

Deciphering the epigenetic code

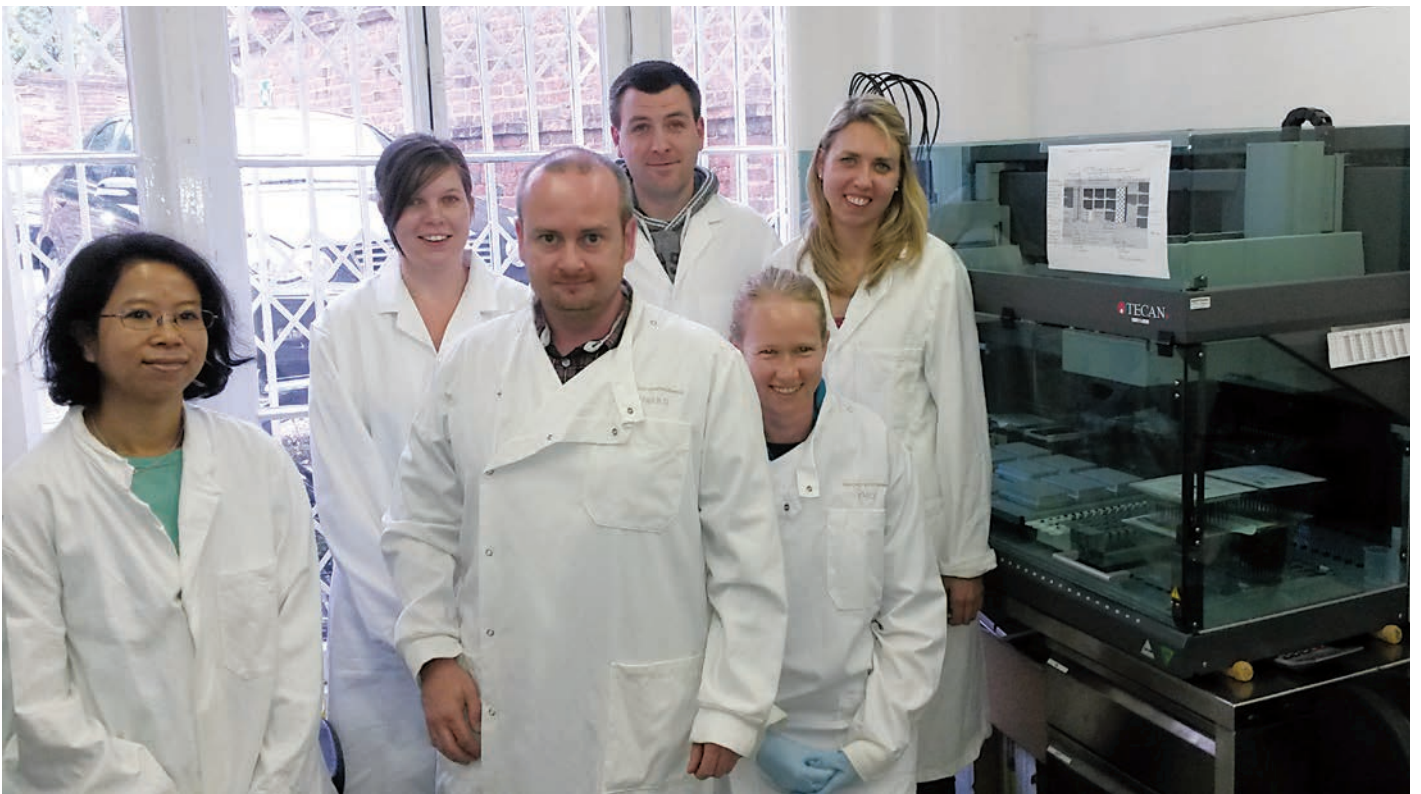
UK-based Oxford BioDynamics has automated its proprietary biomarker discovery platform, *EpiSwitch*[™], on a Freedom EVO[®] 150, helping to establish a NGS, CGH-array and PCR-based pipeline for the discovery of novel biomarkers, as well as a PCR protocol for biomarker-based diagnostic testing.



