News

Isis
University of Oxford
Innovation

Reviewing the latest innovations, collaborations
and technology transfer from Isis Innovation Limited
Edition 34 Autumn 2001

Continued Growth

Left: *Bernard Taylor, newly appointed Chairman of Isis, is Vice Chairman of JP Morgan plc and was a Chemistry undergraduate at St John's College.*

The pace of activity at Isis continues with over 500 projects being worked on by project managers. These projects will result in either new companies being formed or patents being licensed to others for commercialisation of the intellectual property; of all these possibilities towards 20 are being considered as having potential at this time to support new companies. The range of intellectual property managed by Isis project managers is considerable and although the majority of ideas have traditionally come out of the Life Science and Physical Science domains, we are beginning to see more ideas developed in Humanities departments. These, so far, revolve around media, software, distance learning and an example is Oxford ArchDigital Ltd, a spin-out formed to provide archaeological IT consulting and training. *[See page 17]*

Isis has also continued to provide support to recent spin-out managers and on September 12th 2001 about thirty 'spinners' together with Isis and University Research Services Office staff met at Harris Manchester College to share experiences. Russell Smith of Prolysis and Trevor Nicholls of Oxagen talked about the common problems associated with forming a new company and life after the 'spin'. The event was very well received and will be repeated from time to time.

The regular lectures followed by the dinners in College remain the heart of the Oxford Innovation Society. These events assist in the flow of information to society members and allow informal discussions with key members of the academic staff to take place. On September 20th 2001 the OIS meeting included Professor Jonathan Austyn presenting his research on dendritic cells and Dr Clive Dix presenting the latest developments from PowderJect Pharmaceuticals, who very kindly sponsored the dinner.

Also on 20th September at the AGM I took over from Sir Peter Williams as Chairman of Isis Innovation Ltd and I would like to take a moment to thank Peter for all that he did for Isis during his tenure as Chairman. As scientist, innovator and industrialist he supported and guided Tim Cook and the executive team to become one of the UK's leading technology transfer teams. He is a very hard act to follow and I am delighted that Peter's wise counsel will continue to be available to us as he remains on the board of Isis as a non-executive director.

The opportunities for the continued development of both Isis and of the Oxford Innovation Society have never been greater. Notwithstanding the recent turmoil in financial markets, the commercial demand for better ideas and improved technology is unabated. This, combined with the prolific idea generation within the University of Oxford creates our opportunity. Isis is confident its recent successes will continue.

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Dendritic Cells – New Therapeutic Targets

Oxford Innovation Society Lecture – September 2001
Jonathan M Austyn, Nuffield Department of Surgery, University of Oxford

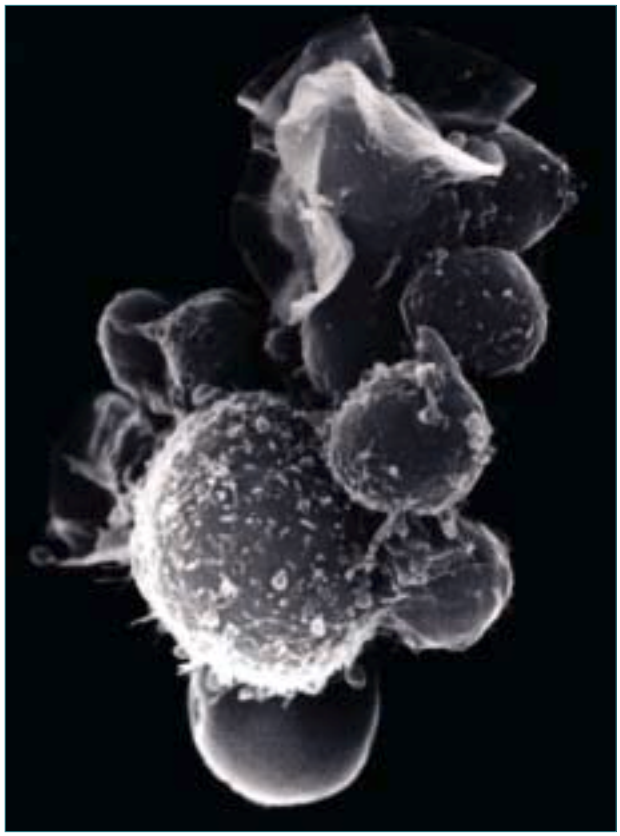
Dendritic cells (DC) play crucial roles in the immune system. There is good evidence that some types of DC are responsible for the initiation of immune responses by lymphocytes to foreign antigens, such as microorganisms, transplants, and certain tumours. More recent evidence suggests that other types of DC may be responsible for the induction of unresponsiveness, or tolerance, of lymphocytes to normal self-components. Because of their potency in inducing and regulating immune responses, there is considerable international interest in the possibility that DC could be used in therapeutic strategies to turn on or to turn off immune responses to our own benefit.

In recent years we, in collaboration with colleagues in Oxford and in Europe, have gained insights into how certain micro-organisms can modulate DC functions

DC are a specialised type of 'antigen-presenting cell' (APC). Like other types of APC, DC in non-lymphoid tissues can display a representative sample of their intracellular contents, that can include foreign antigens if present, in the form of peptides bound to MHC molecules at the cell surface. In response to inflammation and infection, these DC then change their properties, in a process termed maturation, and they migrate to secondary lymphoid tissues, such as lymph nodes and spleen, where lymphocyte responses can be initiated and regulated. DC in these sites have three important functions. They can 'present' foreign peptide-MHC complexes to T cells that have appropriate receptors for such complexes ('signal 1') and they can deliver specialised 'costimulatory' signals to the T cells ('signal 2'). The combination of signal 1 plus signal 2 normally leads to T cell activation, and expression of the lymphocyte's helper or cytotoxic functions. Importantly, delivery of signal 1 in the absence of signal 2 can result in unresponsiveness or tolerance of the T cell. Perhaps depending on the type of microbe they have encountered, DC can also synthesise distinct sets of cytokines (hormones of the immune system), or other molecules, that can polarise immune responses ('signal 3'), leading to different immunological outcomes.

The field of DC immunobiology has been greatly transformed over the past few years by the capacity to generate large numbers of these cells *ex vivo* from progenitors in culture for clinical and experimental purposes. Our own studies have utilised this technology to generate human DC from circulating blood monocytes, and to generate mouse DC from bone marrow progenitors, after culture in appropriate cytokine combinations. In recent years we, in collaboration with colleagues in Oxford and elsewhere in Europe, have gained insights into how certain micro-organisms can modulate DC functions, and we have also started experimental and clinical studies that may contribute to new strategies for immunotherapeutic uses of DC.

Chemokines are a group of chemoattractant cytokines that play an important role in the migration of immune cells into and within non-lymphoid tissues. In particular, so-called 'inducible' chemokines are produced at sites of inflammation that control the entry of cells from the blood into the tissue. In contrast, so-called 'constitutive' chemokines are produced in other sites, particularly in lymphoid tissues, and these control the entry of cells to these particular regions. We have demonstrated that immature and mature human DC respond to distinct sets of chemokines. Immature DC, roughly corresponding to the stage in non-lymphoid tissues, express chemokine receptors such as CCR5 and respond to a set of inducible chemokines. In contrast, mature DC, roughly corresponding to the stage in lymphoid tissues, express chemokine receptors such as CXCR4 and respond to a set of constitutive chemokines. Presumably these chemokines regulate the migration of DC from the blood stream into and through non-lymphoid tissues, and their subsequent migration into secondary lymphoid tissues. Interestingly, CCR5 and CXCR4 also act as co-receptors for infection of certain cell types by human immunodeficiency virus (HIV). Broadly



Above: *Scanning electron micrograph of two dendritic cells with characteristic 'veils' of cytoplasm (top and behind left) interacting with lymphocytes (small round cells to the right), one of which has become activated as a consequence (large round cell towards the bottom of the picture).*

speaking, the former receptors are used by so-called M-tropic strains of HIV, while the latter are used by so-called T-tropic strains. We have now shown that the gp120 component of M-tropic, but not T-tropic, HIV can act as a chemoattractant for immature DC. Moreover, after gp120 binding, DC down regulates responses to inducible but not constitutive chemokines. Our interpretation of these findings is that M-tropic strains of HIV may increase the local density of DC in the vicinity of infection, such as the mucosae, leading to a greater chance of more virus being acquired by the DC and being carried into lymph nodes. Here explosive production of infectious virus particles may occur during the interaction of DC with T cells.

