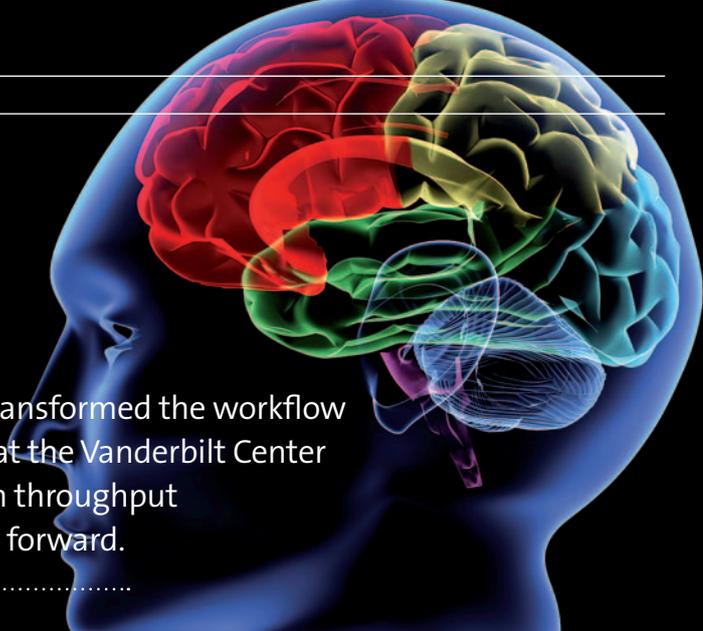


The right tools to drive drug discovery

A Freedom EVO® 200 dedicated to ADME screening has transformed the workflow of the Drug Metabolism Pharmacokinetic (DMPK) Group at the Vanderbilt Center for Neuroscience Drug Discovery (VCNDD), creating a high throughput contemporary ADME facility that is driving drug discovery forward.



Scott Daniels, Director of the DMPK Group

As the name suggests, the DMPK Group in the Vanderbilt University Medical Center Department of Pharmacology's Center for Neuroscience Drug Discovery focuses primarily on targets aimed at treating neurological disorders, such as Parkinson's Disease, Alzheimer's Disease, schizophrenia and various diseases of cognitive impairment, as well as Fragile X Syndrome, a leading genetic cause of autism, and anxiety disorders. The Group has a special interest in modulating metabotropic glutamate receptors and muscarinic receptors to potentially treat these neurodegenerative and neurocircuitry conditions with greater therapeutic benefit and fewer side effects than current therapies. For this, and other similar projects, it partners with several companies and organizations also working in these areas and is heavily involved with the National Institute of Mental Health and NIH's molecular libraries program (MLPCN).

In 2010, with the transition to three lead optimization programs, the workload of the DMPK Group was approaching a critical level and inevitably errors in manual handling and throughput were an issue. In order to tackle the high throughput nature of some of the assays, plans were put in place to build a contemporary drug metabolism facility. The laboratory was already equipped with some automated pipetting systems, but these were not capable of achieving the necessary throughputs and the experimental integrity – consistent temperatures and consistent shaking – so the hunt for alternatives began. A key consideration was the types of *in vitro* systems routinely used – microsomes and liver S9 fractions – which are of such a consistency that they need to be shaken at just the right RPM to prevent settling and precipitation.

Dr J. Scott Daniels, Assistant Professor of Pharmacology and Director of DMPK for the VCNDD, explained why the Group decided on the Tecan Freedom EVO 200 early in 2011: "Firstly, the instrument is a quality product that is easy to operate and it was competitively priced, which has to be an issue. However, we were also very impressed with how keen Tecan was to work with our laboratory at the ground level, to help us build up our HT DMPK operation. Although many suppliers might promise a high level of customer service, our experiences with Tecan support have so far been exemplary and started before the instrument was even in place. Once everything was ordered, Tecan's first step was to provide our laboratory manager, Ryan Morrison, with software to start writing the programs, with several hours of software support with an application specialist. Ryan was able to build preliminary workflows so we could hit the ground running when the instrument was installed and had it running online very quickly."