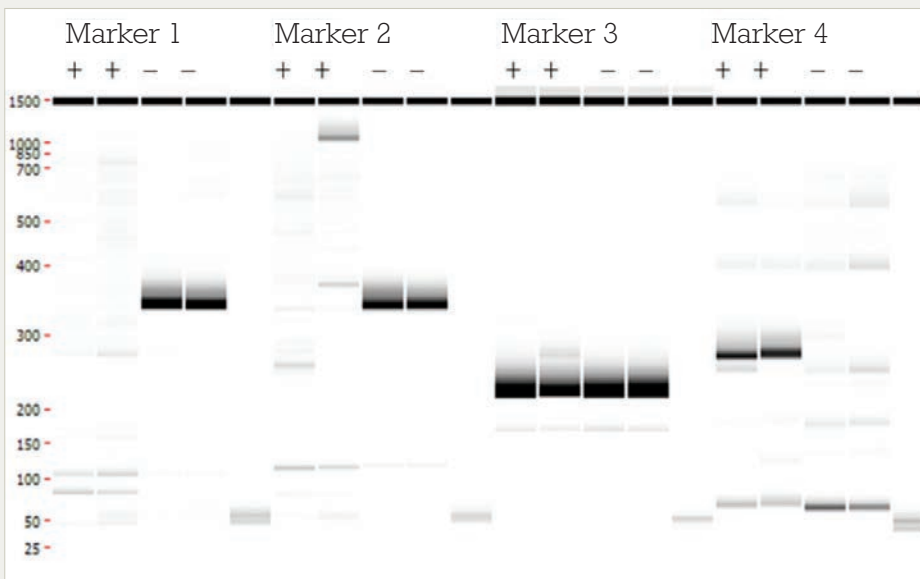
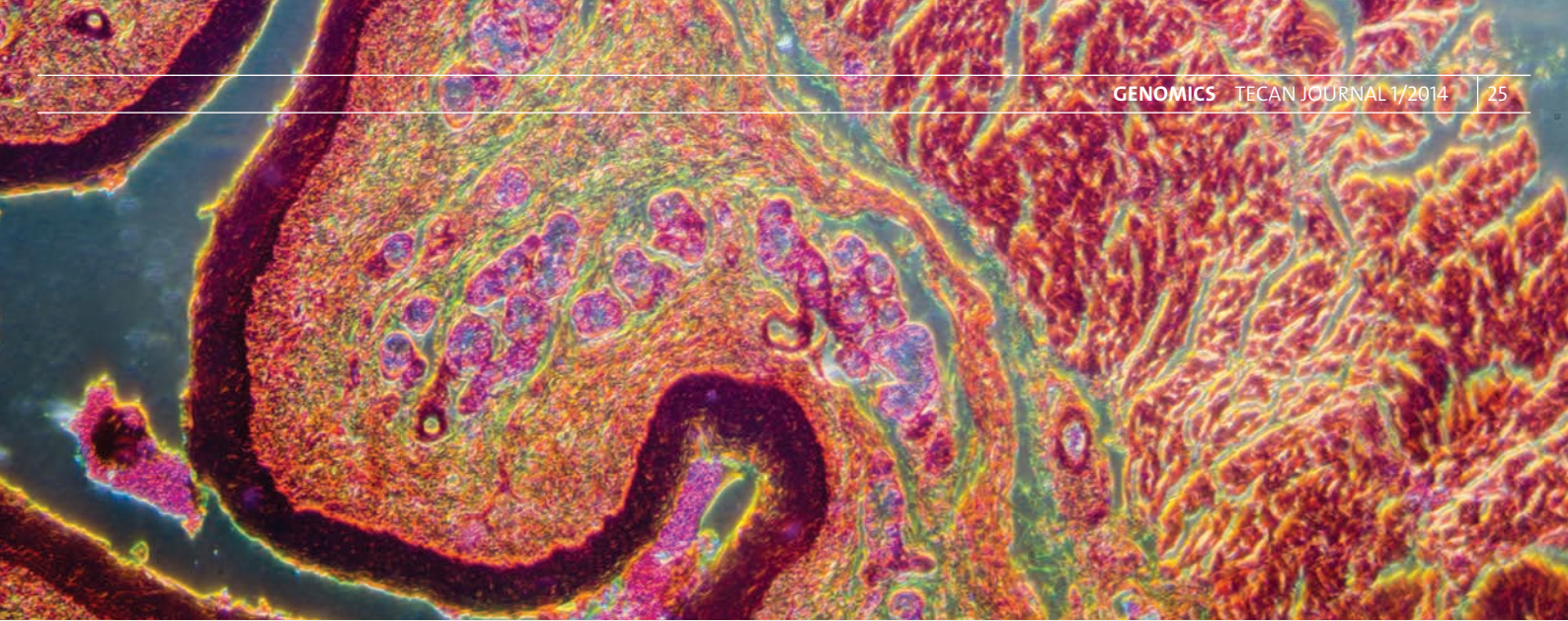
“Automating the *EpiSwitch* process with the Freedom EVO and Air LiHa has improved reproducibility and enabled us to increase our throughput.”