Another example of how pathogens may subvert the immune response by modulating DC function is provided by the malaria parasite, *Plasmodium falciparum*. As part of its life cycle, this protozoal parasite can infect human red blood cells, where it multiplies and develops into a different form. Remarkably, exposure of immature human DC to malaria-infected erythrocytes was found to prevent their subsequent maturation in response to appropriate stimuli. It seems likely *in vivo* that such exposed DC would be unable to initiate immune responses against the malaria parasite, conferring a selective advantage upon it. Only strains of the organism that express proteins permitting direct adhesion between the infected erythrocytes to DC had this effect. It is of particular note that the molecules of DC involved in such adhesion include receptors that are normally responsible for the clearance of cells dying in a regulated manner through the process of apoptosis. It has now been shown that ligation of these receptors by monoclonal antibodies that are specific for them can also modulate DC function is similar respects, resulting in a failure to acquire 'signal 2' for T cell activation. Importantly, the modulated DC secrete the cytokine IL-10 instead of IL-12 in response to appropriate stimulation, suggesting that the immune response can be further modulated by the parasite via an alteration of 'signal 3'. Clearly these insights may have therapeutic impact, in that such agents (e.g. monoclonal antibodies) could conceivably be utilised to modulate DC function in relation to strategies for immunotherapy of autoimmune diseases or for overcoming transplantation rejection. We have previously demonstrated the potential power of this approach in experimental studies of heart transplantation. Under appropriate conditions, it was possible to generate mouse DC with a stable immature phenotype that were resistant to maturation. Pre-treatment of recipients with as few as half a million of such DC, seven days before transplantation of hearts from a completely different strain of mice, resulted in long-term acceptance of the grafts. Clearly the development of related human cells could have a major clinical impact.

The recent definition of a variety of antigens that are expressed by tumours but not by most normal adult tissues, together with the capacity to generate large numbers of human DC, has led to the initiation of a number of clinical

Most recently, we have initiated another clinical trial in Australia, using a potentially widely applicable, approach for immunotherapy of women with advanced ovarian cancer

Above: *Professor Jonathan Austyn*

trials of DC-based immunotherapy for cancer. To date most strategies have involved peptide pulsing of a patient's DC, generated from blood monocytes and matured *ex vivo*, prior to infusion back into the patient. However this approach requires the prior identification of the particular tumour antigens and MHC (HLA) molecules expressed by that individual. Towards a more general approach, we performed a small, phase I clinical trial in Oxford in which DC were generated from the blood monocytes of cancer patients with skin metastases. The DC were then administered directly into accessible skin lesions, without peptide pulsing, since the DC might acquire the tumour antigens locally before migrating to the lymph nodes and inducing a response against the cancer. The procedure was well tolerated, and other aspects of the trial were encouraging, but clinical responses were not observed. Most recently, we have initiated another clinical trial in Sydney, Australia, using a different, but potentially widely applicable, approach for immunotherapy of women with advanced ovarian cancer. The rationale is to prepare messenger RNA (mRNA) from tumour that has been surgically removed, to grow DC from blood monocytes that are obtained by leukapheresis, and then to administer RNA-pulsed, mature DC to the patients after a standard course of chemotherapy, directly into defined lymph nodes. The mRNA should encode a representative sample of all the antigens

Clearly, the field of DC immunobiology is entering an exciting new phase, and expectations are high. But what of the future?

expressed by that tumour, and we would expect these to be expressed as peptide-MHC complexes by the DC, obviating the need to define individual tumour antigens and to match to the patient according to the results of tissue typing. This clinical trial is now in progress.

Clearly, the field of DC immunobiology is entering an exciting new phase, and expectations are high. But what of the future? Approaches using *ex vivo* generation of DC tend to be labour-intensive, time-consuming and really feasible only in centres of excellence in the developed world. Recent insights into the immunobiology of DC should facilitate the development of more rational *in situ* strategies for vaccinology and immunotherapy. Such strategies based on utilising DC as new therapeutic targets are now being explored.

Selected Bibliography

Austyn J.M. 1999. Death, destruction, danger and dendritic cells. *Nature Medicine*. 5(11):1232-1233.

Lin C-L., Sewell AK, Gao GF, Whelan K, Phillips RE and Austyn J.M. (2000). Macrophage-tropic HIV induces and exploits dendritic cell chemotaxis. *Journal of Experimental Medicine* 192:587-593

Urban B.C., Ferguson D.J.P., Pain A., Willcox N., Plebanski M., Austyn J.M., Roberts D.J. 1999. Plasmodium falciparum-infected erythrocytes modulate the maturation of dendritic cells. *Nature* 400:73-77 (Comment in: *Nature* 400:25-26).

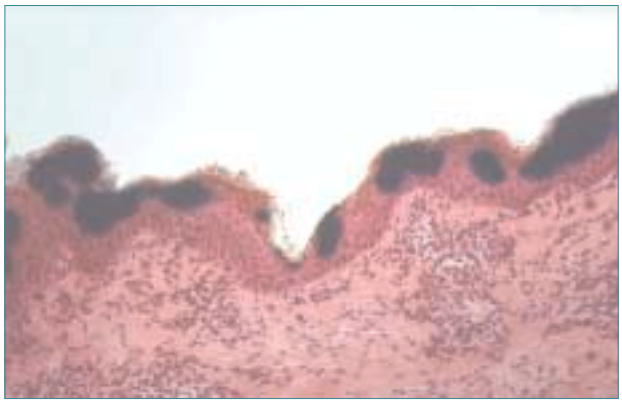
Lutz M.B., Suri R.M., Niimi M., Ogilvie A.L.J., Kukutsch N.A., Rößner S., Schuler G. and Austyn J.M. (2000). Immature dendritic cells generated with low doses of GM-CSF in the absence of IL-4 are maturation-resistant and prolong allograft survival in vivo. *European Journal of Immunology* 30:1813-1822

Austyn J.M. 1996. New insights into the mobilization and phagocytic activity of dendritic cells. *Journal of Experimental Immunology*. 183(4):1287-1292.

Epidermal Powder Immunisation with Protein and DNA vaccines

Oxford Innovation Society Meeting, Sponsor Presentation – September 2001
Dr Clive Dix, PowderJect Pharmaceuticals plc

POWDERJECT PHARMACEUTICALS PLC



Above: *ß-gal expression in epidermis*

Background

PowderJect Pharmaceuticals is a leading vaccines and immunotherapeutics company with projected sales of ~£100 million for the current year financial year and an exciting pipeline of new products based on powder injection. The commercial opportunity is based on three key drivers: (i) meeting a strong demand for vaccines for non-juvenile prophylaxis; (ii) introducing enhanced, consumer-oriented vaccines; (iii) developing 'next generation' therapeutic DNA vaccines. The vaccines market is growing rapidly, with current global sales of $6.5 billion and is forecast to reach $20 billion by 2010. Immunotherapeutics (vaccines that treat disease) are predicted to widen the market significantly and PowderJect will be well positioned to capitalise on the market opportunity.

The Company has a strong product range through Evans Vaccines and SBL Vaccin including nine marketed/approved products, three products in Phase III, a strong development pipeline based on powder injection and a strong portfolio in influenza, diarrhoea and hepatitis B. The influenza market is worth $350 million and is growing rapidly. PowderJect is the UK market leader and has a 20% share in the USA. The travellers diarrhoea vaccine market is predicted to grow to $400 million by 2005 and PowderJect has the only product available. The Company has state of the art manufacturing in Liverpool and Stockholm, with significant potential for capacity expansion, and core competencies in cell-based manufacturing and live-virus manufacturing capabilities.

PowderJect has a world-lead in DNA vaccines and by stimulating both aspects of the immune system in human studies has achieved both antibody and cellular responses. Doses used are between 1 to 4 µg, approximately a thousand-fold lower than for traditional liquid/needle injec-

Table 1: *PowderJect's Product Pipeline*

Preclinical	Clinical	Marketed / Approved
PJ Fluvirin® conventional	**PJ hep B DNA therapeutic** (ph I)	**Fluvirin®** (influenza, worldwide)
PJ hepatitis B conventional	**PJ hep B DNA prophylaxis** (ph I)	**Arilvax®** (yellow fever, Europe)
PJ D/T conventional	**Arilvax®** US (phase III)	**BCG** (tuberculosis, UK)
GSK PJ DNA programmes	**Dukoral®** EU (phase III)	**Dukoral® Travellers Diarrhoea** (Nordic)
PJ influenza DNA vaccine	**Dukoral®** US (phase III)	**Clostet®** (tetanus, UK)
PJ HSV DNA vaccine	**ETEC** (phase III)	**Hepacare®** (hepatitis B, Europe)
		Cholera Vaccine® (Nordic)
		Polio injectable
		Diamorphine

