Senate Enquiry into Gene Patents March 2009

Response of the Peter MacCallum Cancer Centre

Prepared by: Dr Gillian Mitchell (Director, Familial Cancer Centre), Professor Stephen Fox (Director of Pathology), Professor David Bowtell (Director of Research), Professor Joe Sambrook (Distinguished Fellow) Jerry de la Harpe (Director of Commercialisation and Associate Director of Research)

Summary:

- Gene sequences should be excluded from patents
- Current law regarding gene patents must be addressed and clarified
- Gene patents will markedly impede the integration of genetics into clinical medicine due to the cost of genetic testing
- Gene patents will markedly impede research into the role of genetics in the development of disease and/or determining the clinical utility of any new gene discovery

The Institution:

- The Peter MacCallum Cancer Centre (Peter Mac) is the only institution in Australia solely dedicated to the integration of clinical management of cancer with research into the biological basis, prevention and treatment of cancer.
- The close working relationship between the clinical and research Divisions means that we have a strong emphasis on the translation of discoveries from the lab to the clinic, as evidenced by the world-wide renown of the institution and its basic science and clinical researchers, its success in the national and international grants arena, and publication record.
- Peter Mac has one of 12 Familial Cancer Genetic services in Australia, providing expert advice and care in the management of inherited cancer risk.
- Peter Mac also houses one of the most sophisticated molecular cancer pathology services in Australia. Testing for germline mutations and molecular changes in tumours to guide therapy is routine.
- We are therefore in an ideal position to comment on the impact of gene patents on clinical and research activities.
- Our submission is a summary of the current situation and our suggestions for the future of gene patenting. It is not exhaustive as it will be the function of the Senate enquiry to hear the finer details of the arguments from all the stakeholders.

General Comments:

- The understanding of the genetic basis of disease is increasing at an exponential rate.
- We are now seeing the clinical fruits of the basic science research into the genetic basis of disease enabling us to start to tailor clinical management and treatment to the specific underlying genetic abnormalities rather than relying on a more generalised treatment approach.
    - Cancer is at the frontline of molecular medicine as it is a disease of defective genetic information

- Examples include the discovery of the mutated CKIT oncogene as the basis of the development of most Gastro Intestinal Stromal Tumours (GIST) and the targeted drug, imatinib, which has profoundly improved the prognosis of GIST [1].

- As the genetic basis of disease is better understood and used to develop targeted treatment, we will see an ever increasing demand for the assessment of a person's genetic makeup or their tumour's genetic characteristics in order to personalise the treatment of their disease. This can only improve disease outcomes and consequently be more cost effective for society in the long term.

- We are in the midst of a revolution in DNA sequencing technology that will greatly increase the potential availability and use of genetic testing.

- We recognise the importance of patents to protect and facilitate the transfer of novel intellectual property for the benefit of the community at large and the creators of that property. Without patents, it would be impossible to see any return on the investment by academic institutions, granting bodies or commercial parties. However, we consider for the reasons outline hereafter that genes are a special case and should not be subject to patenting in the usual way. In particular, the gene patents currently in place are based on flawed logic:

    - According to the principles of patent law, because genomic DNA is a naturally occurring substance it is not patentable. A similar analogy is the discovery of a new species of orchid in a rainforest – it is "discovered", not "invented" and so cannot be patented. However, in the case of genes, the argument has proceeded that once the genomic DNA is removed from the body it is now an isolated substance and so can be patented. We disagree with this view, as the form and structure of the DNA has in no way altered with its removal. In the same way that the biological processes for the creation of a human being cannot be patented we believe that the DNA sourced from a human should not be patentable per se. The general Australian public would seem to strongly support this view.

