conference report

efficacy; however, because the gene therapy sector itself has been fraught with difficulties, commercialization is no more certain than with other RNAi strategies.

There are several key RNAi projects in or close to the clinical stage (Table 1). It is interesting to note that the race to be the first to enter clinical trials has been hotly contested between several VEGF-targeting siRNAs against the same ocular disorder – AMD, for which there is no current therapy. Also noteworthy, the first RNAi project to enter the clinic has not come from one of the major players but from a small Philadelphia-based company – Acuity Pharmaceuticals. Acuity's anti-VEGF oligonucleotide, Cand5, entered Phase I safety trials in AMD patients in October 2004 and is expected to complete this phase of clinical trials in 2005.

However, the bigger players have been hot on its heels. Sirna Therapeutics has now followed suit, commencing its first Phase I trial for Sirna-027 in November 2004. Not to be outdone, its major rival Alnylam has its own anti-AMD siRNA ready to begin trials in 2005. It will be interesting to see which project will be the winner of the next race – the first to make it to market.

A gold rush?

Many small companies are already clamouring to join the RNAi bandwagon. If the technology is not scuppered by safety issues or delivery problems, a huge expansion in the RNAi therapeutics sector is likely to occur over the next 2–3 years. However, the gene therapy debacle must be remembered. Gene therapy was hailed as a panacea and its popularity burgeoned during the past decade, only for the sector to dissolve into disappointment and frustration as efficacy and safety concerns halted project after project, with only one minor marketed product emerging thus far.

The human genome project has given RNAi developers a gold mine of untapped therapeutic targets on which to test their new technology. Unhampered by the need to develop small molecules through traditional means, and with RNAi technology itself generating screening models for each new target, the generation of actual drug candidates seems almost too easy. This might be a rare example of a newcomer living up to its advance publicity. However, the moment of truth will be the arrival of the first RNAi drug on the market, and its commercial success. Only then will RNAi overcome the most important target for silencing – the sceptics.

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YBF 2004: welcome to the future

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Second annual Young Bioinformaticians Forum (YBF)
Said Business School, Oxford, UK
20th October 2004

In the past, provision of training in bioinformatics has been nebulous and haphazard, with courses varying dramatically in content and context: some emphasize the 'bio' aspect of the subject, whereas others focus on the informatics side. Bioinformatics is more than writing a Perl script, and much more than simply running BLAST (basic local alignment search tool). Fortunately, bioinformatics training has now changed beyond all recognition, becoming altogether more rigorous and has even begun to infiltrate the undergraduate curriculum.

As part of that process, the second annual *Young Bioinformaticians Forum* (YBF) one-day meeting was held on 20 October 2004 at the Said Business School (Oxford, UK). Run as a joint venture between the UK Bioinformatics Forum, which recently launched a new web portal for bioinformatics news, discussion and events (www.bioinformaticsforumuk.net), and the Royal Society of Chemistry Molecular Modelling Group, YBF 2004 used the modest success of last year's inaugural meeting as a foundation to build a more substantial and impressive event. YBF 2004 also drew support from the Said Business School, the South East England Development Agency and the Intermediary Technology Institute (Life Sciences). The meeting was also supported by its main media partner – BioMedCentral.

Theme and variation

The meeting was divided into three main themed sessions: (i) microarrays and clustering; (ii) systems biology and beyond; and (iii) protein evolution. Additional presentations by Martin Blythe (Edward Jenner Institute for Vaccine Research), who described research on the prediction of antibody epitopes, and Xueping Quen (University of Edinburgh, UK), who illustrated research on predicting and

1359-6446/04/$ – see front matter PII: S1359-6446(04)03319-7

conference report

classifying protein–protein interactions, were the introductory and concluding talks of the meeting, respectively.

Blythe illustrated that as bioinformatics has grown it has also diversified, developing new sub-disciplines to fill new thematic niches, for example, immunoinformatics, which is the development and application of computational techniques to problems from immunology. One of the key goals of immunoinformatics is the prediction of epitopes. Whereas T-cell epitope identification *in silico* is now well-developed, the prediction of epitopes bound by antibodies remains primitive. By performing a rigorous analysis of state-of-the-art antibody-epitope prediction methodology, Blythe demonstrated that existing methods work only marginally better than random estimates of epitopes.

