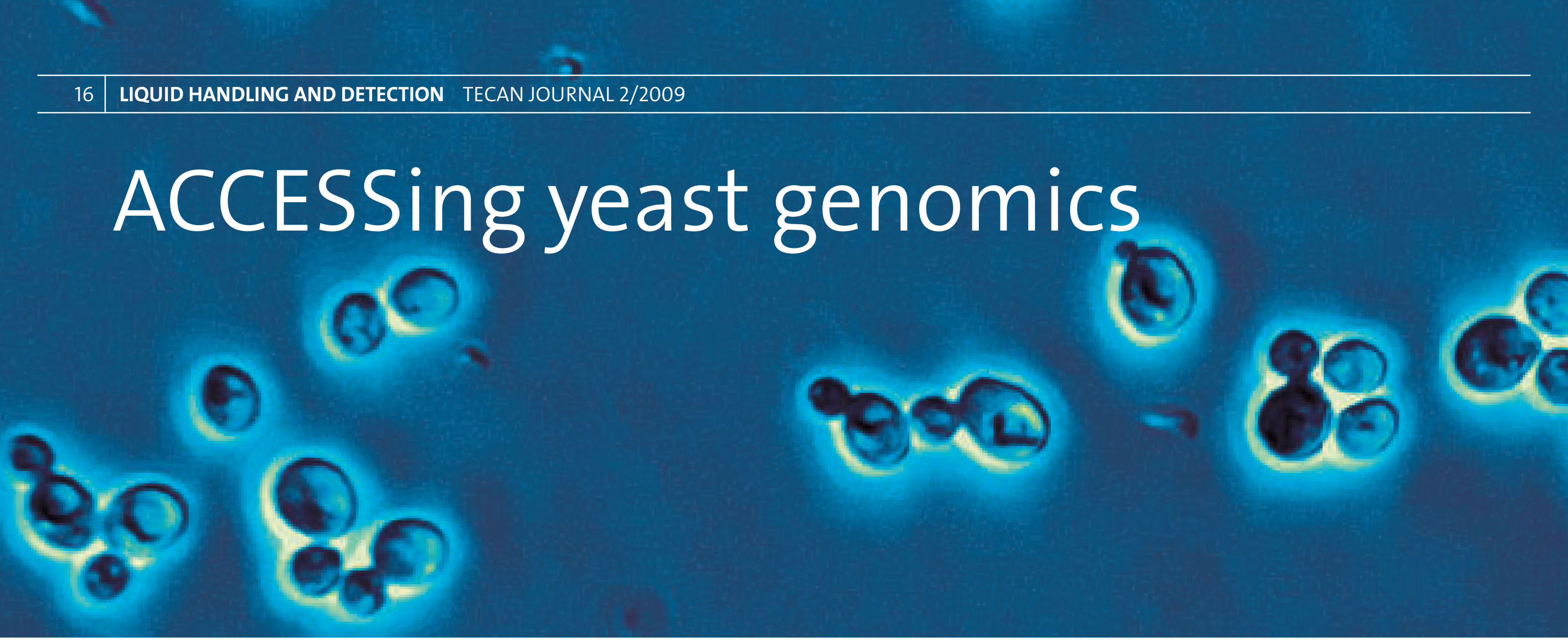
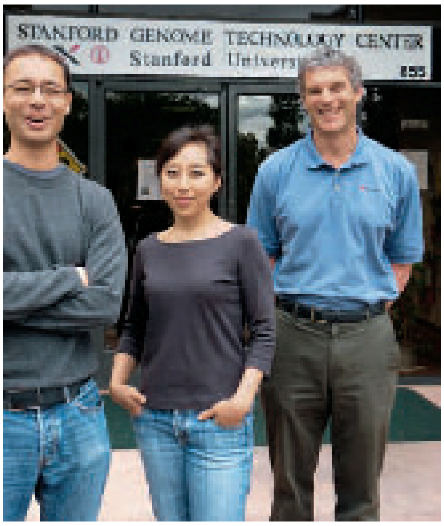
ACCESSing yeast genomics



Tecan systems are providing an integrated solution to researchers at Stanford Genome Technology Center for the study of yeast genomics. The laboratory's ACCESS robot project is combining several Tecan technologies to develop a fully automated platform for phenotype analysis.



