



A Fully Integrated Academic drug Discovery Center

Dr Magid Abou-Gharbia, Associate Dean for Research at the Moulder Center for Drug Discovery Research, explains how the Center's faculty facilitates the transition of academic science into viable clinical candidates and commercial products.

As Big Pharma searches for novel approaches in an ever-more competitive world, the industry is turning to external entities, research institutes and academic centres for help in generating new ideas. One example is The Moulder Center for Drug Discovery Research, which was established in Temple University's School of Pharmacy in 2008 and serves as a multidisciplinary research hub focused on the development of novel therapeutics in an academic setting.

Dr Magid Abou-Gharbia, Associate Dean for Research at the Moulder Center for Drug Discovery Research, is a renowned expert in the field of drug discovery, frequently seen on the speaker-circuit at industry events. *Speciality Chemicals Magazine* was pleased to hear him explain the role of The Moulder Center for Drug Discovery Research where, he said, the faculty and staff have over 250 years of industrial drug discovery and development experience that they use to facilitate the transition of academic science into viable clinical candidates and commercial products.

Moulder Center's mission is focused on:

1. Discovery of new clinical candidates using modern drug discovery techniques and cutting-edge science
2. Education and training of students, postdoctoral fellows, faculty, and future research scientists, in the application of modern drug discovery techniques
3. Collaborative research within Temple University as well as externally with research institutions, universities and the pharmaceutical industry
4. Translational research to bridge the gap between pre-clinical and clinical research by identifying novel tools for translational medicine (biomarkers, imaging ligands).

The Moulder Center maintains a state-of-the-art facility capable of integrating the basic and applied sciences necessary to discover the medicines of tomorrow. Medicinal chemistry is a key component of viable drug discovery programs, and the Center's faculty and staff is well versed in drug design, small molecule synthesis, solid phase peptide synthesis, microwave chemistry, and a host of other enabling techniques. Purification of candidate compounds is facilitated by a range of analytical and preparative chromatography equipment capable of providing milligram to multi-gram quantities of highly pure material for biological evaluation. Compound design is facilitated by advanced computational software including the molecular modeling software packages Benchware and Sybyl and the Dotmatics Informatics Platform (Dotmatics Ltd), high throughput screening data management, structure activity relationship (SAR) analysis, and data visualization.

In vitro screening is another key component of modern drug discovery; the Center has established a high throughput screening (HTS) to the needs of modern drug discovery programs. The laboratory is built around two Janus Automated Workstations (Varipspan and MDT) capable

of supporting 96-well or 384-well platforms using multiple *in vitro* and cellular assay paradigms for the study of enzymes, receptors, ion channels and transporter proteins. The Envision 2104 Multi-label reader provides capabilities to detect diverse platforms including absorbance, fluorescence, luminescence, Alpha Screen and fluorescence polarization. High throughput radiolabel binding and uptake assays are supported with a Perkin Elmer Topcount NXT-HTS Microplate scintillation counter. In addition, label-free methods using LC/MS/MS are routinely utilized for *in vitro* drug metabolism studies. The Center's HTS capabilities are supported by a 40,000 member small molecule diversity-based screening library including linear and cyclic peptides, the Prestwick 1,200 member library of FDA approved drugs, and a 5,000 member library of natural product extracts. A collaborative program with the Natural Products Discovery Institute provides added natural products diversity to our library. Three tissue culture suites support the development of cell based assay and maintenance of cultur/ed cells.

The Moulder Center is also equipped with modern bioanalytical and pharmacokinetics laboratories capable of assessing drug-like properties of candidate compounds using advanced *in vitro* ADME screening systems and sophisticated *in vivo* pharmacokinetic studies. Its *in vitro* ADME assays measure aqueous solubility, chemical stability, stability in physiological fluids, liver microsomal stability, hepatocyte stability, plasma protein binding, microsomal partitioning, CYP450 inhibition, permeability, and cytotoxicity. Small animal *in vivo* pharmacokinetics studies are supported by an array of analytical HPLC/MS system and a fully staffed vivarium capable of housing a wide range of small animals.

The Moulder Center works in close partnership with the school of Proteomics Research Facility which provides accessible proteomics capability for biological and biomedical research. This research facility has state-of-the-art supported by staff with expertise in proteomics, tissue microanalysis and relevant bioinformatics. This facility is capable of conducting expression profiling, protein identification, posttranslational modification characterization, protein and peptide separations, capillary electrophoresis, multidimensional protein identification, and isolation of individual cells from tissues to facilitate studies on the pathogenesis of disease.

The school's cGMP lab is thoroughly equipped with the latest technologies to support and ensure the expert production and packaging of clinical supplies and the manufacture of high-quality solid dose forms. The facility manufactures oral capsules, tablets and powders as well as placebos for clinical trials and is one of only 6 academic cGMP labs in the nation. It provides the Moulder Center with preclinical support for *in vitro* and *in vivo* formulation as well as formulation development for systemic, topical or transdermal delivery.

The Moulder Center for Drug Discovery Research is well equipped to support modern drug discovery programs and is actively engaged in the search for new collaborators. For more information, visit the Moulder Center website at www.moulder.temple.edu.