

Unlimited throughput with Tecan and Illumina's combined technologies creates a powerful new toolset for understanding the genetics of complex disease

Illumina, a San Diego (CA)-based company, has integrated Tecan liquid handling workstations into its revolutionary, end-to-end solutions for large-scale genotyping applications. The collaboration has been crucial for the development of a number of products, including Illumina's production-scale BeadLab systems, which were deployed by major investigators world wide as part of the International HapMap Project and, more recently, Illumina's bench-top BeadStation. Both of these platforms offer automated liquid handling capability using Tecan's flexible workstations.

Illumina initially started talking to Tecan to automate the GoldenGate® Assay, Illumina's custom genotyping assay that can multiplex up to 1536 targets per sample. Illumina's microplate compatible Array Matrix processes 96 samples in

parallel and this scale of sample throughput was crying out for automation, so Illumina turned to Tecan for help. Tecan liquid handling workstations can be used to automate the pre-PCR steps or both the pre- and post-PCR steps involved in the assay, streamlining the workflow and reducing the potential for human error. Processing these assays with Tecan workstations combined with Illumina's BeadArray™ Readers, allele-calling software and tied together with LIMS essentially formed the BeadLab systems.

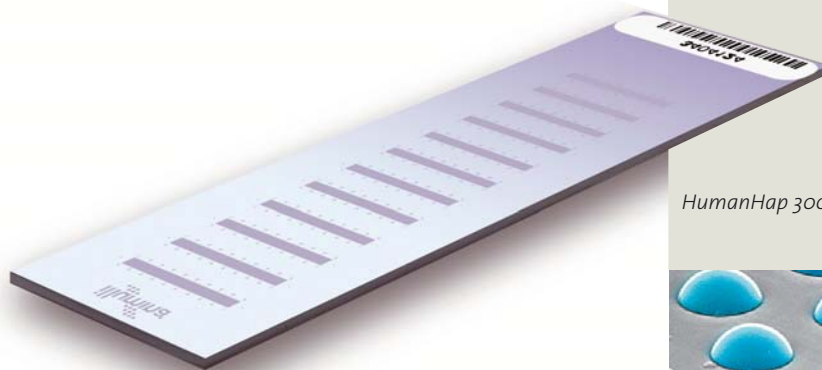
“Many of our scientists had worked previously with Tecan's systems in production sequencing environments,” said Bill Craumer, Director of Corporate and Marketing Communications at Illumina. “They valued the

flexibility of automated, robust pipetting into either tubes or plates with high precision, so it was natural to specify Tecan workstations for our genotyping BeadLab.”

Illumina was both a principal investigator and a supplier of BeadLabs for other principle investigators in the \$100 million International HapMap Project and, by extension, Tecan was a key contributor to the Project's success. Illumina has installed BeadLabs automated with Tecan workstations at virtually every HapMap research center, including the Wellcome Trust Sanger Institute, the Broad Institute, Génome Québec and Japan's RIKEN. The International HapMap Consortium was established in 2002 to develop a haplotype map of the human genome, with the aim of identifying common patterns of DNA sequence variation in the human genome¹. Sets of nearby single nucleotide polymorphisms (SNPs) on the same chromosome are inherited in blocks and the pattern of SNPs on a block forms a haplotype. Although the haplotype may contain a large number of SNPs, only a few SNPs are needed to uniquely identify the haplotype. The HapMap Project has mapped the haplotype blocks and the specific SNPs that identify the haplotypes, which are called tag SNPs. Each institution in the consortium was assigned a certain chromosomal region to map, resulting in large amounts of data that were made publicly available from 2003 onwards² and, in 2005, the completed haplotype map was announced³. The mapped tag SNPs can now be used instead of the ten million SNPs to examine the entire human genome for variation, such as in

BeadStation with Freedom EVO





HumanHap 300

association with a particular disease or phenotype. Depending on the population studied, between 250,000 and 500,000 tag SNPs provide comprehensive genomic coverage, and these large-scale disease association studies are currently ongoing.

