Research Focus

An Australian network to support the understanding and control of parasites

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The Australian Research Council (ARC) and the National Health and Medical Research Council (NHMRC) Research Network for Parasitology will focus and coordinate the fundamental, strategic and applied parasitology research in Australia. It will raise the standing of Australia in the field, assist in the community understanding of parasitology, and maintain and improve the capacity of Australia to keep its stock, crops, wildlife and people free from disease. On an international scale, the ARC/NHMRC Network will work with other countries to develop new technologies for the detection and control of parasites.

A research network for parasitology

The Australian Government formulated a series of national research priorities in December 2002 and enhanced them in December 2003. The priorities include 'an environmentally sustainable Australia', 'promoting and maintaining good health', 'frontier technologies for building and transforming Australian industries' and 'safeguarding Australia' (http://www.dest.gov.au/sectors/research_sector/policies_issues_reviews/key_issues/national_research_priorities). In August 2004, the Government announced the establishment of 24 national research networks that were to be financed by its major granting agencies – the Australian Research Council (ARC) and the National Health and Medical Research Council (NHMRC) – to help establish the scale and focus needed to address these research priorities. One of the new research networks was the ARC/NHMRC Research Network for Parasitology (http://www.parasite.org.au/arcnet/). The establishment of this network was an acknowledgement of the importance of parasites and the diseases they cause in humans and animals to the economic and social welfare of Australia; furthermore, it highlighted the fact that the efforts of Australian researchers have markedly advanced the understanding of all aspects of parasitic lifestyles. This contribution is shown by the number of published articles by researchers in Australia and by the reputation of Australian researchers for delivering the solutions needed to fight and control parasites and the diseases they cause.

The ARC/NHMRC Research Network for Parasitology brings together >50 research groups from 24 universities and research institutions, from every Australian state and territory. Each of these research groups has extensive links to several companies and industries. In addition, the network is backed by the Australian Society for Parasitology (http://www.parasite.org.au/), which has extensive links to the pharmaceutical industry, veterinarians, clinicians, politicians and many community groups. The funding of Australian parasitology research surpassed AUS$23 million in 2004 and is approaching AUS$100 million overall for the lifetime of current grants.

Objectives of the ARC/NHMRC Research Network for Parasitology

(i) To focus and enhance the fundamental, strategic and applied parasitology research capabilities of Australia to understand parasitism, parasite biology and parasitic disease.
(ii) To use this understanding to discover and develop sustainable control strategies to improve and maintain the health and wellbeing of humans and animals.

Additional details about the network can be found at http://www.parasite.org.au/arcnet.

The researchers brought together by the ARC/NHMRC Network represent a wide spectrum of research interests and expertise that reflects the multidisciplinary nature of parasitology. This includes experts in: immunology and vaccine development; cell biology and biochemistry; pathogenesis; genomics, proteomics and functional genomics; molecular modelling and bioinformatics;

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evolutionary biology; molecular and population genetics; epidemiology; spatial analysis (e.g. global positioning and geographic information systems); biodiversity and taxonomy; diagnosis; and biosurveillance. The network will build on this strong and diverse framework to enhance and focus the Australian parasitology research effort to make major contributions to each of the Australian national research priorities (Box 1).

Initiatives of the ARC/NHMRC Research Network for Parasitology

The network is not a new funding agency for Australian parasitology research; neither its current character nor the funding base enables such a function. Instead, it is a facilitator of collaborative research. Australia is a vast and sparsely populated continent and its major cities are separated by large distances; likewise, its parasitology research community is scattered. The network has created several initiatives to bring this research community closer together and to facilitate the sharing of expertise, information, and major equipment and infrastructure. The network aims to:

(i) foster and finance the exchange of staff between national and international research institutions to maximize access to key infrastructure, equipment, expertise and supervision and to encourage the growth of new collaborative relationships;
(ii) search actively for world-class recruits to enhance the Australian parasitology research effort;
(iii) organize and fund conferences, workshops and meetings for scientists, industry representatives, end-users (e.g. farmers, veterinarians and wildlife experts), government representatives and community groups, including participation by international experts;
(iv) create a website that will foster national and international collaborations by providing access to parasite databases, parasitology researchers and parasite genomes, in addition to bioinformatics analysis tools, parasitology research resources and protocols; this would prevent the duplication of research and promote the adoption of uniform protocols, which would fast-track the Australian research effort. Similarly, genome databases and bioinformatics tools would leverage existing resources and contribute new databases that complement existing information or provide a specific focus to the activities of network members.

These initiatives are already bearing fruit, despite being in operation for only nine months. Collaborations, many with an international component, between different laboratories have been established or fostered as a result of network-sponsored researcher exchanges, including financing international experts to spend time in Australian laboratories and financing young Australian researchers to spend time in other national or international laboratories. Thus, new international collaborations have been established between Australian institutions and: (i) the Rockefeller University (http://www.rockefeller.edu/); (ii) the Hebrew University of Jerusalem (http://www.huji.ac.il/huji/eng/); (iii) Guy's and St Thomas' Hospital (http://www.guysandstthomas.nhs.uk/index.htm); (iv) Harvard Medical School (http://hms.harvard.edu/hms/home.asp); (v) the George Washington University (http://www.gwu.edu/); (vi) the University of Glasgow (http://www.gla.ac.uk/); and (vii) McGill University (http://www.mcgill.ca/).

