

Sample management for pharmaceutical research in Japan

Pharmaceutical research scientists at Japan Tobacco Inc. (JT) rely on Tecan's Genesis RWS™ workstations and REMP Tube Punching Module™ (TPM) for their sample management, to handle the enormous number of compounds with pharmaceutical potential that are being studied in their laboratory.



JT researchers (from left to right): Hiroshi Sahara, Nobuko Fujimoto, Miwa Kamabe and Akira Ohta

“ We evaluate hundreds of thousands of compounds for their effect upon a target molecule ”

No longer just a tobacco company, JT in Tokyo, Japan, has three pillar business operations of tobacco, foods and pharmaceuticals. Since 1987, JT has been striving to build a distinctive research and development-driven pharmaceutical business of international recognition, aiming to create original drugs for a variety of fields like diabetes, lipid metabolism, immunology, inflammation, viral diseases and bone disorders.

Senior researcher Dr Akira Ohta manages compound samples for seed discovery, where he and his colleagues are working on the early stages of drug discovery and are responsible for the management and supply of compounds. “We are searching for seed compounds; substances with specific or unique effects upon potential target molecules, like enzymes, receptors and functional proteins or protein-protein interactions,” explained Dr Ohta. “To

find these compounds, we first evaluate hundreds of thousands of compounds for their effect upon a target molecule and, from these, a few thousand are selected for further tests. This second round of evaluations involves different tests, using different concentrations to study dose response, and tests to determine whether there is specificity to the target. These tests require a larger amount of the compound solutions of a greater volume, or of a higher concentration, are prepared and stored to be called up when required. The process of repeated evaluations continues on each compound over several rounds to narrow our focus, selecting substances with special effects from a large starting number, and eventually reducing this to 20 or 30 seed compounds. Once a few seed compounds have been identified, many related compounds are synthesized, and those which are considered suitable for pharmaceutical applications are selected for further development.”



JT's Central Pharmaceutical Research Institute in Osaka



Genesis/TPM/Carousel set-up



Close-up of TPM in the Genesis

Dr Ohta's group has two Genesis RWS workstations in the laboratory – one equipped with liquid handling modules to dissolve and aliquot the compounds into individual tubes, while the other uses an integrated robotic manipulator (RoMa) arm to transport racks of tubes to and from the Tube Punching Module, and Tecan's Carousel HS™. The TPM cherry picks the compounds by punching out the required tubes from Source Tube Racks (STBR) and into Destination Tube Racks (DTBR), and the DTBRs are stacked in the Carousel to be taken away and used for the evaluation of the compounds. The group uses REMP's 384 Tube Technology™, which comprises 384 individually sealed tubes, secured within one tube rack. The compound solution is dispensed into each of the small, 40 µl tubes, which are then heat-sealed and stored. Dr Ohta explained why he is particularly pleased with this set-up: “Integrating the 384 Tube Technology into our workflow was straightforward,

and was an economical use of our funds. This system helps to minimize the absorption of moisture during the cherry picking step, improving the quality of the compound solution. Our standardized procedure involves dissolving the compounds in dimethyl sulfoxide (DMSO) which is highly hygroscopic and can be affected by water vapor in the air; water absorbed by the DMSO causes the dissolved compound to precipitate. Before we started using the 384 Tube Technology, precipitation of the compound for this reason was common in the DMSO solutions, and resulted in a lower level of activity in the cherry picked compounds compared to original activity levels. Now, with the 384 Tube Technology, the DMSO solution of the compound is sealed within small tubes and directly transferred to the DTBR using the TPM; compound precipitation is kept to a minimum and the related loss of activity of the compounds has been virtually eliminated.”

“The Genesis/TPM system is extremely easy to use, and one person can control the process just by pressing a few buttons or clicking on the PC monitor with the mouse. Although the installation area is relatively small and it occupies minimal bench space, the system is now able to pick hundreds of tubes in an hour. Using an automated and barcoded system such as this for so many plates is essential to eliminate the human error that would be inevitable if we attempted to handle this kind of throughput manually.” Dr Ohta concluded: “For the future, we are looking for a system capable of storing the compounds frozen in the STBR with direct, automated access, and of a size around REMP's Small-Size Store™ (SSS) or Mid-Size Store™ (MSS), for even greater efficiency in our sample management. The recent merger of Tecan and REMP gives us even greater confidence that we will receive an integrated maintenance and technical service for our instruments.”