Illumina has now deployed tag SNPs on its new HumanHap BeadChips, which can query up to 500,000 different SNP loci on a single microarray. The BeadChips rely on Illumina's Infinium™ assay, which allows interrogation of the human genome at single base resolution without needing PCR or ligation steps. Precise liquid handling is critical to the Infinium assay so, once again, Illumina chose Tecan for automating the application. Tecan worked closely with Illumina to provide the Te-Flow™⁴ flow cell technology on the Freedom EVO® family of workstations to enable parallel processing of 24 BeadChips simultaneously. The Freedom EVO can be used to automate every step of the Infinium genotyping process, offering pre-optimized and ready-to-run protocols, and allowing much more efficient management of large sample numbers. Most HumanHap BeadChip users have at least one Freedom EVO with a modified robotic manipulator (RoMa) arm to help achieve higher sample throughput and allow LIMS integration for positive sample tracking.

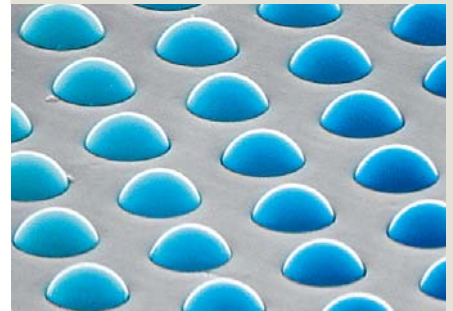
“A key driving force behind this strategic partnership was to deepen our understanding of customers’ needs and provide the technology they really want,” explained Christoph Beck at Tecan. “Illumina was able to successfully automate the Infinium assay with BeadChips by combining our high precision,

robust liquid handling technology with the Te-Flow cell flow technology. At Tecan, we can provide customers with access to our instruments’ application programming interface, and this made it much quicker and easier for Illumina’s developers to integrate the workstations into their own software environment, and tailor the instruments’ performance to exactly meet requirements.”

As a result of Illumina and Tecan’s combined technology, researchers can now routinely generate millions of genotypes per day. “Reliability and quality are critical for our customers, and the fact that Tecan’s workstations integrate so nicely into a LIMS-controlled environment for all required production capacities is really important,” said Bill.

“Over the last five years, Tecan’s relationship with Illumina has evolved from that of an equipment supplier to a highly strategic collaborator, and Tecan has provided essential value to Illumina and to our customers,” added Alex Chan, Illumina’s Associate Product Manager, Systems & Software.

Illumina has also started offering Tecan’s Freedom EVO workstations as a standard upgrade to bench-top BeadStations for users that want the automated, liquid handling capability for smaller scales of throughput. In the future, Illumina anticipates incorporating Tecan automation options with its gene expression applications.



Illumina’s beads-in-wells technology. The 3 μm features are the smallest in the microarray industry

Illumina’s BeadArray technology

The BeadArray technology involves the random assembly of oligo-coated 3 μm beads into wells etched into one of two different substrates:

- 1) the 96 sample Sentrix Array Matrix (which was standard for the HapMap Project), where each array is composed of 50,000 fiber optic strands
- 2) the Sentrix BeadChip, designed for denser, whole genome applications. The BeadChips are available in six different configurations and can contain up to 12 million beads (or features) each, and every feature is represented on average over 30 times, providing really high confidence calls

References

1. The International HapMap Consortium (2003) The International HapMap Project *Nature* 426: 789-796
2. International HapMap Project <http://www.hapmap.org>
3. Altshuler D, Brooks LD, Chakravarti A, Collines FS, Daly MJ, Donnelly P & International HapMap Consortium (2005). A haplotype map of the human genome *Nature* 437: 1241-1242
4. Patented Te-Flow technology is exclusively distributed by Tecan Switzerland AG

For more information, please visit:

<http://www.hapmap.org>

<http://www.illumina.com>

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