PJ = PowderJect powder injection vaccine

Vaccination with PowderJect Gene Delivery

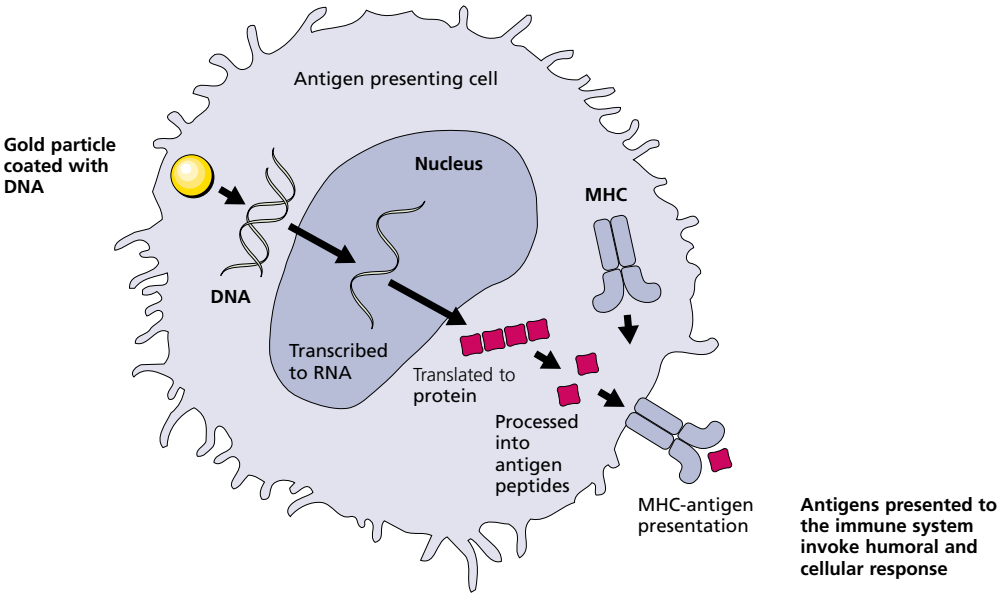


Figure 1: *PowderJect efficiently delivers DNA intracellularly to elicit a protective or therapeutic immune response using 1,000 fold less DNA than injection*

Using the PowderJect device, vaccines are formulated as a fine, dense powder, and a helium gas jet accelerates the particles into the skin

tion, giving a significantly reduced DNA raw material cost at pilot scale at $400 per 1000 mg lot. Eight DNA vaccine clinical trials have either been completed or are ongoing and the Company has a $300 million collaboration in the field with GlaxoSmithKline.

Powder injection needle-free delivery technology and DNA vaccines

The epidermis is an efficient immunologic organ and is rich in Antigen Presenting Cells. Keratinocytes are also found in the epidermis and are a rich source of pro-inflammatory and immunological cytokines. Langerhans cells located in the epidermis pick up antigens and migrate to the dermis and draining lymph nodes and play a key role in antigen processing and presentation. However, it is difficult to reproducibly access the epidermis by needle and syringe. In contrast, the PowderJect System® is uniquely designed for delivery to the epidermis. Using the PowderJect device, vaccines are formulated as a fine, dense powder (DNA is precipitated on gold), and a helium gas jet accelerates the particles into the skin. Delivery is needle-free, avoiding the disadvantages of needles, and is directed at the immune competent epidermis. Indeed DNA-gold particles have been shown to efficiently and reproducibly target the epidermis (see Figure 1 above).

Studies have also shown that antigen delivered to the epidermis are carried by the Langerhans cells in the skin. Via this approach the skin immune system can be modulated to elicit a broad-based immune response.

Clinical Studies

Clinical studies using PowderJect's DNA vaccine technology have focused primarily on hepatitis B. A Phase I HBsAg DNA vaccine in naïve vaccinees showed that dermal PowderJect vaccine administration was well tolerated at all doses tested. All subjects showed a humoral response and seroprotected to > 10mIIU/ml: the first protective immunity induced in humans by a DNA vaccine Cellular responses induced both CD4+ and CD8+ T cell mediated sAG-specific immune responses in all evaluable subjects.

Left: *Dr Clive Dix, Senior Vice President Research and Development, PowderJect Pharmaceuticals plc*

A further study of a DNA vaccine to prevent hepatitis B infection in individuals non-responsive to licensed vaccines was also very encouraging. This was an open label study of 6 subjects in each of two cohorts. Group 1 included individuals with 6 or more doses of licensed vaccine, while group 2 included those with 3 or more doses of licensed vaccine. Three candidate vaccine doses (a prime plus two boosts) were administered. The results showed that the novel hepatitis B DNA vaccine was well-tolerated and that the vaccine was immunogenic. Group 1 showed a 50% response rate and group 2 gave an 80% response rates offering protective immunity to those who had failed to sero convert following administration of existing commercial vaccines.

To summarise, preclinical and clinical data in a number of different diseases shows that PowderJect DNA delivery to the epidermis has a number of technical advantages: (i) it drives a strong cellular response; (ii) it induces protective antibody responses; (iii) it introduces DNA directly into the cell; (iv) there is *de novo* synthesis of antigens; (v) it is efficient – 1,000 fold less DNA than intramuscular delivery; (vi) there is potential for safe delivery of adjuvants and cytokines; (vii) multiple genes are possible; (viii) it is effective for *in vivo* and *ex vivo* cellular protocols.

Extracellular epidermal powder immunization with conventional protein vaccines

Delivery of protein powder using PowderJect delivery also targets the immune competent epidermis. Preclinical studies with extracellular PJ delivery of trivalent influenza vaccine showed significantly higher antibody titers than with conventional intramuscular injection. Further studies using HIV gp120 and HBsAg as antigen have demonstrated that PowderJect delivery of protein vaccines may improve vaccine efficacy by eliciting cellular, humoral and mucosal immunity. Skin delivery clearly offers immunological advantages and may also be compatible with water soluble adjuvants.

Independent market research shows that 95% of patients prefer PowderJect

In conclusion, the PowderJect System® offers a number of advantages. It is patient-friendly since it is needle-free and avoids the discomfort associated with needles, overcomes needle phobia issues and avoids needle-stick hazard. It is easy to use and there is no sharps disposal. The PowderJect System also offers a cost-saving potential for self-administration since it avoids complex handling and/or reconstitution issues and there is no need for an expensive cool chain. It gives an improved immune response and independent market research shows that 95% of patients prefer PowderJect.

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Induction of Immune Tolerance

Isis Project Number 665

Therapeutic areas

Malaria and many other human diseases associated with malfunction of the T-cell immune response.

Introduction

Inappropriate immune response, particularly T-cell response, has been shown to be involved in the initial development and further progression of many human diseases, such as Plasmodium falciparum malaria.

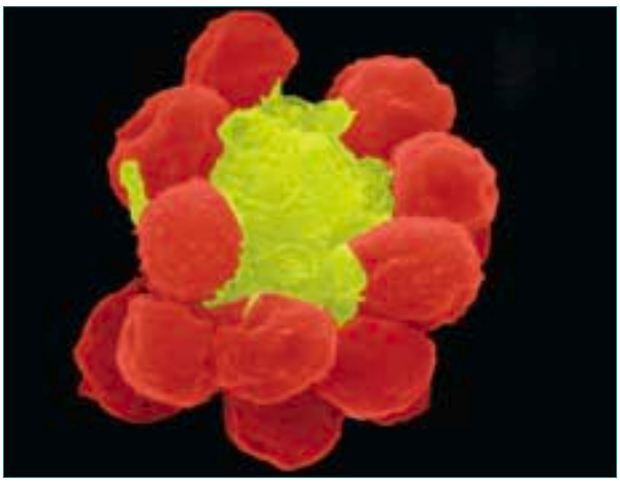
Understanding the obstructions to the development of protective immunity to severe infection with Plasmodum falciparum is crucial for rational approaches to prevent the disease. Furthermore, the development of pharmaceuticals able to control such immune defence mechanisms is highly desirable in order to alleviate the distressing symptoms associated with this disease.

The inventors have now identified a further mechanism by which the malarial parasite prevents the infected host from mounting an effective immune response and preventing recurrences of the disease.

The Oxford invention

Oxford inventors have observed that human erythrocytes that are infected with Plasmodium falciparum are capable of adhering to human dendritic cells. The inventors found that the immature dendritic cells exposed to infected erythrocytes are no longer able to mature into full antigen-presenting cells or to stimulate T-cell proliferation when subsequently exposed to an immune stimulus.

The Oxford inventors have now discovered that dendritic cell maturation on exposure to an immune stimulus can be influenced by molecules which bind to CD36 or to CD51 or both via the bridging molecule thrombospondin (TSP) and which act as agonists.



Above: *Plasmodium falciparum-infected red blood cells adhering to immature dendritic cells*

Applications

1) The invention provides a method for identifying a molecule which is agonist of cell surface receptor CD36 and/or CD51 as expressed by mammalian dendritic cells and a method used to identifying a molecule capable of preventing adherence of erythrocytes infected with a malarial parasite to human dendritic cells.
2) The invention provides a pharmaceutical composition suitable for inducing immune tolerance useful for the treatment of autoimmune diseases associated with dendritic cell maturation and T-cell proliferation.
3) The invention supplies a method of treating mammalian dendritic cells in vitro to induce immune tolerance.
4) The invention provides a method to measure maturation of dendritic cells.
5) The invention allows the development of a pharmaceutical composition useful for the treatment of malaria which comprises a molecule capable of preventing the adherence of red blood infected with the malarial parasite to human dendritic cells.