    - Patents are granted when inter alia an invention is novel and inventive (or innovative). We contend that genes are not novel or inventive as they already "exist" and are readily disclosed in that existing form. No innovative step can be identified in the isolation of existing DNA. This may be contrasted with developing new methods for identifying the genes and/or their mutations in order to improve the efficiency of their detection or reduce the cost of their detection; such new methods may well be novel. However, the use of a novel method to identify a gene sequence should not, in our opinion, necessarily constitute a right to patent that sequence. In this instance, only the method should be protected.

- As a consequence of the prevailing position that isolated DNA is subject to a patent application, patent offices in the US and Europe have granted patents on gene sequences which have formed the basis of the development of commercial tests for gene mutations across the developed world. We consider that the patent officials were not appropriately briefed to make the decision about the patentability of DNA sequences and certainly were not able to consider the consequences of such an action. Examples of undesirable consequences include the action by Myriad genetics in its pursuit of enforcing its BRCA gene patent(s) [2].

- Permitting gene patenting means that there is no incentive for the gene patent holder to continue to improve its commercially available genetic test, particularly not to continue to drive down its cost and efficiency. An example is the variable pricing of a BRCA1 and BRCA2 genetic test in different countries when performed by Myriad Genetics or its

licensee. Furthermore the cost of this test has not reduced appreciably in the US despite the continuing reduction in costs of genetic sequencing over time. Patenting the method rather than the sequence permits the patent holder rights over the method, but also encourages them to continue to improve it – if they do not do so then they risk being superseded by another body which develops a more effective methodology.

- We propose that the Australian Government develops a way to manage the currently issued gene patents and does not grant further patents over gene sequences. We are sensitive to the reciprocal agreement between Australia and the US patent bodies, but this should not prevent Australia taking action based on its interpretation of what constitutes a patent.
    - We recognise that many gene patents are already in existence. If withdrawing current patents is too complex, then we propose that the government should strongly consider requiring all existing Australian gene patent holders to grant compulsory licences to Government-funded laboratories/research institutions engaged in providing a service to the public and to exempt them from paying more than a token annual licence fees or such other costs.

We also refer the Senate Enquiry to the Royal College of Pathologists of Australia's submission to the ALRC enquiry on Gene Patenting and Human Health in October 2003 which eloquently summarises in detail many of these arguments and it is striking that these arguments are still valid six years later.

Specific Questions to be addressed in the Senate Enquiry:

The impact of the granting of patents in Australia over human and microbial genes and non-coding sequences, proteins, and their derivatives, including those materials in an isolated form, with particular reference to:

The following responses from the Peter Mac will focus on the consequence of gene patents as they relate to the prevention, diagnosis, treatment and research into the biological processes of cancer. We have not written an exhaustive review of this area as this will be covered in detail during the Senate enquiry, rather we have highlighted what we see as the pertinent issues and given our opinion on their relative importance and the effect of gene patents on them:

(a) the impact which the granting of patent monopolies over such materials has had, is having, and may have had on:

(i) the provision and costs of healthcare,

There are few concrete examples of the impact of patent monopolies on healthcare as the widespread clinical use of genetic testing has been relatively limited. A good example is the Myriad BRCA1 and BRCA2 testing [2] and other examples are described by the Royal College of Pathologists of Australia in their report to the ALRC enquiry on Gene Patenting and Human Health in October 2003.

We are concerned that these few examples herald the likely difficulties we will experience once the indications for genetic testing in terms of cancer prevention. We note that:

- genetic information is increasingly important to select specific cancer treatments as we are already starting to see in breast (PARP inhibitors [3] and platinum chemotherapy agents in BRCA mutation carriers), ovarian (PARP inhibitors and question about the additional role

of taxane chemotherapy in BRCA mutation carriers [4, 5]) and colorectal cancer (the relative ineffectiveness of 5FU-based chemotherapy in people with Lynch syndrome [6]).