The ARC/NHMRC Network for Parasitology also recognizes that the fostering of collaboration and the sharing of information among such a disparate and geographically separated group of researchers require a commitment to information technology and adoption of the benefits of 'e-research'. Databases are being developed to share information about research capabilities, collaborative links, protocols, and employment and training

Box 1. Priorities of the ARC/NHMRC Research Network for Parasitology

The ARC/NHMRC Research Network for Parasitology has identified several key objectives for parasitology research in the context of the following national research priorities.

An environmentally sustainable Australia

By assessing the susceptibility to, and monitoring the prevalence of, parasitic disease in wildlife, the network will generate new information that will aid the management of terrestrial and marine ecosystems. The specific objectives of the network are to enhance and focus the Australian parasitology research effort to assess parasite diversity in Australian fauna and to ensure the sustainability of wildlife and ecosystem health.

Promoting and maintaining good health

The young and the elderly are most susceptible to parasitic diseases, in both the developed and the developing world. To address this, the network will focus on the development of new vaccines and treatments for local and global populations and the creation of new technologies to monitor and prevent the contamination of waterways with infectious stages of zoonotic parasites (a major source of disease). The specific objectives of the network are to increase and concentrate the Australian parasitology research effort to understand host–parasite relationships and to develop sustainable parasite-control strategies.

Frontier technologies

A central goal of the network is to develop new molecular tools and information resources. This includes the development of databases and data-management systems to enable network researchers to harness the vast quantity of information that is being generated by an increasing number of genome-sequencing projects. Developing new bioinformatics tools will create unprecedented opportunities to identify new vulnerabilities or targets in parasites for control. The specific objectives of the network are to augment and focus the Australian parasitology research effort to discover and develop molecular and bioinformatics tools for studying parasite biology and to discover and develop antiparasitic vaccines and therapies.

Safeguarding Australia

The ARC/NHMRC Network will enable the development of technologies to aid the surveillance of the border areas and neighbours of Australia for exotic, emerging and re-emerging parasitic diseases. Thus, the specific objectives of the network are to strengthen and train the Australian parasitology research effort to understand the epidemiology and transmission dynamics of parasites and to develop better surveillance systems.

opportunities. In addition, specific parasitology projects are being undertaken. For example: (i) the network has supported the analysis and dissemination of the results of the scabies-mite expressed sequence tag collection; (ii) network-supported researchers are developing databases that focus on the biology and ecology of parasites to complement available genome databases; and (iii) the network has recently made available a microarray service that includes expert assistance and access to microarray databases and analytical tools (http://vbc.med.monash.edu.au/~powell/vbc-microarray/vbc-microarray-capabilities.html). These initiatives are the result of a close collaboration between the ARC/NHMRC Network and the Victorian Bioinformatics Consortium (VBC) – the network provides funding for personnel and the VBC provides the required infrastructure and expertise in bioinformatics.

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Red blood cells that do and red blood cells that don't: how to resist a persistent parasite

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Sixty years ago, Haldane proposed that certain abnormalities in red blood cells could be selected as malaria-resistance genes. Population studies have confirmed that many human polymorphisms confer resistance to severe malaria, although the mechanisms of protection remain unknown. A recent article proposes a new mechanism for explaining the protective effects of hemoglobin C (HbC). HbC-containing red blood cells have modified displays of malaria surface proteins that reduce parasite adhesiveness and could reduce the risk of severe disease.

The malaria hypothesis

The epidemiology of malaria can give important insights into the host and parasite factors that contribute to the pathogenesis of this disease. For example, the innate resistance of Africans (who lack the Duffy antigen on the red blood cell surface) to vivax malaria inspired the hypothesis that *Plasmodium vivax* requires the Duffy antigen for erythrocyte invasion – a notion that has been proved in subsequent studies [1].

More famously, the coinciding geographic distributions of malaria transmission and the thalassemias prompted Haldane to propose the 'malaria hypothesis', which stated that common abnormalities in red blood cells have been selected because of the fitness advantage they confer against malaria [2]. Haldane's speculation centered on the frequency of thalassemia in Mediterranean populations, for which he predicted that the deleterious effects of the homozygous state would be balanced by the increased fitness afforded to heterozygous individuals by resistance to malaria – hence manifesting a 'balanced polymorphism'. This increased fitness is commonly presumed to mean protection from the deadly malaria syndromes (e.g. cerebral malaria and severe malarial anemia), which are thought to kill at least one million African children each year [3].

'Sickle hemoglobin' (HbS) is the best-known abnormality of red blood cells that is associated with protection from malaria. HbS decreases the risk of severe malaria by >90% in some populations [4], but in its homozygous form it is fatal early in life without modern treatment. Other hemoglobinopathies {e.g. hemoglobin C (HbC) [5,6] and hemoglobin E (HbE) [7]} and deficiencies in red blood cell enzymes (e.g. glucose-6-phosphate dehydrogenase deficiency [8]) have also been linked to protection against severe malaria. The population-based studies relating abnormalities in red blood cells to protection have supported Haldane's initial hypothesis.

Mechanisms of resistance to malaria

It is unclear how any of these abnormalities in red blood cells can confer protection. Haldane speculated that the smaller erythrocytes of thalassemics, which are resistant to osmotic lysis, might also be 'more resistant to attacks by the sporozoa which causes malaria' [2]. Other researchers have obtained data supporting several mechanisms by

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