Painting Genes in Parallel

Tecan's GenePaint provides multiple, parallel ISH, FISH, or IHC analysis

Knowledge of the tissues and cells that express particular genes is key to understanding gene function. In situ hybridization (ISH), a popular method for deciphering gene expression, is a slow, labor-intensive, error-prone operation that limits parallel investigation of multiple genes and tissues to what may be carried out quickly by hand. These attributes essentially preclude slide-staining efforts from the high-throughput analyses that are so critical to functional genomics research. But a new system from Tecan Group, Mannedorf, Switzerland, could change all that.

Based on an established pipetting robot platform, GenePaint—invented by Gregor Eichele of the Max Planck Institute of Experimental Endocrinology, Hannover, Germany—delivers high-throughput performance for ISH, fluorescence ISH (FISH), and immunohistochemistry. The system’s automated flexibility eliminates 80% of the manual steps of conventional ISH by performing all fixing, staining, washing, and hybridization operations in a temperature-controlled environment. It also integrates specialized reagent kits familiar to molecular biologists (for example, the system handles low-signal samples through a tyramine signal amplification [TSA] kit). The combination of features could make IHC, ISH, and FISH practical and essential tools for functional genomics researchers.

PARALLEL AND AUTOMATED Normally performed on standard glass microscopic slides, ISH requires addition of as many as 50 different reagent and wash solutions, at specified temperature and within a narrow timeframe. Reproducibility is critical for comparing results across a large collection of slides and over several experiments.

“Like most ISH operations, TSA can be done manually,” notes inventor and codeveloper Eichele, “but the process is tedious, and over a large number of slides [it is] very tricky to perform reproducibly. By automating everything, you eliminate the uncertainties of human interaction. GenePaint gives excellent control over critical parameters such as pipetting volume, and incubation time and temperature. In the case of excess binding it’s possible to add wash steps as needed without worrying about the added time. If you tell the machine to pipette an extra 10 times, it doesn’t care.”

ESTABLISHED ROBOTIC PLATFORM GenePaint consists of a Tecan Genesis pipetting robot equipped to allow automated high-throughput ISH slide processing, plus ISH-optimized pipetting and reporting software. GenePaint’s flow-through technology, based on the interaction between gravity and capillary forces, results in very high reproducibility, according to Josef Syfig, a marketing specialist at Tecan.

“Pipetting steps and reagent preheating are performed automatically by the Genesis robot’s eight pipetting tips,” he notes. The flow-through slide chamber is key to GenePaint’s automation capabilities. The chamber, which holds paraffin-embedded or frozen sections on as many as 192 standard 25 x 75-mm slides, protects samples and reagent solutions from physical disruption and desiccation. GenePaint uses hybridization chambers placed on a protruding platform, 48 of which are arrayed within a “thermorack” maintained at ±1°C by an external circulator bath. Depending on the protocol, temperature changes as large as 30°C are achieved in less than 10 minutes.

Tecan’s Gemini software controls prehybridization steps, probe addition, hybridization, temperature, stringency washes with preheated reagents, chromogenic detection, and counterstaining, with little or no supervision. The system simultaneously processes up to four thermoracks, or 192 slides, in one daylong analysis. Depending on slide sample density, researchers can analyze as many as 300 sections per day, which is a throughput level suitable for large-scale genome-wide investigations. For experiments that do not require high throughput, GenePaint offers a manual mode that analyzes up to 10 slides.

BROADENING HORIZONS Eichele conceived of GenePaint about three years ago. The completion of the human and mouse genome sequences were imminent, and he saw that traditional, time-consuming hybridization methods were not up to the challenge of the chromosome- and genome-wide studies that were sure to follow. He realized that automated, unattended pipetting capabilities were required to tame the tedium of parallel ISH experiments. “Early on ... we became aware of the need for specialized hardware and software as well.”

Eichele began serious work on chromosome 21 using a prototype instrument last year. The system’s automated, parallel processing power gave his team access to broader, deeper swaths of gene/protein-tissue space than ever before, allowing them to assess expression of 161 murine genes in nearly 6,500 mouse tissue sections.

“Before GenePaint,” says Eichele, “we simply couldn’t perform this type of work, no matter how much equipment or how many instruments we used.”

For More Information
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—Angelo DePalma