- Full genomic sequencing – determining the sequence the entire genome of individual person – is now an inevitability. Over the next few years the cost and the speed of full genome sequencing will decrease to the point where a complete human genomic sequence can be assembled for a few thousand dollars over the course of a day or two. This will lead to a quantum leap in understanding the causes of human genetic diseases and to far more accurate assessments of personal risk in, for example, diabetes, cancer and a wide range of cardiovascular diseases. Identifying more individuals who are at risk of developing cancer will enable the most appropriate cancer screening or prevention strategies to be offered thereby decreasing the overall burden of cancer to the individual and the wider community.

The selection of treatment for breast, colorectal and ovarian cancer in people with certain genetic mutations, will translate into a demand for genetic testing from all of the people who present with these three most common cancers affecting Australians. This already occurs for the HER2 gene that is altered in 15% of breast cancers and is routinely screened to determine who receives trastuzumab (Herceptin) chemotherapy [7]. More recently, is the discovery that colorectal cancers with a mutant KRAS gene in their tumour specimens do not benefit from the addition of EGFR-inhibitors to their chemotherapy schedule [8]. In neither example the gene is not patented, the detection system is.

Although these examples are based on tumour rather than germline genetics it is not difficult to see how germline testing for treatment selection would quickly take hold once specific targeted treatments become widely available.

- It is important that we have readily accessible and affordable germline genetic testing – especially if we can avoid delivering expensive treatments to those people who may not benefit from it. Healthcare costs are increasing, particularly new targeted agents for cancer treatment, and so national healthcare budgets would be best served by directing expensive treatments to those who would most benefit. If the cost of the genetic test is excessive, due primarily to the cost of the licence to do the genetic testing, then any healthcare savings generated by more effectively targeting treatment will be lost by the cost of identifying the likely responders in the first place.
- It is clear that if a single body holds a specific gene patent, then there is no incentive to continue to develop the methods with the goal of reducing costs while maintaining the quality of the process. For example, although the costs of gene sequencing have dramatically fallen in recent years, the cost of a Myriad BRCA genetic test has not fallen over the years in parallel.

(ii) the provision of training and accreditation for healthcare professionals,

The provision of training and accreditation for healthcare professionals working in the molecular pathology field could be greatly reduced if the consequence of gene patenting results in genetic tests only being undertaken in private laboratories, which are permitted to undertake the testing either because they hold the patent or by having purchased a licence from the patent holder. This occurs in the USA where only Myriad Genetics Inc. undertakes the full mutation screen for all diagnostic BRCA1 and BRCA2 genetic tests. As far as we are aware, Myriad has not granted any licences for other US laboratories to undertake a full BRCA mutation screen.

- In Australia, if this same situation is allowed to occur for the more common hereditary conditions, such as the BRCA1 and BRCA2-associated syndromes, then this would severely reduce the ability of our public laboratories to offer genetic testing in other genes. The common gene tests provide a critical mass for laboratories allowing them to undertake occasional testing for rarer mutations. These are not attractive to large companies and so are vulnerable to becoming orphan diseases with no genetic test available if the public laboratories are effectively closed due to the loss testing for the more common genetic conditions.
- Losing core "screening work" would result in many public laboratories closing, with a consequential adverse effect on clinical activity, which would otherwise benefit from the close working relationships between the clinicians, who manage the patients and the molecular pathology team, which performs the test and interprets the results. Often gene test results are not clear cut and require close consultation between the clinic and laboratory to determine their clinical significance.

(iii) the progress in medical research, and

It is easy to see that issuing patents for the isolation of individual genes will greatly inhibit the clinical applications of full genomic sequencing. The genomic landscape would be heavily littered with legal obstructions that would effectively block an entire field of research, would stifle commercial development and would the effectively prohibit the medical benefits that would otherwise flow

(iv) the health and wellbeing of the Australian people;

We believe that understanding the genetic basis of cancer and using this information to better define an individual's future cancer risks, as well as targeting specific cancer treatments more effectively must improve the health and well-being of the Australian people. Not being able to access useful genetic tests because of their cost will eventually impact on the health outcomes for the Australian people