Ryan described the system the Group now runs on a daily basis: "We have a Freedom EVO 200 workstation fitted with three robotic arms – an eight tip Liquid Handling Arm, a MultiChannel Arm™ 96 and a RoMa Arm. On the deck, there is an incubated six-position IKA® shaker that Tecan had customized for us so that it has a really tight radius, plus a Safire²™ microplate reader for a high throughput kinetic solubility assay. There is also an additional incubator, a linear shaker incubator that sits on the back of the deck, and hotel stacks for planned Caco-2 transporter assays. For ease of use, we are using all disposable tips. In the initial stages, I was very impressed with the 3D modeling



Tammy Santomango shows the Group's Freedom EVO, equipped with disposable tips for maximum sample security



3D modeling helps Ryan Morrison to maximize use of the available deck space

software and the 3D renderings of how the workstation would look with all the modules that we would need to run our assays to plan out the space on the deck. Sitting down with the Tecan application specialist and having the time before installation to get used to the programming was really helpful."

"We currently have three high throughput *in vitro* ADME screening assays running on the system: an intrinsic clearance assay, a plasma protein binding assay with RED (rapid equilibrium dialysis) plates, and a cocktail-style cytochrome P450 IC₅₀ assay. We are looking at adding two more assays in the near future and, although the assays are not running concurrently at present, we could very easily run them on the same day if our throughput increased, as laid out on the 3D simulator in the development stages."

Scott continued: "In just one day, our Tecan system can help us screen compounds for their metabolic stability, their extent of protein binding, and whether there is the potential for drug-drug interactions. It has revolutionized our throughput in *in vitro* subcellular work, and we're now looking at its potential in screening at a molecular level."

"Overall, our system is very flexible, very efficient and has tightened up our reproducibility and error rate, saving considerably on compounds, microsomes and FTE time, simply because we no longer need to repeat failed Tier 1 assays. Another big advantage is that it builds in capacity, freeing up time for other bench work, data crunching or the next step of detailed PK Tier 2 assays."

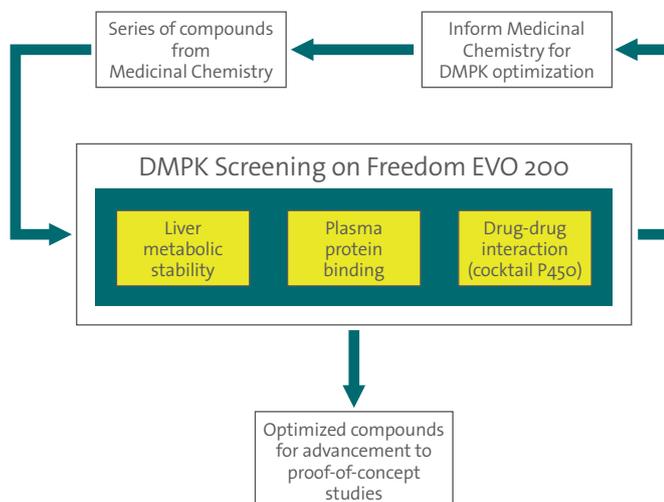
He concluded: "From struggling with single pipettors on the bench, we have progressed to a fully automated linear platform with which we can perform several bread and butter assays every single week to help drive the drug discovery pipeline. That is what we wanted to achieve, to drive the science, and to take risks in novel targets in a way that companies just cannot do given the current economic climate. We had a mission and we tackled it, and Tecan really lived up to its promise, partnering with us to make our facility into an efficient, high throughput contemporary ADME group."

To find out more on Tecan's options for ADME screening solutions, visit www.tecan.com/adme

To find out more about VCND, visit www.vcnnd.com

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Tecan Freedom EVO 200 workflow



The laboratory's workflow is centered around the Freedom EVO's high throughput capabilities