Centre for Gene Research

April 1998

From your Director

How do you see yourself as a scientist in the 21st century - a possum caught in the glare of the on- coming future, a shark swimming alone in the scientific sea or a soaring white pine tree (nga kahikatea) securely rooted in a knowledge base and beaming with national intent? These are (with some artistic license) the scenarios being proposed by the Foresight Project. Those of you who attended the recent Foresight road show (held March 18) got a taste of what lies in store for us. The review of R S & T priorities, the introduction of full cost recovery and the setting of sector strategies are likely to move the goal posts once again and change the face of New Zealand science. We in the academic scientific community will have to change our mind-set from thinking of science as following an intellectual challenge to one of achieving specified outcomes. Gone are those romantic days (were they ever real?) of an academic with a good idea, a small dog and running water being able to successfully bid for funds. Where does this leave us? A similar exercise was carried out by the Australian Science and Technology Council, but that report was basely shelved in favour of the usual ad hoc expediency. Will this happen on this side of the ditch? The signs are that there will be a significant change in the way bids for funding will occur. The emphasis will be on a 'provider' having a research portfolio aligned to outcomes, bidding across outputs with a mixture of targetted and non-targetted projects. The question for us is who will be the 'provider' for us and what will be our portfolio? The structures of CRI's are better placed to do this than this University. The assertion is that the creation of wealth in the future will be knowledge based is encouraging. We are in the knowledge

'business', so our future should be assured(?). The message of the Foresight road show was: get involved.

On the local scene I am pleased to report that the new ABI 377 DNA sequencer has been installed. We gratefully acknowledge the importance that Research & International placed on upgrading the DNA sequencing facility and to the University equipment committee for providing the funds. Behind the scenes was the 'gentle hand' of Professor George Petersen making sure the right decisions were made. As part of the sequencer bundle some ABI sequence analysis software was also purchased. This is being evaluated and there will be further information in the form of workshops and hands-on training. The other bit of good news is that an order has been placed for the ABI quantitative PCR instrument. Funds for this were obtained from Lottery and the Division of Health Sciences.

Finally the CGR Website is almost ready to be launched. It will have some interactive features and will incorporate a member's database and the on-line DNA sequencer order forms. Watch this space.

James Kalmakoff

Gene Structure & Function

In 1997 the theme " Gene Structure & Function" was granted to the Centre for Gene Research as part of the University's Research Management Plan 1997-2000. The Centre has recently received approval for a budget to run a Workshop on Emerging Technology (DNA chip applications, proteome analysis, Taqman - quantitative PCR applications, bioinformatics) and a Symposium on Research Funding (Swimming with the Sharks) and/or Scientific Communication. Anyone interested in participating or organising these events, please email the Director. The present CGR Committee is planning to extend its membership to include participation from the younger Associate Members who have all the original ideas, energy and are at the coal face of doing science. Volunteers are required, nominate yourself or your colleague.

Accountability: But Where is the Science?

I was recently in the position of looking over a feedback report from a FRST application and was struck by some of the comments that were made on what was an unsuccessful application. Much of the report did not discuss the scientific quality of what was submitted; instead there was talk of end-users, pathways of communication and "research outputs that contribute to outcomes". Much of this terminology reflects an attempt to make science "accountable". It is argued, perhaps with some justification, that for many years New Zealand science (and New Zealand scientists) were not accountable for the money they received. Hard questions were asked of the value of science that was produced in return for the investment of taxpayers money (despite its ugliness, the vocabulary is strangely infectious). The battle over whether scientists were accountable and whether there was a good return on the investment is now won and lost, but I wonder if it was not a straw man that was tried.

However much we dislike the new style of doing things, I suppose we have more or less got used to it. But it seems that since things have changed once, they should change again, and now we have the Foresight Project to guide our footsteps to scientific success. This project takes the somewhat dubious premise that the best way to figure out how to get somewhere is to imagine oneself at one's goal and look back at how one arrived. No doubt this approach has some merits, but it is fundamentally flawed in its inability to incorporate novel developments. Since novel ideas are the stuff of science, applying this somewhat mechanistic idea to doing science seems to me to be just plain silly. At best this approach might allow novel ideas to be considered, at worst it will result in pedestrian near-science. The cynical might argue that reorganizing science funding is just another way of avoiding spending money on science. It may not be entirely coincidental that the government has fallen behind its own funding targets in the last year or so.

What then are we to do? There are two classical dangers to steer between. Ignoring the problem is no guarantee that it will go away; almost certainly it will not and we will be lumbered with the consequences. However, getting involved with the exercise may lead to contamination. Consultation should involve not just the soliciting of

opinions but actually listening to what is said. Sadly, the first part of the process is often all that transpires. The Foresight Project does offer an opportunity to be involved. Visit their web site and say your piece. If enough people say the same thing, there is a possibility that some notice might be taken. However lame this sounds, it seems to be the best that we can do.

I have always thought that were I to keep a dog it would be to save me barking at strangers. If I were to keep the dog busy filling in reports of when it barked, for how long and how loud, at what and why, I should not be too surprised if burglars sneaked in unobserved. Perhaps scientists, like dogs, are best left to do what comes naturally.

Craig Marshell

Protein Prattle

The Protein Microchemistry Facility is running more effectively again with the return of Diana Carne from parental leave. Thanks to our patrons who patiently waited their turn in 1997 - despite the hassles we ended up doing about as much service work as in the previous year. It looks like 1998 will be even busier based on first quarter throughput.