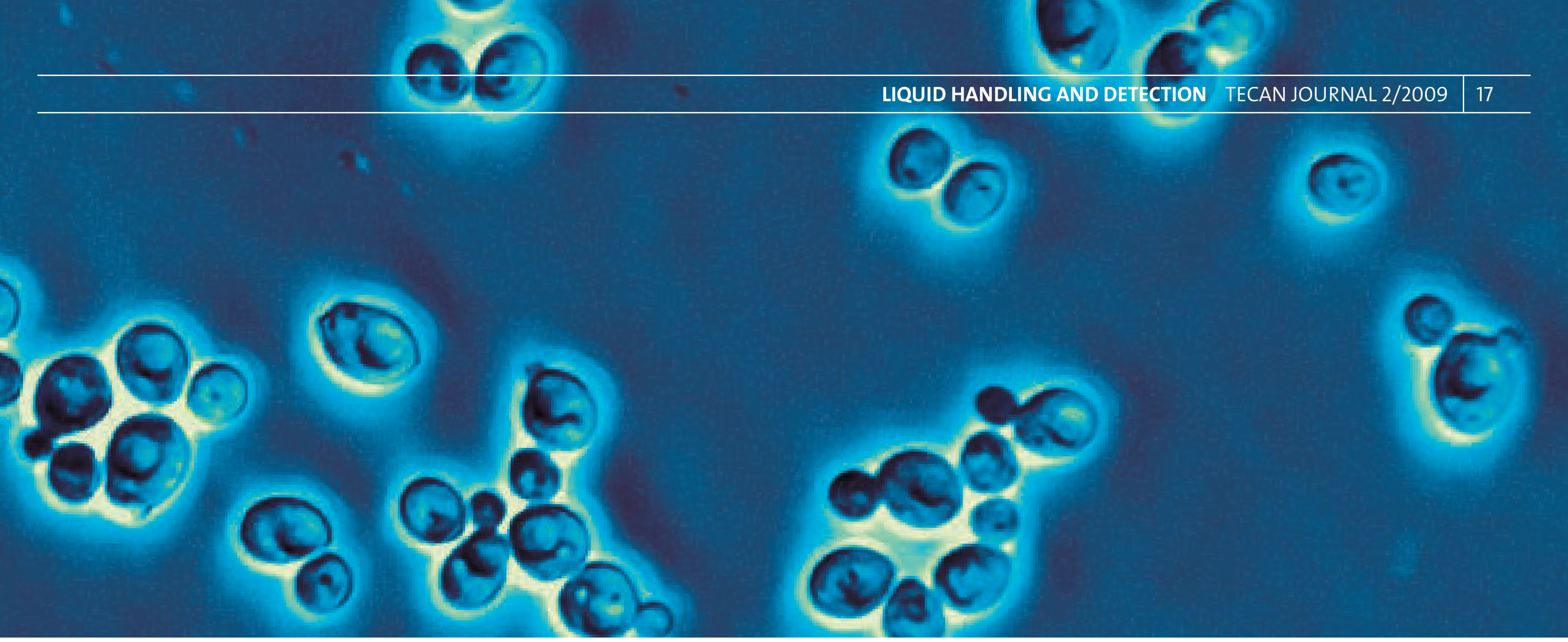
l to r: Ulrich Schlecht, Julia Oh and Michael Proctor.

Although the yeast genome is relatively small in comparison to higher eukaryotes, this 'simple' system is still comprised of nearly 6,000 genes spread across four chromosomes and its study is very relevant to the understanding of complex cell biology. The Genome Technology Center at Stanford University in California, USA, in collaboration with the University of Toronto, Canada, has a strong research interest in the functional genomics and chemogenomics of yeast, and is developing powerful tools to assist in the investigation of this model organism. The Center currently has several yeast research projects running, including establishing a growth phenotype for every gene in the genome, reciprocal hemizygosity studies (to characterize complex multi-gene phenotypes) and screening libraries of small molecules for compounds affecting yeast phenotype. Such ambitious projects require high throughput genetic techniques, and the Center is at the forefront of developing new genomic technologies including an automated cell, compound and environmental screening system (ACCESS) robot for haplo-insufficiency and over-expression profiling in yeast(1, 2), as well as high resolution phenotypic analysis of other single cell organisms.