Commercialisation opportunity

The patent applications are available for licensing and Isis is actively seeking partners for the licensing and commercial development of this technology.

Identification and Use of CD8+ T Cell Epitopes in Applications for Allergic Disease

Isis Project Number 945

Therapeutic area:

Treatment of atopic diseases such as asthma, eczema and hayfever.

Research at Nuffield Department of Clinical Medicine, University of Oxford, has resulted in identification of novel T cell epitopes relating to dust mites allergens.

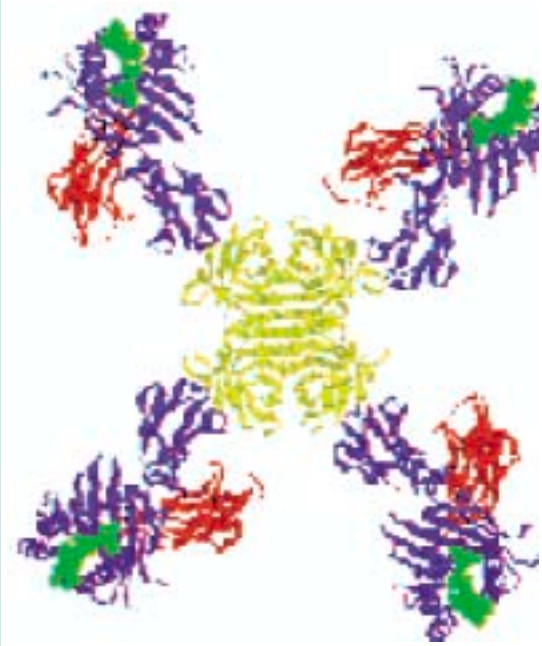
Atopic diseases contribute greatly to health expenses, costing the US alone $6 billion a year.

Background

Atopic disease is an affliction in which an immune reaction occurs in response to usually innocuous substances. Although allergens can come from a variety of sources, dust mite allergens play a significant role in atopic diseases. Dust mites are found in households everywhere, being particularly abundant in bedding and carpets. The dominant allergic protein from dust mite faeces, DerP1 is thought to be especially important in atopic diseases such as eczema, rhinitis and asthma, which affect around 15% of children. Atopic diseases contribute greatly to health expenses, costing the US alone $6 billion a year.

Problem

Current treatments for atopic diseases concentrate on relieving the symptoms rather than treating the disease. Immunosuppressants leave the patient dangerously open to infection, and antihistamines, mast cell stabilisers, bronchodilators and leukotriene antagoists all have their own side-effects, and do not provide a long-term cure. Clearly a more effective, safer therapy would be an advantage.



Above: *Schematic representation of a HLA-peptide Tetrameric Complex*

The Oxford invention

A novel research project from the University of Oxford has resulted in the identification of CD8+ T cells specific for DerP1 in atopic individuals. New evidence strongly suggests that CD8+ T cells are important in disease pathogenesis.

Commercialisation opportunity

This technology has many possible applications, including diagnostic use, for disease monitoring, in therapeutic areas, or for vaccination. A patent application has been filed (number 0108752.7, claiming priority from 6th April 2001) and Isis is actively seeking partners to develop this fascinating, novel concept.

Nutritional Supplement

Isis Project Number 1031

Work in the Lipid Metabolism Group at the Radcliffe Infirmary, University of Oxford, has resulted in the development of a palatable, high-fat drink that can be used as a nutritional supplement or as a concentrated source of energy.

Background

The human body requires a certain proportion of fat in order to function properly. Fat contributes over twice as much energy per gram than carbohydrate or protein, and so is important during exercise, providing around 50% of the body's energy requirements. This can rise as high as 80% towards the end of long endurance events. Fat is also responsible for transporting vitamins A, D, E and K.

At present there is no product on the market which is able to deliver large amounts of fat, orally, in a palatable form

Problem

Athletes, particularly endurance athletes, may need to consume up to 6,000 calories a day to maintain their energy levels. Due to its higher energy value, fat would be the most convenient way of providing this energy. Convalescing patients may also require fat supplements. However, at present there is no product on the market which is able to deliver large amounts of fat, orally, in a palatable form.

The Oxford invention

An exciting new research project has resulted in the development of a high-fat drink which is palatable and provides a large amount of fat in a very concentrated way. Experiments have suggested that products using this technology should have a good shelf-life and could be sold at normal grocer-type outlets. The main advantage, however, is that the composition of this drink can be adjusted to deliver specific fatty acids as a nutritional supplement, or to provide a concentrated energy source.

Commercialisation opportunity

We believe there to be large markets for this product in both the commercial and public sectors, for example as an energy supplement for athletes, for veterinary use, for use in hospitals, and to treat specific nutritional and dietary deficiencies. The supplement would also be very important in research, as it would allow the effect of specific fatty acids on metabolism to be studied in depth. A patent application has been filed and Isis Innovation would welcome inquiries from potential partners interested in commercialising this technology.

Above: *The use of fat emulsion in a research experiment, to increase a specific kind of fat in the circulation.*

An Improved Bone-Implant Interface

Isis Project Number 761

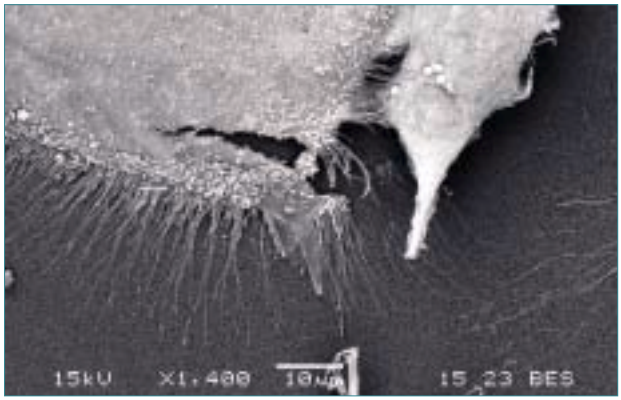


Figure 1: *Scanning electron micrograph showing the colonisation of a sample similar to the Bone Implant Coating by bone cells under* in vitro *conditions. (Bioactive materials have not been inserted into the pores in this sample.)*

A new porous inorganic coating has been developed by researchers at the Department of Materials, University of Oxford, in co-operation with the Centre for Surface Biotechnology, University of Uppsala, with the aim of reducing, or eliminating, the loosening of replacement joint implants.

Background

Replacment implants for replacing broken or diseased bones or teeth are based on special metals or ceramics having inert surface characteristics. This lack of chemical interaction can lead to a weak bond between the implant and the underlying bone, which often leads to aseptic loosening within only 5-10 years. The rate of implant loosening can be slowed by mechanically roughening the surface of the implant to provide features onto which the bone can attach. Another method is to cover the surface in a bioactive material, which encourages the bonding of bone to the implant.

Problem

The promotion of bone growth on the surface of implants using coatings of bioactive glass or hydroxyapatite are expensive, and the coatings are brittle. Mechanical methods of promoting bone to implant adhesion have only a temporary effect as the bone does not grow onto the implant. These drawbacks limit the working life of current implants, which requires additional operations to fit new implants when the old ones loosen.

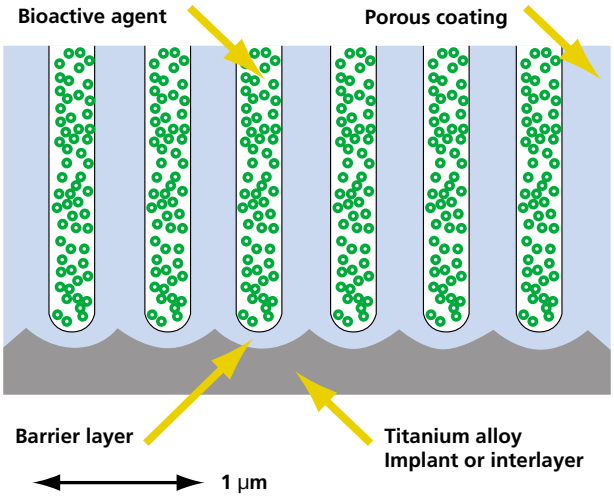


Figure 2: *A schematic cross-section of the coating.*

The Oxford invention

Surfaces covered with bioactive materials can have interfacial bonds with the newly formed bone that are as strong as the parent bone itself. The Oxford invention consists of a process for forming a porous inorganic coating on suitably prepared metals, ceramics, plastics and composites, the pores of which can be loaded with bioactive materials in order to promote bone, or other tissue, growth. Bone cell growth and proliferation on the surface of the implant is promoted, resulting in a significantly stronger bond to the parent tissue. Consequently, the rate of implant failure will be significantly reduced and the service lifetime of implants will be increased. Further increases in implant lifetime are possible by the use of 'slow-release' bioactive compounds, which may be loaded into the pores of the coating.

