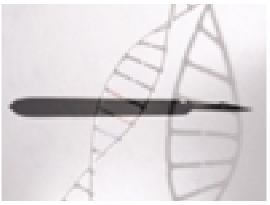


DNA. This insertion, deletion or substitution of whole strings of nucleotides helps explain how so few human genes can encode so many different proteins with so many different functions.

However, despite the intensity of work in this area, many alternative splice variants of human genes have been missed, says Zhengyan Kan, Senior Research Scientist at Rosetta Inpharmatics in Kirkland, Washington DC (http://www.rii.com). 'You'd expect not to see any surprises because we've really studied the human transcriptome quite well,' he said.

But when mouse transcripts rather than human transcripts are aligned against the human genome, there are a lot of novel splicing patterns that have not been observed in human transcripts, says Kan. Humans and mice share so much of their evolutionary past, some of these newly discovered arrangements could be present in humans, he suggests.

Cross-species analysis

Comparing unedited DNA sequences with expressed sequence tags (ESTs) – 400–500-nucleotide fragments of cDNA – is the most common means of identifying splice sites. Aligning these edited DNA fragments alongside the complete DNA sequence reveals which chunks of DNA end up coding for protein and which do not. Importantly, such alignment also shows up the sites where the RNA was spliced before being translated.

'We have predicted novel splice forms for 42% of human genes and 51% of mouse genes through cross-species analysis,' note Kan and colleagues in a paper presented 6–10 January 2004 at the *Pacific Symposium on Biocomputing 2004* in Hawaii, USA (http://psb.stanford.edu/) [1]. Work is now underway to validate these predictions experimentally, say the researchers.

Evolutionary divergence

One key point that the researchers have yet to address is the fact that the accurate identification of intron–exon boundaries relies on the accurate alignment of genomic sequences. By definition, the alignment between a transcript of one species and the genome of another is rarely perfect. This makes it difficult to be sure that what looks like a novel splice pattern is not simply a consequence of evolutionary divergence.

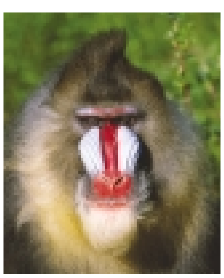
'We don't know whether these are real events in humans yet,' admitted Kan, 'A lot of that could be due to evolutionary divergence.' But this does not undermine his confidence in the approach. 'Mouse transcripts represent a potentially valuable resource for discovering alternative splice variants of human genes,' he concluded.

Reference

1 Kan, Z. *et al*. (2003) Detection of novel splice forms in human and mouse using cross-species approach. (see http://www-smi.stanford.edu/projects/helix/psb04/kan.pdf)

Monkey business over

Branwen Morgan, BMN News



Three years after applying for planning permission to build a new neuroscience center to house their non-human primates, Cambridge University's (http://www.cam.ac.uk) application has been finally accepted, generating an almost audible sigh of relief from many scientists across the UK.

State-of-the-art facility

The 'state-of-the-art' facility at Cambridge University will benefit the animals housed there, say researchers in Cambridge and beyond. Animal rights activists who are trying to prevent the building of the new facilities should ask themselves who their actions are benefiting, they add.

David Morton, Professor of Biomedical Science & Ethics at the University of Birmingham (http://www.bham.ac.uk) notes that, 'the centre could also minimize the number of primates being used in research, for example, by sharing tissues and information on good practices.' Certainly, it would bring together researchers working in different areas of neuroscience who until now how been working in separate laboratories scattered around the campus.

Alistair Kent, Director of the Genetics Interest Group (http://www.gig.org.uk/), says, 'Of course, it would be nice if we didn't have to do them [experiments on non-human primates (NHPs)]. If there was an alternative that could likely lead to results as quickly, as safely and as effectively as doing primate-based research then I, and every scientist I know, would be happy to take it.'

NHPs and practical issues

The complex physical and social requirements of NHPs and their relatedness to humans mean that they

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are only used in research when it is absolutely necessary. They are highly intelligent creatures and the decision to use them in a scientific study is not taken lightly. Under the 1986 Animals (Scientific Procedures) Act, cats, dogs and NHPs are afforded special protection and in 2002 were collectively used in less than 1% of the 2.73 million procedures in the UK.

Scientists that use animals face a number of practical issues in addition to intimidation and physical threats. These include the lengthy processes required by law to obtain and amend licenses for animal experimentation, and the supply of the animals themselves.

Almost all NHPs used in the UK (macaque monkeys and marmosets) are obtained from captive-bred breeding colonies. They have known family histories and are supplied with health profiles from birth to shipment. The majority of macaque monkeys are bred and weaned in their countries of origin, which means that the animals have to endure lengthy transportation periods. When they are shipped to the UK, careful consideration is given so that those animals that have grown up together are transported together, as a result they can be acclimatized to their new surroundings with animals that they know.

The green light?

However, a spokesperson from a leading UK research company told *BioMedNet News* (http://news.bmn.com) that as a result of animal rights groups targeting airline carriers, it is nearly impossible to transport animals directly into the UK. 'Different transportation mechanisms have been introduced to overcome this situation, along with additional feeding stations to minimize the stress to the animals. But this increase in transit time that directly results from animal rights targeting, has effectively compromised animal welfare. Both the time taken to obtain licenses and animal importation issues have caused some primate researchers to relocate their studies to the USA.'

As for Cambridge University, while they finally have permission to build their new neuroscience centre, the escalating costs due to the three-year wait mean that there is no guarantee it will go ahead.

Private prescription:

A thought-provoking tonic on the lighter side

Column by Raymond C. Rowe, AstraZeneca, UK

Please note that these are the personal opinions of the author and do not necessarily represent those of AstraZeneca.

A spectrum of limericks

Invariably in physical chemistry textbooks you will find a section on the electromagnetic spectrum detailing the distribution of electromagnetic waves according to their frequency and wavelength. The various frequency ranges are characterised by the different behaviour in the emission, transmission and absorption of the waves. From the shortest to the longest wavelength (the highest to the lowest frequency), frequency ranges include gamma-rays, X-rays, visible light, heat and infrared and radio waves. Methods of detection vary but include, photography for the short and medium range of wavelengths, bolometry for the infrared region and crystal detectors, vacuum tubes and transistors for the radio waves.

The study of these waves has spawned many Nobel Prize winners for physics, not least Wilhelm Röntgen in 1901 for the discovery of X-rays, Henri Becquerel, Pierre and Marie Curie in 1903 for work on radiation, Guglielmo Marconi in 1909 for the development of wireless telegraphy, and John Bardeen, Walter Brattain and William Shockley in 1956 for the development of the transistor. All of these scientists and their discoveries have been celebrated in limericks. Indeed the electromagnetic spectrum has resulted in a spectrum of limericks.

Gamma-rays

In March 1896, Antoine Henri Becquerel began looking for a crystalline substance that emitted penetrating radiation of similar properties to X-rays, which had been discovered by Röntgen a few months earlier. Becquerel found that luminescent and non-luminescent compounds of uranium made records on a photographic plate wrapped in black paper, even though the specimen

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