- As reported in recent days by the President of the Royal College of Pathologists of Australia, Bev Rowbotham, at the college's annual conferences in Sydney, genetic testing is already "unco-ordinated, inequitable and inefficient," predominantly due to the funding mechanism currently in place, and most genetic services see their role as the "rationer" of access to genetic testing, mainly because of the current costs of tests and the limited budgets available to spend on them.
    - Clinical genetics teams have been anxiously waiting for the costs of genetic testing (predominantly sequencing costs) to continue to fall, as well as hope for a greater slice of the healthcare budget in order that we can widen our net to include more people who might benefit from such testing.
    - If genetic testing costs do not reduce, either as a consequence of close guarding of gene patents by patent holders or if new gene patents continue to be granted and we cannot access them as the genetic testing budgets do not increase sufficiently to match the commercial testing costs, then we will not be able to translate these exciting genetic discoveries into an improvement in the health of the Australian population.
- It is reasonable for a nation to consider establishing a national screening program for common cancers, however, it is difficult to believe that there is an "average" cancer risk in a population; i.e. that all women have the same breast cancer risk, that all men have the same prostate cancer risk and that all adults have the same colorectal caner risk except for a few, rare individuals at very high risk of the disease. Rather it is more likely that there is a spread of cancer risks across the general population, with a few at very high risk, a proportion at

what would be currently designated as a “moderately” increased cancer risk and the majority at significantly less than what is currently considered an “average” cancer risk.

    - This latter group would not benefit sufficiently from current population-based cancer screening programs which would be better targeted to those at a higher risk.

- The current problem is identifying those who are/are not at increased risk.
    - Recent research into the genetic predisposition to breast and prostate cancer has demonstrated variations in more common genes (single nucleotide polymorphisms, SNPs) that individually only increase cancer risk for an individual person to a low-moderate degree, but in combination may increase risk more significantly and certainly are likely to account for a reasonable proportion of the population who do go on to develop cancer.
    - Although we are some way from developing a meaningful clinical genetic test using these SNPs, they hold great promise for the future. So far most SNPs with an associated cancer risk have been identified by publicly-funded consortia that publish their results widely and are not exerting any intellectual property rights to them.
    - However, it is not difficult to imagine that a private company may not be so altruistic. In fact may SNPs in other genes have been patented for this reason as outlined in the Royal College of Pathologists of Australia’s response to the ALRC Inquiry in 2003.
- What is more likely to enter the clinical arena in the near term is using genetic information to determine likely response to specific targeted cancer treatments.

(b) identifying measures that would ameliorate any adverse impacts arising from the granting of patents over such materials, including whether the Patents Act 1990 *should be amended, in light of the any matters identified by the inquiry; and*

- If it is finally decided by the Senate Enquiry that gene sequences can be patented, or if it is felt that it is too late to change the status quo even if it should not have been allowed to occur in the first place, then we suggest the most effective way of ameliorating any adverse impacts arising from this decision would be to have a system of compulsory licences for public laboratories set at a cost that can be afforded by the healthcare system.
    - Patent holders would still be able to compete for the genetic testing work if they offer a more effective/more cost effective test than can be performed by the public laboratories which will ensure healthy competition and keep healthcare costs to a more reasonable level.
- The UK and a number of other European governments have elected to undertake BRCA mutation testing in their public laboratories without acknowledging the Myriad patent(s) due to the health benefits of their populations. As far as we are aware these governments have not negotiated a licence with Myriad to do the BRCA testing in their own public laboratories.

(c) whether the Patents Act 1990 *should be amended so as to expressly prohibit the grant of patent monopolies over such materials.*

We believe that the Patents Act 1990 should be amended so as to expressly prohibit the grant of patent monopolies over such materials as they are not inventions or novel but are simply discoveries of the basis of human life. The argument that DNA is somehow different once it is isolated from its natural state in the human body, and forms the basis of current patent applications, is simply not acceptable.

Reference List

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