Commercialisation opportunity

This technology has been patented by Isis Innovation. Companies interested in pioneering the use of this technology to coat any type of medical implant should contact us to learn more about this invention. Given the early stage nature of this promising coating technology approaches from companies producing implants for veterinary use would be especially welcome.

Improvements in Breast Cancer Diagnosis

Isis Project Number 1098

Oxford inventors have developed a means of visualising the physiological parameters extracted from contrast-enhanced magnetic resonance imaging (CE-MRI) used to diagnose breast cancer. These parameters help the clinician interpret quickly the complex physiological processes occurring.

Background

MRI is widely used to image soft human tissue, and there has been much effort to analyse the signal so as to differentiate between normal and diseased tissue; conventional MRI has not yet been able to do this. To sustain their aggressive growth tumours generate millions of microvessels that increase the blood supply around the tumour. CE-MRI uses this physiology, particularly in breast cancer imaging of younger women and where x-ray mammography has been inconclusive. A contrast agent is intravenously injected immediately prior to imaging. Different tissues have different take-up rates; cancerous tissue has a high uptake because of the leaky microvasculature while normal and fatty tissue show little uptake.

Problem

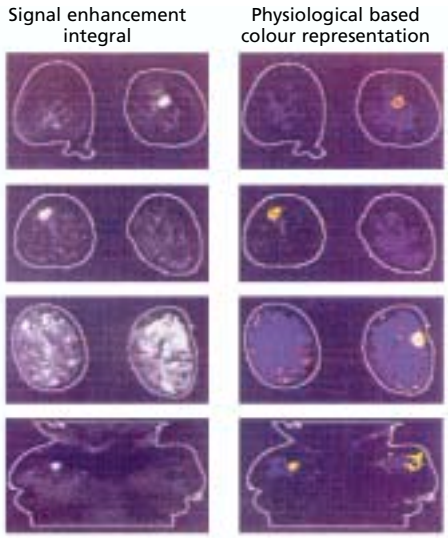
Erroneous assumptions, such as that signal enhancement is linearly related to contrast agent concentration, have led to poor specificity in breast cancer diagnosis. In fact the relationship is both non-linear and is highly dependent upon the intrinsic nature of the tissue under examination. Current diagnostic procedures also rely on detailed and time consuming analysis of signal-time curves by a clinician.

The Oxford invention

The invention is concerned with improved characterisation of the physiology of the breast being imaged, and the calculation and display of physiologically meaningful parameters. These parameters represent the physiology or structure of the breast, and may each be represented by a different colour whose intensity is representative of the value of the parameter. This technique contrasts with the common use in medical imaging of 'false colour', which is often applied to improve the visibility of imaged features relative to a standard grey scale, but has no physiological relevance.

Figure 1:

*Example images of malignant tumours using conventional signal enhancement (**left**) and physiological colour representation (**right**). The colour representation shows highly vascularised regions as yellow or white and necrotic areas as red or blue.*



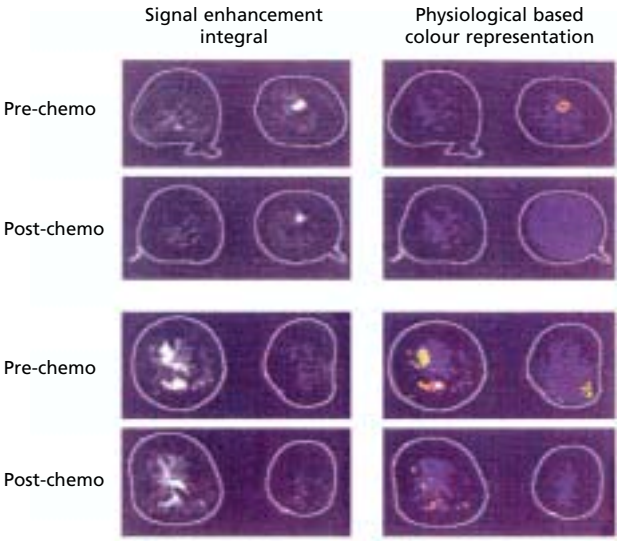


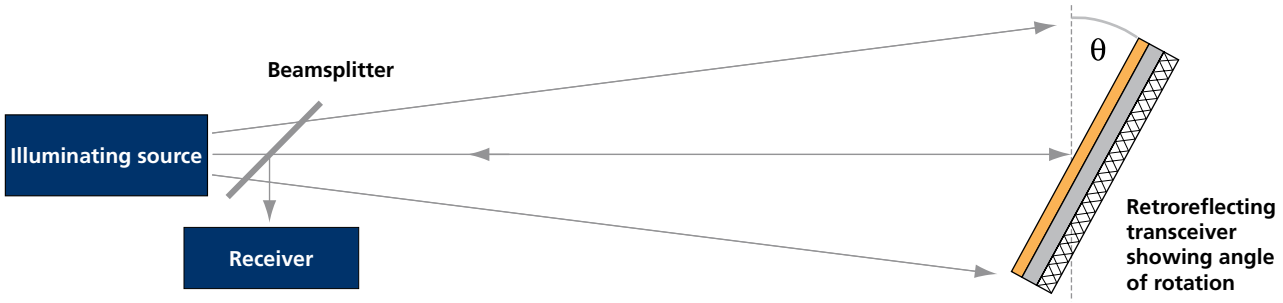
Figure 2: *Pre/post chemotherapy assessment based on signal enhancement analysis (left) and physiological colour representation (right). In both of these examples the signal enhancement analysis suggests that the tumours have partially responded to chemotherapy with shrinkage of the enhancing region. However, the colour representation suggests that the physiological basis for the enhancement has altered with little remaining malignant tissue, indicated by the lack of yellow/white colour following chemotherapy. These results were supported by histology, which indicated that there was little remaining tumour after chemotherapy.*

Commercialisation opportunity

This invention is now the subject of a patent application, and companies interested in developing the technology commercially are invited to contact Isis Innovation.

Modulated Microwave and Optical Retroreflectors

Isis Project Numbers 282 and 532



Above: *Schematic of the optical retroreflector system showing illuminating and reflected signals.*

These inventions describe retroreflectors that return the beam of radiation to the illuminating source and impose a code or information on the return beam by modulating it. It is envisaged that this technology will find application in detection, tracking, positioning and identification.

Background

There is an increasing requirement to enable detection and identification of targets. This can range from providing information for traffic tolling and airspace management to patient supervision in hospitals, security passes and stock control. Here the target automatically provides routine data relating to its type, position, speed or indeed medical notes.

Problem

Present simple retroreflectors comprising 'corner' structures are sometimes employed to enhance both optical and microwave radiation reflections from targets. However, these cannot easily be modulated so it is difficult to establish communications links between the target and illuminator. Current active transponders are costly and have high power consumption so are unsuitable for many applications.

The Oxford inventions

The inventions consist of retroreflectors, which reflect signals back to their source, and additionally can be modulated to provide information transmission back to the illuminating source. Retroreflectors for both microwave and optical frequencies have been developed. Typically the microwave device will be used for longer range applications such as vehicle monitoring whereas the optical system will be suitable for, for example, the smartcards for use in PDAs or 'personal' information carriers.

The return signal can be modulated to provide a means of transmitting data relating to identification, position, speed etc. The ability to pick out coded returns may be used to enhance the readability of a display, enabling detection within any background clutter. Since the incident radiation is retroreflected, the only necessary electrical power is that required to drive the modulating mechanism. This low power may be achieved by a small battery or another modest power source such as a solar cell.

The microwave retroreflector comprises a flat array structure where antennas, switches and connections are all contained on a single printed circuit providing a cheap, robust and visually unobtrusive unit. The optical system is equally inexpensive and simple to manufacture.

Commercialisation opportunity

An option agreement is already in place for the microwave retroreflector in marine applications. However, Isis Innovation is keen to discuss suitable arrangements with companies who wish to develop and utilise the microwave technology in the other available fields and those who are interested in utilising the optical technology.

Unipath – Collaborative Pioneering

New OIS Member

UNIPATH

Unipath is the world's leading women's health consumer diagnostics company with a strong presence in most key markets with its leading brands, Clearblue™ and Clearplan™. Unipath's headquarters are based in Bedford, UK where it employs over 400 people.

Research, development, production and sales and marketing are all undertaken at Bedford where products are distributed to over 80 countries. The company also has offices in Germany, Sweden, Holland and the USA.

Unipath's products are built around a technology that the company has pioneered and patented known as rapid assay technology. This highly flexible diagnostic technique can be adapted to handle most bodily fluids or sample types and can detect large or small molecules.

Our products are sold into two distinct market places. The first is where products can be used by women in the privacy of their own home and the second where tests are used by health professionals.