Refinements to our operation procedures instituted during 1997 are proving effective and hopefully we can continue to achieve an improved turn around time for service work. Interaction during the job and preliminary reporting of results are now done routinely by email. A new web site will be online soon offering service request forms and information sheets. We are retaining the team approach to running the Facility adopted in 1997 so if Diana is not available then either Chung Kon or myself should be able to assist. Chung is doing a PhD in my lab so we are fortunate that his experience with the MALDI-TOF mass spectrometer and amino acid analyser will be available for another three years or so.

Most protein microsequencing is done from blotted samples now and it certainly is a very effective approach, subject to the appropriate sort of membrane being used! Please remember that it is ESSENTIAL to use PVDF membranes only - anything else will not survive in the sequencer and a major replumbing exercise will be the horribly expensive

consequence (we had a close call in 1997, phew!). We supply high density PVDF (ProBlott, from Applied Biosystems) on a single sheet basis and will also accept samples on PVDF membranes from two other suppliers: Transblot (BioRad); Immobilon P and Immobilon PSQ (Millipore).

Last year we put our support behind the Australian National University (Canberra) bid to get a C- terminal microsequencing service established in Australasia - this was successful and an Applied Biosystems instrument is due to be installed 'any day now'. We will serve as the intermediary between local patrons and the ANU lab, ensuring that sample preparation is appropriate and assisting with data interpretation. With the current C-terminal chemistry you can expect 'half a dozen or so residues from about a nanomole' of sample which is fine for the expected primary use, characterisation of recombinant proteins (Pro is not sequenced). Likewise this year we will offer to 'farm out' mass spectrometry work to other labs in NZ and Oz when analyses with our current MALDI- TOF instrument are incomplete or inadequate.

I feel that this kind of resource sharing is an appropriate way of dealing with the increasingly gloomy prospects of funding major instrument purchases and, equally importantly, the major costs of their ongoing operation - its also fun and productive to interact with other labs doing the same sort of work! We can be heartened that the long awaited shift from genome sequencing to functional genomics is now upon us and with it a massive shift in focus to the gene products - viva proteomics! Hopefully the Facility can help increasing numbers of researchers with their quests for understanding gene function.

The Protein Microchemistry Facility (Room 123) is located on the first floor (east end) of the Biochemistry Department. For general enquiries in 1998, contact us by phone (479 7542), fax (479 7866) or email (protein.microchemi stry@stonebow.otago.ac.nz). Chung Kon might be tracked down in the Hubbard lab, at phone 479 7938. Dr Mike Hubbard can be reached by phone (4797831), fax (479 7866) or email (mike.hubbard@stonebow.otago.ac.nz).

Mike Hubbard

News from the Sequencer

The big recent event has of course been the commissioning of the ABI377XL sequencer. There have been a few of the inevitable teething problems and learning experiences, but things are going well now with the quality of some of the sequences being quite exceptional. Thanks for your forbearance! We would emphasise that one thing has not changed - DNA of the appropriate concentration and cleanliness is required to guarantee good results. We have appreciated the technical support from ABI in Australia and the visit today of the Perkin-Elmer's new rep. in New Zealand, Stacey Farmer. Some of you will know that Stacey was previously with the U. Waikato sequencing facility and so has extensive experience with the 377.

One of the advantages with the 377 is in the new BigDye Terminator chemistry. The acceptors are dichlororhodamine dyes. These have significantly less spectral overlap at their maximum excitation efficiency than the rhodamine dyes used with the 373, and their sequencing products show much reduced background noise. The result: cleaner signals and less peak overlap, giving greater base- calling accuracy at longer readlengths. The aim is for 650 bases at >98% accuracy. The 377 also has a number of technical advantages over the 373, including a better laser and optics, shorter run times and easier gel pouring and handling. Overall, it looks a great machine!

We are purchasing a DynaQuant Fluorimeter for the determination of DNA concentrations, to help us in our trouble-shooting when things don't work as well as we would like. Because of time constraints, we plan at this stage to check only those templates that do not give satisfactory results rather than all templates sent to us.

Note that we are using the cgr-list for information as it comes to hand -if you have not subscribed to the list, now would be a good time to do so!

Software available for evaluation

The Centre for Gene Research was able to purchase 10 copies of each of two software packages from ABI at a greatly discounted price (<25% of normal) as part of the deal negotiated for the new 377XL sequencer. Each copy is licensed for installation on a single computer only and

indeed shuts down with no warning or saving of data if more than one copy with the same registration number is in use. The Committee of the CGR has decided to offer the software to interested members for a two-week evaluation period with a view to purchase. The purchase price will be $300 per package.

The two packages (both Macintosh based) are:

1. Autoassembler version 2.0. This is a sequence assembly program and can handle at least 1000 sequences of 500 bp. It allows on-screen editing of chromatograms and essentially fulfils the function of DNAstar Seqman demonstrated at the last CGR users meeting. The blurb claims the software has no known limitations or bugs. It certainly has the nice feature of lining up all the chromatograms under each other to facilitate editing.

2. Sequence Navigator version 1.01 (comes packaged with Factura). I have not really tested this package but Factura allows for batch editing (topping and tailing) of chromatogram files according to criteria the user sets. Navigator is a DNA and protein sequence comparison program and essentially allows you to align multiple sequences and view their chromatograms simultaneously. Its major use is to identify heterozygotes or mutations in near- identical sequences eg the tutorial involves a screen for p53 mutations. To me, it seems quite similar to SeqEd but able able to handle many more sequences. It is obviously a more specialist piece of software than Autoassembler.

If you would like to evaluate one or both packages on a trial basis for two weeks, please contact Clive Ronson by e-mail. At the end of two weeks, you will need to return the software and remove it from your computer, or indicate a desire to purchase. Note both packages come with ABI mousepads that are sure to become collectors' items and are nearly worth the purchase price alone!

Clive Ronson

A Grassroots Organisation of Active Research Scientists