Dr Michael Proctor, a research and development scientist at the Stanford Genome Technology Center, explained their investigations: "Our laboratory's work, in association with our collaborators Dr Robert St Onge from Stanford, and Dr Guri Giaever and Dr Corey Nislow from Toronto, is focused on establishing the functional genomics of *S. cerevisiae*, using a combination of chemogenomics and knockout mutants to establish the phenotype associated with up or down regulating any given gene. Phenotypes are often quantitative and influenced by multiple genes, so it is important for the data we generate to be robust and reproducible, and this is where automation is a great advantage. Another advantage of automation is that it allows the development of experiments which would otherwise be too complex or error-prone to be run routinely."

"For a number of years we have been developing the ACCESS platform to eliminate many of the manual steps of plating, growing, screening and data analysis of yeast cultures in liquid medium. This has resulted in much higher resolution data and improved reliability, and we are now able to identify very small changes in the growth curves of our yeast cultures. Our latest system is based around a Freedom EVO® 150 liquid handling workstation, integrating incubator shakers, plate readers and pipetting stations to allow inoculation, re-plating and saving samples to a cold station. This system is designed to be extremely flexible, allowing multiple users to run different assays in parallel for maximum productivity. The Freedom EVO's RoMa arm transports microplates between the various devices, and the LiHa arm performs inoculation steps as necessary."

"We have multiple temperature controlled plate shakers and a Safire²™ microplate reader arranged on our Freedom EVO platform, and are currently evaluating an Infinite® M1000 microplate reader for integration into the ACCESS system. This platform provides us with a high throughput capacity, enabling many cultures to be grown and monitored in parallel. We also



have three non-liquid handling versions of ACCESS, for pre-screening and inhibitory concentration (IC) assays. These systems have up to seven Tecan microplate readers, which offer excellent condensation dissipation and temperature control characteristics. We run a combination of assays at any time, with 2,000 samples a day on average, although this is well below the capacity of the system using 384-well plates. When we first began using Tecan readers we used 24-well plates, but quickly progressed to 48-well plates. We now use a combination of 48- and 96-well plates for most of our screening work, although we have also achieved a high level of success with 384-well plates. One of the greatest benefits of Tecan's microplate readers is that they are not restricted to one plate format. You can use any plate type, and there is the option of scanning the plate and defining the parameters automatically using pre-set or customized protocols stored in a database, giving almost infinite flexibility."

"Operation of the ACCESS platform is controlled by LabVIEW™ software which has been developed in-house. This coordinates with our LIMS system, also developed in-house, and with the workstation's Freedom EVOware® and the microplate reader software. It also schedules tasking of the instruments, and coordinates analysis of data. This approach simplifies complex pipetting operations for the user, and offers us the facility for rapid sequential measurements of optical density, fluorescence and luminescence as required. The software is also capable of automatically determining several growth parameters, autonomously governing inoculation, addition of screening compounds and storage of samples. The LIMS is capable of large scale analysis and coordination of data and assays. This enables the ACCESS platform to run many multi-step, multi-plate assays with just a few barcode scans of the instruments, source and growth plates. "

"We have now been using Tecan instruments for over nine years, and over this time we have expanded our set-up to include more and more Tecan equipment, enabling us to very successfully increase the magnitude of our project. In total we have close to thirty Tecan instruments – spread over three laboratories in the USA, Canada and Germany – and these have been very reliable workhorses, shaking and reading every 15 minutes, 24 hours a day and running almost constantly as the ACCESS platform has developed over several years."

The Freedom EVO platform at Stanford University.

Acknowledgements

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1. Giaever et al (2004). Chemogenomic profiling: identifying the functional interactions of small molecules in yeast. *Proc Natl Acad Sci USA*, 101 (3), 793-8.

2. Hoon et al (2008). An integrated platform of genomic assays reveals small-molecule bioactivities. *Nat Chem Biol*, 4 (8), 498-506.