Home tests include:

Clearblue™: The world's leading home pregnancy test, detecting minute concentrations of a key pregnancy hormone, hCG, giving a result that is over 99% accurate in 1 minute.
Clearplan™: A simple method of detecting changing luteinising hormone (LH) levels to help a couple conceive.
Clearplan Easy™ Fertility Monitor: A simple and accurate method of pinpointing peak fertility.
Persona™: A monitor plus test stick system used to test using samples on 8 days of a menstrual cycle, to track fertility and provide a woman with an objective but natural method of contraception.

Tests for use in clinics and laboratories are sold under the Clearview brand and include:

Clearview™ HCG (pregnancy testing)
Clearview™ Chlamydia MF (rapid detection of chlamydial antigen in both sexes)
Clearview™ Strep A (streptococcal Group A antigen)
Clearview™ IM (detects infectious mononucleosis heterophile antibody in plasma, serum or whole blood)
C. Diff A (rapid detection of Clostridium difficile toxin A)

The world of biotechnology is vast, and although we at Unipath have a bright and talented Research & Development Group, we must always look outwards to others with whom we can work and learn. Isis provides us with a 'hunting ground' where we can explore and perhaps return to Bedford with a new and exciting opportunity to compliment our existing business.

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Acambis plc

New OIS Member

Acambis

Left: *Dr Michael Darsley, Senior Director, Vaccine Research, Acambis*

Acambis is a biopharmaceutical company discovering, developing and manufacturing vaccines to prevent and treat infectious diseases. It has a broad portfolio of vaccine product candidates, including six currently undergoing clinical trials. It also has technology platforms that provide the basis for further vaccine product candidates. Acambis has operations in Cambridge, UK and Cambridge, Massachusetts, USA, and currently employs around 160 people.

Acambis' extensive vaccine product pipeline contains both anti-viral and anti-bacterial vaccines, areas in which Acambis has extensive expertise and experience. Products in development include vaccines to prevent and/or treat travellers' diarrhoea, stomach ulcers, West Nile virus, dengue fever and Hepatitis C.

In December 2000, Acambis concluded a major strategic alliance with Baxter Healthcare Corporation, one of the world's leading healthcare and pharmaceutical companies. Baxter is investing £28m ($40m) in new Acambis equity, ultimately resulting in Baxter owning approximately 20% of Acambis. The alliance also includes an agreement for Acambis to manufacture certain of Baxter's vaccines at Acambis' manufacturing facility in Canton, MA, potentially generating over $200m in revenues to Acambis over the next 10 years. The alliance provides Acambis with significant financial strength and substantial revenue-generating potential.

In September 2000, Acambis was awarded a major contract by the USA Government to develop and manufacture a new smallpox vaccine. The contract is for 20 years and has an estimated value of $343m. The award of this contract is a clear endorsement of Acambis' leadership in the development of live viral vaccines.

In March 2001, Acambis initiated an alliance with Berna Biotech that combines its oral typhoid vaccine with Berna's experience in the manufacture and formulation of live bacterial vaccines. Berna will also contribute its oral cholera vaccine to the alliance, providing an opportunity to create, for the first time, a single dose, oral, combination vaccine to protect against both typhoid and cholera.

Dr Michael Darsley, Acambis' Senior Director of Vaccine Research, commented: 'At Acambis, we are constantly searching for new opportunities in the areas of both validated protective antigens and novel delivery systems in our work to develop vaccines against infectious diseases. We perceive that membership in the OIS could bring us accelerated notification of new technologies available for license from Isis, as well as enabling us to develop other relationships through facilitating contacts with University researchers.'

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Option taken on bone implant technology

Oxford technology and Accentus expertise improve success of hip replacement procedures

accentus

Replacing a diseased hip joint with a metal / plastic articulation was originally developed by Sir John Charnley in the early 60s. Since then the success rate of the procedure has improved to the point that almost one million such arthroplasties are performed annually around the world. The survival rate for such implants is at least 90% after ten years.

However, with increasing lifespan, the cost of re-operating on the remaining 10% is becoming an increasing burden on global healthcare providers. One subset that exhibits less than satisfactory results are those patients under sixty years old. The failure rate of the artificial hip from normal wear and tear is currently much higher for this relatively younger and more active group.

In the mid 1980s, a group of London-based surgeons trialed a metallic prosthesis coated with a ceramic material called hydroxyapatite, which is a normal constituent of natural bone. Such materials had been previously applied to dental implants and had shown promotion of new bone growth around the prosthesis, resulting in improved long-term fixation. Fifteen years later, the consequence of such products has been an improvement in the outcome for younger patients receiving an artificial hip.

Until now such coatings have only been applied using a high temperature plasma-spray technique that is both expensive and time-consuming. This resulted in a much more expensive prosthesis which most healthcare providers could only afford to use for particularly difficult cases or for the very young patient.

A recent development in the Department of Materials, at the University of Oxford, could have the outcome of such technology being offered to a much higher number of patients. Scientists working under the direction of Dr Jan Czernuszka have developed a room temperature electrophoretic method of applying hydroxyapatite coatings to orthopaedic implants. Initial testing has shown these coatings to be highly bioactive and highly porous. This second quality opens up the exciting opportunity of incorporating other molecules such as antibiotics into the hydroxyapatite at the time of deposition, which is not possible using existing techniques. As long-term infection is another major cause of implant failure, this advance could have considerable appeal to the global orthopaedic community.

Isis has recently entered into an option agreement regarding the further development and exploitation of this technology with Accentus plc. Accentus is the intellectual property development subsidiary of AEA Technology, based at the Culham Science Centre. Accentus is active in the development and licensing of intellectual property arising from the activities of the AEA Technology group. It also acts as a development partner for other organisations wishing to develop basic intellectual property into exploitable products or services. The company is currently involved in projects in many fields. These include Electrocat™, an advanced system for the destruction of particulates and hydrocarbons from the exhaust systems of diesel engines; and Silver II™ for the destruction of toxic organic material using novel combinations of catalysis, process and materials technology.

Dr Martin Pickford, the Business Director of the Medical Device Sciences Group within Accentus, is convinced of the long term potential for this Oxford technology to improve the clinical outcome of total hip replacement in the younger patient: 'By combining the knowledge of the hydroxyapatite coating within the University with the expertise in metal surface modification and process engineering existing within Accentus, we are confident in our ability to work together to produce a viable manufacturing process which can then be licensed to orthopaedic manufacturers around the world'.

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Bringing Archaeology into the digital age

Oxford spin-out launches web-accessible image database

Oxford University's Institute of Archaeology has launched Oxford ArchDigital Limited (OAD), a new spin-out company to provide Information Technology training and consultancy services to individuals and organisations involved with the discovery, conservation and presentation of the past.

Traditionally the collection and analysis of archaeological data has been an extremely lengthy process due to the vast amounts of information that needs to be examined, classified and presented. Advances in the flexibility, reliability and access to digital storage and analysis have caused archaeologists, museums, heritage bodies and historic preservation societies to move increasingly towards IT based solutions. This is a process in which OAD co-founder Dr Gary Lock has been a prime mover.

'Due to the complexity and interlinked nature of the data, the collection and analysis of archaeological and similar information is an extremely laborious process,' notes Gary. 'IT not only gives us new ways to store and analyse the archaeological records but also new ways to present it. To do this effectively, one needs both an in-depth understanding of the past as well as advanced computer skills.'

Fellow OAD co-founder Dr Tyler Bell has extensive experience in archaeological fieldwork and the high-end computer applications used to display and analyse archaeological data. He has developed numerous integrated data systems for research projects incorporating GIS (Geographic Information Systems), CAD and web databases, and also builds computer reconstructions of ancient and modern architecture for 'fly-throughs' and lighting studies.

In response to the increasing demand for practitioners to acquire the necessary IT skills, OAD offers a full range of Training modules. These are run from a dedicated facility in central Oxford. The courses are the responsibility of Dr Tom Evans, who has been involved with fieldwork and management in commercial archaeological companies in both the UK and US. The company's Training modules are focused on the effective use of electronic data collection, management, analysis and presentation for individuals and organisations involved with the study of the past or geographically based research.

Consultancy services offered include the design and development of databases, GIS, 3D reconstructions and data-driven dynamic web sites to suit any field project, archive or museum collection. These are of particular value to heritage bodies, commercial archaeological units, researchers, developers and groups within the geographical sciences in need of specialised or comprehensive IT solutions. The company's ToadView image database can be seen on the web site at www.oxarchdigital.com.

Dr Tim Cook, Managing Director of Isis Innovation, said: 'Oxford ArchDigital is Isis' latest spin-out company and interestingly, does not come from a science department, but archaeology. We are looking forward to supporting OAD as it establishes itself in this exciting new field'.

Tom Hassall, President of the International Council on Monuments and Sites, UK and former chief executive of the Royal Commission on the Historical Monuments of England (RCHME), brings unparalleled experience to OAD in the heritage industry. 'Such a body that combines professional training and consultancy services has been needed for some years,' comments Tom.

