, minimizing losses during the assay. The film is completely transparent, so the optical properties of the slide are unchanged and the analytical protocols do not need to be altered."

Rita Fallico checking a slide processed on the automated FISH system

"While developing the microfluidic chip, Tethis searched for a partner to provide the best available liquid handling platform for automation of the assay. We wanted a liquid handling system that could manage everything – the samples, reagents and probes – and chose a Freedom EVO 75, equipped with a two-channel liquid handling (LiHa) arm, as the starting point for automating our FISH assay. Once the Freedom EVO had been adapted with accessories to accommodate the microFIND chip, we had autoFIND-F75, a fully automated system for miniaturized FISH. At the moment, there are a limited number of ways in which laboratories can automate this type of procedure, and these usually result in increased consumption of reagents. autoFIND-F75 fully automates the FISH assay without increasing the cost of the test, reducing the volumes of sample, reagents and probes that are required and producing the processed sample on a glass slide, ready to be placed on a microscope for analysis."

Massimo continued: "The assay also has the ability to process scarce cell samples, which is important in situations where



Fully automated microfluidic FISH analysis

the sample contains only a few cells, for example multiple myeloma. With standard FISH protocols, analyzing this type of sample can be quite difficult, but with our assay it becomes easier and more affordable. Our microFIND technology offers users the unique opportunity to perform FISH assays starting with specimens of living cells, and avoids cytogenetic pellet preparation and manipulation. The nanotech coating sticks even non-adherent cells to the slide surface, which are then processed for FISH analysis. This approach is particularly suitable for situations where the initial specimen contains just a few cells, as it is vital to avoid the loss of cells which occurs during cytogenetic pellet preparation. Using our automated procedure, if you begin with 2,000 cells, you will finish with 2,000 cells, so there will be plenty of cells to analyze."

"Using the autoFIND-F75 system, based on the compact Freedom EVO 75 platform, we can process up to 64 tests per batch, and with the larger Freedom EVO platforms we could obviously increase this further. The initial development period, during which Tethis adapted the hardware, was followed by an in-depth collaboration with Tecan on a number of topics, for example the graphical user interface (GUI) and the optimization of tip positioning parameters to ensure the highest possible reproducible results. Tip positioning is quite critical for microfluidics, where just a tenth of a millimeter is crucial. We are now in the final phase of development, defining assay protocols and working with our customers to validate them."

Emanuele Barborini, Head of Tethis Research, commented: "The microFIND approach to FISH may provide many advantages for clinical laboratories. But however good your product is, you still need to convince the potential users that it will be beneficial to them to adopt the technology, and the product must fit easily into hospital and laboratory routines. Adapting the Freedom EVO platform to accommodate the microFIND chip has allowed us to handle a complex methodology and offer our customers an instrument that provides automated, high throughput FISH, which appears very simple and is easy to use."

To find out more on Tecan's Freedom EVO 75, visit **www.tecan.com/freedomevo75**

To find out more on Tethis and microFIND, visit **www.tethis-lab.com**