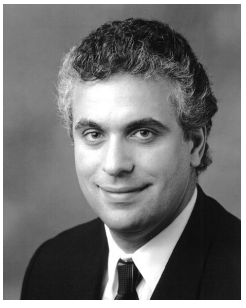
Reaping the rewards



Drug discovery is the subject of unprecedented advances in genomics, combinatorial chemistry, ultra-high-throughput screening and information technology. These technologies promise to discover proprietary validated targets and chemical entities faster and more economically than before. Furthermore, the quality of drugs going into development might improve if profiling of drug candidates, performing *in vitro* substitute adsorption-distribution-metabolism-excretion (ADME)-toxicology and genotyping subjects in clinical studies, is undertaken at an earlier stage.

In their quest for time-based competitive advantage in drug discovery and development, research-based pharmaceutical and biopharmaceutical companies are faced with make-versus-buy decisions. Many companies are choosing the latter and are working with so-called 'tool-companies'. However, it is not enough just to buy the technology, and companies also need to change the way they work and to develop the necessary internal skills to maximize the return on their investment. Furthermore, the risk, expense and demands on management necessary for the new technology may be too much for some companies to maintain and will be key drivers for the industry consolidation which we are currently in. Such companies have the option to minimize that risk and create a competitive advantage by outsourcing key aspects of their discovery programs to service providers that are differentiated by advanced technology. Consequently, those companies without the critical mass to assimilate the new technologies will be able to focus on high-value creating activities such as disease-mechanism elucidation and lead optimization.

The new generation of technology includes assay miniaturization and ultra-high-throughput screening (UHTS), which are featured in this issue of *Drug Discovery Today*. There are several benefits to miniaturization and UHTS:

- greater accessibility to reagent-limited targets
- avoidance of certain types of patent claims (through the use of native receptors in cell lines)
- conservation of valuable chemical libraries
- improved data quality through process improvement
- much faster data generation and manipulation
- significantly reduced running costs.

In order to access these benefits, some pharmaceutical companies have made large investments in collaborations with technology and service providers. UHTS can range from large integrated, centralized systems offering library management through to screening and data management, to simple but powerful bench-top modules. In all these instances, database integration, flexible system control and data analysis are particularly critical for UHTS.

Many of the early concerns about assay miniaturization (such as evaporation and cell growth on a miniaturized scale) have been overcome. Future challenges include the establishment of industrially robust systems. Fluorescence, in its various forms, is firmly established as the standard for miniaturization and has the versatility to accommodate a broad range of cell-based and biochemical assays. It will be desirable for UHTS to be sufficiently flexible and modular to accommodate a range of readers and high-density formats such as 1536-well plates, 3456-well Nanowell™ plates (Aurora Biosciences, San Diego, CA, USA) and perhaps higher-density formats including chip-based screening devices. A frequently overlooked design feature for advanced miniaturization formats, particularly those based on the lab-on-a-chip concept and flow-through systems, is the requirement to interface to large chemical libraries, which are primarily stored in 96- and 384-well plates within automated storage systems. These systems represent a

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substantial sunk cost in capital equipment and infrastructure and are unlikely to be phased out in the near future.

UHTS: the future

UHTS on a miniaturized scale needs more than new technology. This technology must be robust enough for production-scale operation to industrialize drug discovery. One of the most challenging aspects for production-scale miniaturization is the microfluidics required for library reformatting and reagent addition into high-density screening formats at UHTS. I expect that these new capabilities will benefit not only drug discovery screening, but also large-scale genotyping and other diagnostic applications.

As we industrialize and miniaturize screening, we can see the benefits of this process. The technology itself is exciting, but we should not be so seduced by it that we lose sight of the key objectives. Pharmaceutical companies have a wealth of new targets and chemical libraries. The advances in technology, such as UHTS, will help these companies to discover new, safe medicines faster and more productively. Efficient and effective deployment of the technical advances we are witnessing is both a major challenge and an opportunity for both providers and users, as we seek to reap the medical and commercial rewards of the new technologies for drug discovery.

Harry Stylli

Company collaborations…

A research collaboration has been formed between **GPC AG** (Munich, Germany) and **Boehringer Ingleheim** (Vienna, Austria) to focus on discovering new oncology targets and their expression profiles. Under the terms of the agreement, GPC AG is required to utilize its ExpressCode™ technology platform to produce gene expression profiles and functional information on potential targets identified by Boehringer Ingleheim.

A strategic alliance has been formed between **Genset** (Paris, France) and **Algène Biotechnologies Corporation** (Montreal, Canada) for research into Alzheimer's disease. Algène has compiled an extensive collection of clinical samples from Alzheimer's patients to which it has applied gene mapping and statistical analysis platforms. This research has found a number of chromosomal regions that might contain genes associated with Alzheimer's disease. Under the terms of the agreement, Algène will licence both its gene mapping results and its existing Alzheimer's disease-DNA collection exclusively to Geneset. Geneset will then use its integrated genomics technologies to generate proprietary bialleic markers, perform high-throughput genotyping of the complete sample collection, and then analyze the data using advanced biostatistics and bioinformatics.

A co-marketing alliance has been formed by **Amersham Pharmacia Biotech** (Uppsala, Sweden) and **AlliedSignal** (Morristown, NJ, USA) to produce large-scale DNA/RNA synthesis instrumentation to reduce the valuable time and resources of pharmaceutical manufacturers. Under the collaboration, AlliedSignal's Burdick and Jackson facility will provide its suite of high-purity synthesis reagents and solvents for use with Amersham Pharmacia Biotech's OligoPilot™ and OligoProcess™ DNA synthesis systems.

In the September issue of Drug Discovery Today…