The management and overall strategic development of OAD are the responsibility of Nick Case, a chartered accountant with experience of running a software company. He has additional experience in the fields of venture capital, corporate development and M&A.

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It's all part of the process…

The public and commercial launch of Novarc, a joint project between the University and Ford Motor Co.

September 4th 2001 was a red-letter day in the history of Novarc Limited, Isis Innovation's twentieth spinout company. It heralded the public and commercial launch of the company, which is the commercial realisation of Oxford University and Ford Motor Company's joint research and development of sprayforming technology – a process dedicated to the manufacture of tools exploiting electric arc spraying. Both Dr Patrick Grant, Department of Materials, and Dr Stephen Duncan, Department of Engineering Science, who lead the Oxford University program, were instrumental in setting up Novarc.

Following a launch to the relevant trade and regional media, the company, headed up by managing director Dr David Field, is already generating revenue in the first two months of its existence and the signs from the marketplace are that Novarc is set to capitalise on the technology into the long term.

So, why is the sprayforming process and Novarc's exploitation of it being looked upon so enthusiastically by the engineering and manufacturing sectors? Here, Dr Field explains a little more about the process, the history of the development and the role of Isis.

'Throughout manufacturing industries, be it automotive, aerospace, medical or any other sector, any reduction in lead times that can be gained in introducing new products to the marketplace is extremely valuable from a commercial perspective.

'One of the greatest limiters on the introduction of new products is in the design and manufacture of prototype and full production tools and dies. In addition, conventional toolmaking procedures are invariably laborious and place a heavy financial burden on manufacturing budgets.

'Sprayforming is set to change that – the technology has the capability to cut up to 75% off the lead times of conventional

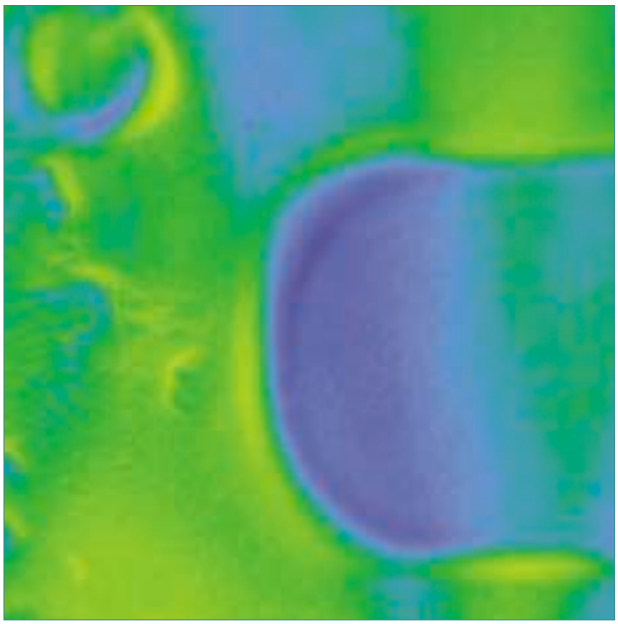
Above: *(L) Dr David Field, Managing Director, Novarc Limited and (R) Herb Askew, Project Manager, Isis Innovation*

techniques. However, while the use of electric arc spraying, particularly with zinc metal, is increasingly common in the manufacture of 'soft' tools for prototype work, its utilisation in high volume production runs is limited. Novarc can produce hard, steel tools for production applications in the same time scale.

'The process is applicable to a wide range of tools, including plastic rotational moulding, plastic and rubber injection moulding, reaction injection moulding, composite panel moulding tools, metal stamping and pressing, as well as forming and sand core moulding tools.

'Once a design for a part has been completed, usually via CAD/CAM technology, a three dimensional model is created in a low cost modelling board and a ceramic cast taken to create a reverse replica refractory pattern utilising freeze casting. The freeze cast is heated but not sintered to drive off moisture and leave a net shape part ready for the next stage of the process. Tool sets can be manufactured for any size of part, from a door handle to potentially a complete body panel for a vehicle.

'The refractory pattern is then placed in a chamber, where an automated robotic system sprays the cast with molten steel. This creates a fully hardened, net shape shell of the working surface of the tool. The ceramic is then removed and the tool cap, or shell, is ready for assembly. Much of Novarc's core technology lies in the on-line control system developed at Oxford for the robot and spray guns.



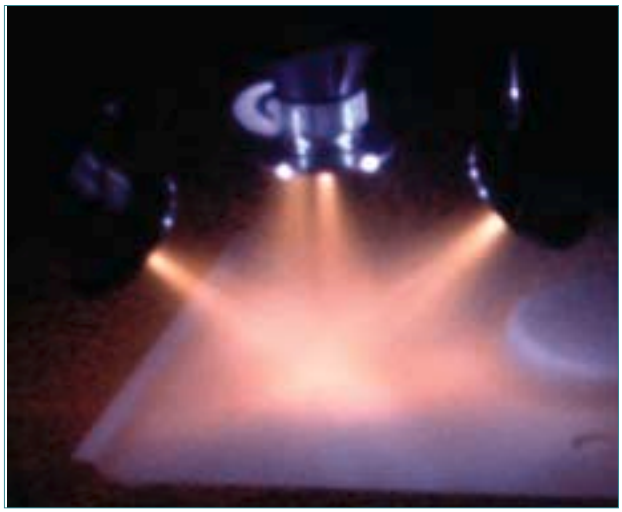
Above: *Thermal image of tool undergoing Sprayforming. The areas imaged in blue are running cooler than the areas shown in yellow.*

'While costs for one off tools are comparable to conventional tools, significant economic advantages are gained where multiple tools are required – due to the spreading of upfront set up costs.

'Currently, we are working on 600mm x 600mm tools at our Begbroke facility and it is only a short time before the company is able to handle far larger tools.

'Ford Motor Company is leading the development of large tools and systems. Through their wholly-owned subsidiary, Ford Global Technologies Inc. (FGTI), Ford acquired the rights to sprayforming technology from British-based company Sprayform Holdings back in 1999. Novarc has now licensed the key intellectual property rights of the technology from FGTI and continues to enjoy the automotive manufacturer's patronage and influence. Novarc has an exclusive license to sell turnkey spray forming systems in Europe and can sell tools and dies throughout the world.

'Obviously, Isis has also been pivotal in the formation of Novarc, following Oxford University's involvement in the development of sprayforming technology. Isis brought together the team and investors and put in train all of the steps required to incorporate and complete the start-up. The relationship is ongoing and Dr Herb Askew represents the University on the Novarc board.



Above: *Thermal sprayforming of development tool for Airflow Streamlines plc by Novarc*

'In addition to the support of Isis Innovation and Ford, Novarc also benefits from close ties with Beeson Gregory – the investment bank specialising in small-cap, high-growth companies – via its subsidiary IP2IPO. IP2IPO is a company that forms partnerships with universities, working with them to create value from their intellectual property. IP2IPO is an investor in Novarc. Bringing extra strength to the partnership between the two organisations is IP2IPO's CEO, Dr. Chris Wright. Himself an Oxford chemistry graduate, Wright is also the non-executive chairman of Novarc.

'As an example of the potential of the process, it is estimated that sprayforming could save up to five months of the usual development time for a prototype vehicle in the automotive industry, a time saving that will equate to millions of pounds. This is the size of opportunity that awaits Novarc. With the support of Ford Motor Company, Beeson Gregory and especially Isis Innovation, it is an opportunity we will embrace.'

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Bringing diagnostics closer to the patient

Further success for Oxford Biosensors' revolutionary handheld medical devices

Oxford Biosensors was formed in August 2000 with the objective of delivering a low complexity, convenient and low cost medical diagnostic system for use in primary care to the key market of doctors' surgeries and healthcare clinics. This bold objective was built around the development of an easy-to-use instrument, capable of measuring multiple parameters from the smallest drop of blood, but still only the size of a mobile phone. In August 2001, ahead of schedule, the company demonstrated proof of principle to its shareholders with prototype test strips that operate in conjunction with this proprietary instrument. These initial test strips can measure up to six parameters in less than 30 seconds.

Taking diagnostics closer to the patient is well recognised as a logical consumer-focused trend. To date it has received mixed success and lessons can be learnt from some of the earlier problems that companies have experienced. Most notably, siting relatively complex devices into doctors' offices has not proved successful because these instruments have essentially been miniaturised laboratory analysers which still require skilled users. The US market, with its well-controlled laboratory regulations (CLIA), strongly favours simple systems with minimal user test influence.

