Automation standardizes single-cell assays

Chemical engineers in Cambridge, MA, USA, are using HS 400™ Pro Hybridization Stations to study heterogeneity in populations of cells, characterizing single cells to help understand inter-individual variability in immune response and responsiveness to clinical treatments.

Dr J. Christopher Love, an assistant professor of chemical engineering in Cambridge, MA, is investigating ways of measuring characteristics of single cells in large cell populations. Research into the heterogeneity of cell populations is expected to help vaccine and drug development; understanding how genetically identical cells vary within a population, and identifying the underlying mechanisms, is critical for successfully bio-manufacturing therapeutic substances. Dr Love explained the involvement of his team of engineers in biological projects: "One aspect of chemical engineering is about understanding how to make products from molecules and how to engineer the processes that accomplish that task. In pharmaceuticals today, this means the manufacture of therapeutic substances that are biological molecules, such as enzymes and antibodies, using traditional chemical engineering approaches. The cells that produce these molecules are critical to the whole manufacturing process, so it is necessary to be able to characterize the cells as well as the final product. In our laboratory, we also aim to understand more about the diversity of the immune cells that contribute to autoimmune disorders such as diabetes or multiple sclerosis, or those that battle chronic infections like HIV. We collaborate closely with a number of local clinical laboratories in this research on human immunology, and for developing diagnostic tools for allergy. For example, we are working with a newly-formed institute here in the US, using cutting-edge technologies to develop a vaccine for HIV."

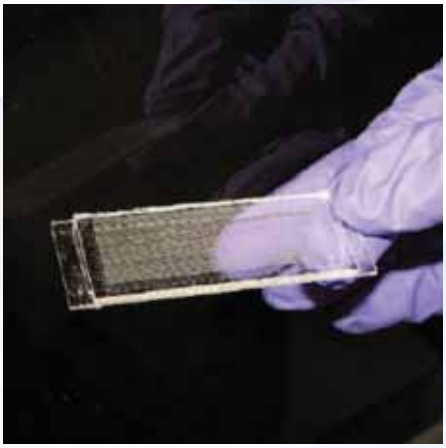
Dr Love continued: "Early in 2008, as we started to explore how to better characterize immune responses so that we might have a better understanding of how vaccines work, we decided to standardize all of our routine steps, including washing slides and processing data, to ensure that results from successive experiments are comparable. To help us achieve this goal, we chose two HS 400 Pro Hybridization Stations. These systems are critical in all the projects that involve the single-cell technologies we have developed. In a typical experiment, we isolate and analyze large numbers of individual cells. Our platform consists of a specialized rubber chip containing a grid of 100,000 individual wells, each

Christopher Love and Navin Varadarajan. The photos are courtesy of Melanie Miller.

able to hold about one cell. To study a population of cells, such as those used in bio-manufacturing, or white blood cells from a clinical sample, the cells are loaded onto the chip and evenly distributed. Molecular secretions from the cells are transferred from the rubber chip onto multiple glass slides – like a miniaturized version of intaglio printing for copper plate etchings – and the slides are analyzed for different cell products. The results resemble a protein microarray in appearance, but the spatially encoded information reveals the function of the individual cells that it maps to. As a recent example, we have been measuring cytokines from cytotoxic T-cells, as data in the literature suggest that cells secreting multiple cytokines respond better to HIV-infection than those producing only one cytokine, helping to prevent HIV infection becoming full-blown AIDS. We can now measure four different cytokines secreted from the same cell, allowing us to start studying T-cell profiles in rare 'elite controllers', people that have HIV but don't progress to AIDS, at the single-cell level."

"We simply insert the slides into the hybridization station chamber for processing, through washing, fluorescent reagent addition and post-washing steps; the HS 400 Pro systems really help us to maintain consistent quality of these printed assays. We have enough variability in clinical samples without having to deal with variations in the assay itself. The systems allow us to run eight slides in parallel, and are being used by students and researchers daily. The hybridization stations also help to automate and improve our workflow, so that we can leave the system unattended to get on with the other parts of the assay, knowing that conditions and methodology are always standardized. This is our first experience with Tecan, and the service has been very good."

For more information on HS Pro, please visit **www.tecan.com/hs400**



Molecular secretions from single cells are transferred onto glass slides, which are analyzed for different cell products.