introduction

It has become increasingly apparent that very few, if any, of the organisations currently engaged in drug discovery have the capability to sustain a viable level of activity without significant input from others. This applies to large pharmaceutical companies with their discovery groups struggling to meet ever-growing requirements for new additions to development pipelines. It is equally true for smaller pharmaceutical and biotech companies, which often lack resources and expertise to exploit their discoveries by progressing them effectively through the development process. The obvious solution is for alliances of various kinds to be formed playing on the strengths of the partners involved. Many such arrangements are in place, ranging from research collaborations and co-development programmes through to more extensive joint ventures and there is increasing reliance on out-sourcing to contract research organisations (CROs).

Many of these alliances have not been unqualified successes, however. One of the articles in this number of ***DDW*** quotes evidence indicating that of about 700 collaborative agreements that were signed within the pharmaceutical industry between 1997 and 2002 at least one-third of them were deemed to be unsuccessful. The same contributors point out that most agreements between pharmaceutical and biotech companies and CROs are on a fee for service basis. They consider that it would be mutually beneficial if the parties entered into true strategic alliances.

There are many risks inherent in partnerships. We include an article in which these risks are identified and suggestions made as to how they can be minimised. 'Forced marriages' between incompatible partners are doomed to failure. Suitable due diligence by both parties should identify such incompatibilities and give appropriate warning signals. The terms of the deal need to be considered extremely carefully at the outset to minimise the chance of difficulties arising and resentments building thus reducing the effectiveness of the deal or destroying it completely.

Early stage companies, by definition, have little or no experience in partnering and often see themselves, rightly or wrongly, as being at the mercy of their bigger and more experienced brethren. One of our articles in this edition considers in a wider context the problems often experienced by founder scientists in biotech companies as they attempt to make the transition to being business managers.

So far this editorial, like several of our articles, has been devoted to the 'business' of drug discovery. No excuse is made for this – if the business aspects are not right then technological advances will not be translated effectively, efficiently and expeditiously into new medicines.

We have not neglected science and technology, however, and we return to a theme which has been present in several of the recent numbers of ***DDW*** – namely the current difficulties in identifying the most fruitful targets for pharmacological intervention and in choosing the best lead molecules for these interventions.

By far the majority of targets are proteins but the role of proteins in most diseases is not clear. We include an article on functional proteomics, a method for establishing functional links of proteins to disease relevant phenotypes. This has promise as a powerful tool for identifying 'druggable' targets and so to selecting relevant leads.

We also introduce a term new to ***DDW***, namely 'transcriptomics'. This is defined by the author as the discovery of drugs that control disease through the regulation of gene expression. As such, transcriptomics bridges the gap between genomics and proteomics and should, therefore, provide fruitful new drug discovery programmes.

High Throughput Screening (HTS) is still widely used in lead identification and various technological advances have enabled ever larger numbers of compounds to be screened. Even these large numbers do not get near to producing total chemical diversity and there is, consequently, an increasing interest in the use of *in silico* structure-based design which comes in two guises, virtual screening and *de novo* design. These are reviewed in our pages and it is concluded that use of these techniques should reduce the attrition rate at the lead discovery stage and thus lead to a more effective drug discovery process.

A consequence of HTS is that very large numbers of compounds have been generated and have to be catalogued and stored appropriately. Our contributor states that some compound stores are little better than 'broom cupboards under the stairs' whereas stores with appropriate accessibility, integrity and flexibility should form an integral part of the drug discovery process. All aspects of compound management are comprehensively reviewed.

An integral component of some programmes of selection of best leads involves *in vivo* mammalian testing which is time consuming, expensive and controversial. In an attempt to overcome these difficulties some non-vertebrate species like the fruit-fly Drosophila have been used but not with great success. More recently zebrafish have been advocated as a suitable species and, perhaps surprisingly, this fish is ranked by the NIH as the third most important experimental organism after man. Our contributors on this topic estimate that studies cost about one-thousandth of equivalent studies in mice. They review the evidence to support the view that results obtained are likely to be predictive of effects in man.

Finally, we have been carrying reviews on recent developments in a variety of therapeutic areas. In this number we depart slightly from this with an article on therapeutic vaccines. Vaccines have been used for 200 years or so in the prevention of diseases like smallpox but new insights into immunological mechanisms have made the use of vaccines to treat , rather than to prevent, diseases a distinct possibility. Our authors cite melanoma and HIV, for example, as two diseases likely to be amenable to this approach.

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