With all this in mind, the development team behind Oxford Biosensors started with a test as simple to use as a diabetic's glucose meter and worked towards the following aims:

- the instrument should be simple to use with minimal user inducible error
- consumables should not require refrigeration
- tests should only require blood from a small finger prick directly onto the test strip
- automatic instrument calibration should be included with every pack of test strips
- results should appear in seconds, eliminating return patient visits or results by mail
- test panels should be designed for particular conditions

Oxford's expertise

During the first year of proving the science, much of the work was carried out through research contracts with the University of Oxford, drawing on the scientific skills and assets within both chemistry and engineering faculties. Obstacles in electrochemical science that had previously prevented multiple sensors to be co-located on a single strip were challenged and overcome to allow several parameters to be measured at once. Consequently, the Company's intellectual assets have expanded from the initial two patents to the currently filed six and a further five in process, providing a strong portfolio of IP.

The real novelty of this technology is the development of the strips to incorporate micron sized electrodes – a similar feature size to integrated circuits – but using low cost plastic and carbon ink substrates. The device has been developed for manufacture from the start, using mass manufacture techniques that lend themselves to high reliability. There are matching patents on electrochemical detection techniques that make optimum use of these microelectrode structures with rapid detection times and broad enzyme applicability.

One sample
One strip
Multiple parameters
Minimum time

Although most of the IP resides in the tiny test strip, the instrument design is still important as it forms the critical user interface. The initial prototype units are small, hand-held devices that allow the user to view all measurements at once or scroll through them. The data can also be stored in the instrument's memory or downloaded to a PC. The next phase will see the design develop into a dockable, rechargeable device that can synchronise information back to electronic patient files, as well as provide a hardcopy from an integrated mini printer.

The system is expected to become a doctor's office platform that will run a number of test strips, each focussed on a particular condition:

Strip#1 will combine markers for **cardiac risk**, where the accepted group of total cholesterol, HDL, LDL, and triglycerides are determined on a single strip.

Strip#2 will be an extension of #1. The **statin monitor** strip will be for patients with elevated lipids who are prescribed statin drugs. It will include a marker for liver disorders, alkaline phosphatase, as well as a marker for myopathy, creatine kinase, to monitor recognised side-effects of statins.

Strip#3 will combine markers for **renal care** and is designed for monitoring the condition of people with kidney disease, measuring creatinine, blood urea, uric acid, potassium and sodium. This is a large market where fast results bring real benefits to both the patient and medic. It is hoped that eventually the device will be used by the patients themselves, so that they can directly see the effect of complying with low salt and protein diets at the same time as feeling the benefits. Such a device would allow doctors to better control and schedule renal care intervention as necessary.

Further strips for **liver function**, **neonates**, etc will follow.

Where now and where next?

At the outset, six parameter strips were planned, with the possibility of working up to many more test parameters on a single strip – a possibility which the Oxford Biosensors team now knows can be done. In reality, however, configuring separate strips for condition-related groups of markers as described above presents a very practical format and there are rarely occasions when more than six parameters would be needed for a single strip.

The Company is now moving from technology development into product development and has already moved most of its activities to premises at the University's Begbroke Science Park, four miles north of the city. Discussions with potential marketing partners have also begun for branding and sales of the product.

Above: *Multiple parameters measured in a drop of blood.*

With a clear understanding of market needs, product design and the required manufacturing process, Oxford Biosensors is proceeding with second round financing to build manufacturing capabilities and an operational infrastructure that meets the regulatory needs of the Global Healthcare Markets and will take the technology to market within a two year timeframe.

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Joint Isis / OION Meeting

Tuesday, 30th October 2001 at the Sir Martin Wood Lecture Theatre, Oxford

Oxfordshire Investment Opportunity Network Ltd

On Tuesday, 30th October 2001, the Oxfordshire Investment Opportunity Network (OION) held a joint meeting with Isis Innovation at the Sir Martin Wood Lecture Theatre, Oxford, to introduce private investors to the wealth of opportunities for investing in local start-ups.

OION, a technology focused Business Angel Network, runs a series of presentation meetings where its network of over 100 investors can be exposed to companies during the crucial fundraising stages. Isis also manages a not-for-profit organisation, the Isis Angels Network, which introduces its business angels to the newly formed spin-out companies emerging from the University of Oxford. Together, Isis and OION sponsored the joint meeting during which seven local start-ups had the opportunity to present their companies to an audience of over 100 individuals looking to invest.

The presenting companies included IFM Company, which will market the Illuminated Flexible Membrane, a novel display product which facilitates optimum viewing in extreme lighting and climatic conditions where conventional electronic display products normally perform poorly; Physiomics plc, which uses patented software technology to simulate medically relevant processes, enabling the creation of virtual patients to predict optimal therapy in diseases like cancer and diabetes; and Hallmarq, which will be shortly installing its first-to-market MRI (magnetic resonance imagining) scanner at a leading equine veterinary practice, an acknowledged diagnostic procedure formerly too expensive and inconvenient for use by vets.

Four of Isis' planned spin-out companies, Oxitec, PharminOx, BioAnalab and NeoParadigm, also presented at the joint meeting. **Oxitec** has proprietary new technology (RIDL) that will greatly increase the cost effectiveness of controlling insect pests in agriculture, and insect vectors in public health, with an anticipated cost savings of up to 90% over existing techniques in a market currently worth tens of millions. **PharminOx** (formerly Oxford Therapeutics) is a spin-out company based on the research of Professor Gordon Lowe FRS, who has discovered a group of terpyridine platinum (II) complexes which possess both antitumour and antiparasitic activity. **BioAnalab** is based on the work of three founders who have over 50 years experience in the development of therapeutic antibodies and are seeking to establish the company because the current level of orders is too great to handle in a University setting. Additionally, no UK company at present offers a service for the specialised analytical testing monoclonal antibodies require during clinical trials. **NeoParadigm** is a bio-medical company with core technology, most advanced for liver applications, which centres on a novel way of maintaining organs that preserves their functionality far better than current methodology and has potential in preservation of donor organs for transplantation, liver support for patients with acute liver failure, and treatment of liver-sited secondary cancer metastases.

The joint meeting, which also featured Isis Director Mr Tom Hockaday speaking on 'Investing in people – building teams for start-ups', concluded with a finger buffet and wine to afford the guests and speakers the chance to network and discuss the new business ideas presented. Following the success of this joint meeting, Isis and OION have plans to collaborate again for a meeting in October 2002.

For further information about Isis' planned spin-outs companies, please contact Jennifer Johnson on 01865 280839. For information about OION, see below.

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University Challenge Seed Fund

£2m invested

The Oxford University Challenge Seed Fund has now invested over £2m of its £4m capital, two years after its inception. The Fund has made 46 investments in all; each aimed at developing opportunities for the commercial exploitation of Oxford University research. The investments range in size from a few thousand pounds to the maximum allowable investment of £250,000. This rate of investment is in line with original forecasts and there is a consistent flow of new investment opportunities to the Fund.

The Fund continues to invest in a wide range of activities: the development of research outcomes within the laboratory; validating preliminary research findings; generating additional data to support international patent applications; exploring the market potential of an opportunity by commissioning specific market research; and as initial investment capital into new spin-out companies.

It is clear that the Fund is now playing an integral part in stimulating the commercial development of Oxford research

The Fund now holds investments in nine of the companies recently spun-out from the University:

- **Mindweavers Ltd**
- **Novarc Ltd**
- **Oxford Ancestors Ltd**
- **Oxford ArchDigital Ltd**
- **Oxford Bee Company Ltd**
- **Oxford Biosensors Ltd**
- **Oxford Biosignals Ltd**
- **OxLoc Ltd**
- **PharmaDM NV**

In addition, two of the Fund's investments have been made into technologies which have been licensed out to industrial partners. It is clear that the Fund is now playing an integral part in stimulating the commercial development of Oxford research.

The background to the Fund is that during 1999 Oxford University was awarded one of 15 seed funds that have been established as part of the Government's University Challenge Seed Fund Scheme. The aim of the Scheme is to fill a funding gap in the UK in the provision of finance for bringing university research discoveries to a point where their commercial usefulness can be demonstrated and the first steps taken to ensure their utility. The Scheme's primary focus is the exploitation of science and engineering research outcomes. Oxford University has established a £4M Fund made up of contributions from the University (£1M) the Government (£1.4M) and the Wellcome Trust (£1.6M).

The key criteria the Fund uses for evaluating proposals are:

- The innovation of the science
- The intellectual property position
- The route to market
- The scale of the commercial opportunity

A researcher wishing to apply for funds should contact either the Project Manager at Isis Innovation with whom they are already working, or Tom Hockaday to be put in touch with the appropriate Project Manager. Isis has produced a booklet that explains the workings of the Fund in more detail. This can be found on the Isis web site at www.isis-innovation.com and copies are available from Isis.

Company Contact

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Meetings

Isis
University of Oxford
Innovation Society

Forthcoming meetings of the
Oxford Innovation Society
will be held on the following dates:

Thursday 6th December 2001

Thursday 21st March 2002

Thursday 26th September 2002

All meetings will be held at 5:30 p.m. followed by a Reception and Dinner for members and invited guests at a University college.

For information about the OIS contact Jennifer Johnson, Marketing Administrator:
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