Winners and more winners

Runner-up in the poster section was Peter Giles (University of Cardiff, UK) with a poster describing MADRAS (microarray array data review and annotation system), a web-based system for the interactive manipulation of transcriptomic data. MADRAS enables a user to visualize and annotate a gene-orientated representation of microarray datasets in a straightforward, uncomplicated manner. Furthermore, it enables the integration of pathway data and disease information, and its visualization includes colour-coded interaction schematics and Venn diagrams.

Sanne Abeln (University of Oxford, UK), who won the main poster prize, described a thorough analysis of statistical trends in how representative genomes from the three branches of the 'tree of life' use different protein folds. Although there are no simple relationships between the different measures of fold usage, Abeln identified that archaea and eukaryotes have fewer distinct folds than bacteria (for similar sized genomes). Abeln also examined how these folds might have evolved, and discovered that although there is a greater incidence of α- and β-folds, when compared with other folding patterns, there are fewer distinct α- and β-folds on larger genomes. Folds with only one superfamily seem over-represented (according to a power law distribution) and a fold occurring on many genomes does not necessarily have several duplications.

Kostas Lykostratis (Ludwig Institute for Cancer Research, UCL, UK) had a slight edge over Bryony MacKenzie (University of York, UK), who gave an entertaining and erudite description of research on establishing a robust phylogeny of bacteria, and was honoured with the title of commended speaker. Lykostratis provided an excellent overview of the effect of shear stress on the function of endothelial cells, demonstrating how it is now possible to integrate mathematical modelling with microarray data: this strategy enables the simultaneous understanding of physiological events at the molecular and cellular levels. Lykostratis also indicated how mathematical models of the macroscopic hemodynamic forces regulating the structure and function of blood vessel walls can be integrated with mesoscale systems models of individual cells and microarray data on the gene expression of sets of actual genes.

And the overall winner is…

The clear and unanimous winner of the title Young Bioinformatician of the Year 2004 was Julia Handl (University of Manchester, UK). Handl described research into developing a novel approach to the notoriously difficult area of clustering. For example, although oranges and apples seem to have significant differences, they are both fruit. Is a pomegranate more like an apple or is it more like an orange? When the clustering problem is poorly specified, or the variation within each cluster is greater than that between different clusters, meaningful or useful clustering often becomes almost impossible. Progression in the development of new methods is hampered by the lack of 'gold standards' against which to judge the quality of any clustering exercise.

The outcome of clustering exercises can be assessed by many, often seemingly contradictory, criteria. Handl described the application of a powerful, multiobjective solution to the problem that exploits these issues to the advantage of the researcher, thus circumventing the difficulties associated with having several criteria. Multiobjective problems are a formal way of describing situations where it is necessary to fulfil several, possibly conflicting, objectives simultaneously. The method presented by Handl offered a promising innovative approach to this obstacle and a variety of real and artificial models were used to demonstrate the applicability of this strategy. Data sets included simulations in which the data were extremely intermixed or highly structured and several real-world examples covered classic data sets (e.g. Iris) and others such as those generated from yeast microarrays. Paul Taylor (Edward Jenner Institute for Vaccine Research), the preceding Young Bioinformatician of the Year, was present to see his title pass to Handl.

Welcome to tomorrow

YBF 2004 set the standard for future meetings, which, we hope, will become an important feature of the conference year. The achievements of all the prize winners and commended speakers should not be underestimated. Although the competition was fierce, it was conducted in a courteous and polite manner. YBF 2004 gave eight speakers – each an able and gifted post-graduate bioinformatician in their own right – the opportunity to highlight their research before a wide audience. The quality of science demonstrated by all the speakers bodes well for the future of the discipline. The potential benefits of bioinformatics to bioscience are as obvious as they are unrealized. In a support role, bioinformatics has proved its worth time and again, but it is often held in disdain by so-called experimental scientists, who view it with contempt, suspicion and ignorance, or often a combination of the three. There are many factors that have contributed to this regrettable situation. However, it is clear that the ideal scientist is open to all possibilities, embraces all disciplines and can use any tool or technique to progress scientific understanding to the benefit of society. The scientist of tomorrow will not be narrow minded – locked into neither informatics nor experiment – but will embrace the best of both disciplines.

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