Oxford BioDynamics Limited (OBD), a healthcare service company spun out from the University of Oxford, focuses on molecular biology investigations into gene expression and epigenetics. Its unique *EpiSwitch* platform, based on Chromosome Conformation Capture (3C), enables the discovery, development and validation of epigenetic biomarkers, aiding the identification and further development of biomarker panels for diagnostic and prognostic purposes. OBD has successfully automated its *EpiSwitch* NGS, CGH-array and PCR-based discovery pipeline and PCR test procedure on a Freedom EVO liquid handling system, improving both reproducibility and throughput.

Dr Alexandre Akoulitchev, co-founder and Chief Scientific Officer of OBD, explained: “Epigenetic biomarkers are very informative, providing a clear indication of whether – and how – a patient’s gene expression profile has changed, as well as the progress of disease progression. In cases where objective biomarkers are required to help identify which patients fit into a particular cohort, we use existing knowledge of the epigenetic deregulation of well-known genes to assess whether any informative biomarkers are present. As an extension of our *EpiSwitch* platform, we have also developed a number of applications that involve deep sequencing and microarrays. This allows us to carry out investigations at the biomarker discovery



Howard Womersley (front) and the Oxford BioDynamics team with the Freedom EVO



Screening for epigenetic markers to detect hepatocellular carcinomas. Diseased individuals are marked with +, healthy donors are marked with -; The sizes of markers 1-4 are 328bp, 324bp, 213bp and 261bp respectively. The electrophoresis was done on a PerkinElmer LabChip GX

stage in an unbiased manner, looking at quite complex disease phenotypes where very little information is available. This approach allows us to identify and filter out specific information about deregulation at the epigenetic level. By combining individual biomarkers and powerful statistical tools, we can develop biomarker panels that deliver good cross-validation with clinical results.”

“When developing this technology, we paid particular attention to compliance with industry-standard procedures, and so our methodology has been carefully designed and perfected. Our ISO-certified reference laboratory, based in Oxford, is responsible for R&D and quality control, as well as the transfer of technology. This enables us to provide customers with a fully validated set of biomarkers, together with a technology that can be licensed and used in house for either diagnostic or prognostic testing in

hospitals and clinics, or for high throughput screening in the pharmaceutical industry.”

Automation is fundamental to the OBD business model, and the Company recognized the importance of developing processes that are efficient and cost effective in a low throughput diagnostic laboratory, but which can also be easily scaled-up and translated onto an automated platform for high throughput applications. “At any one time, we will have several ongoing projects, and flexibility is essential to enable us to switch between them as and when necessary,” said Chief Operating Officer Dr Phil Jordan. “Initially, most projects involved manual processing of quite small numbers of samples but, as we progressed further, we needed methods that offered better reproducibility and higher throughput. Automation was clearly the answer, and we acquired our first liquid handling system – a

Freedom EVO 100 – in 2010. Even then, it was obvious that we would eventually need higher throughput still and, two years later, we invested in a Freedom EVO 150, which enables us to look at roughly 600 markers a day.”

Dr Howard Womersley, Associate Director, Platform Development, added: “We looked at a number of liquid platforms before settling on a Freedom EVO 150 equipped with a MultiChannel Arm™ 96 and an eight-channel Air LiHa, controlled by Freedom EVOware® software. The system is faster than the other platforms that we looked at, and its versatility allows us to switch between different types of labware – 96-well plates, PCR tubes and 50 ml tubes – while its Air LiHa gives us the pipetting accuracy we need over a larger volume range, from 1 to 1,000 microliters. Our requirements change on a daily basis, and the Freedom EVO gives us the flexibility to cope with a dynamic workflow, changing between R&D applications and biomarker screening. Freedom EVOware is quite impressive too; it can do pretty much everything you need, and the scripts can be as simple or as complicated as necessary.”

Dr Akoulitchev concluded: “EpiSwitch is a unique assay looking not just at ordinary DNA and PCR products, but at intact epigenetic biomarkers. Automating the process with the Freedom EVO and Air LiHa has improved reproducibility and enabled us to increase our throughput; the system handles this challenging technology very well.”

To find out more about Tecan’s genomics solutions, visit www.tecan.com/genomics

To find out more about Oxford BioDynamics Limited, visit www.oxfordbiodynamics.com