

9.3 Applied genomics (LINK)

9.3.1 Summary

The Applied Genomics (LINK) programme has been running since 2000, jointly sponsored by the Biotechnology and Biological Research Council (BBSRC), the Medical Research Council (MRC) and the then Department for Trade and Industry (DTI). The objectives of the programme are to encourage collaboration between industry and academia using genome sequence and genetic data to identify new functionalities in biological systems that are capable of exploitation in the healthcare industries.

Interviewees consider the programme to have been successful in both an academic and economic sense. Although much of the work is far from maturity, partner businesses have already benefited directly and potential wider impacts are identified.

Already, some new products have been generated and with many projects, the developments have helped the companies' competitiveness. At least six companies received significant further investment or were acquired for their capabilities that were in part developed under the programme. These investments exceed £500 million and helped to retain capability in the UK.

Substantial indirect impacts of this work are expected in the future as the technology matures. The market for functional genomics already exceeded £450 million in 2002 and is forecast to increase to more than £1,000 million this year. Many of the outputs of these projects have direct or indirect application in the fields of disease prevention, diagnostics and drug discovery. By way of illustration of potential impact a recent report concluded that the cost of developing an innovative drug is estimated at more than £500 million including expenditures on failed projects and the value of forgone alternative investments and the process takes on average 12 years.⁴⁶² Assuming that the work informs that process and avoids even a few months of the total effort spent on failed projects the benefit may be many £ millions per product realised - particularly as it is used early in the development cycle.

The impact of the work will arise from the knowledge generated in this ongoing programme, with 70 articles published and 21 patents filed to date.

A total of £28 million has been invested in the programme, half from the three sponsor Research Councils and half from industry, predominantly SMEs.

⁴⁶² <http://www.abpi.org.uk/statistics/intro.asp> . See also report by Congress of the United States Congressional Budget Office In the cost of developing an innovative drug is estimated at more than \$800 million including expenditures on failed projects and the value of forgone alternative investments, and the process takes on average 12 years (Congress of the United States, Congressional Budget Office study (2006) Research and Development in the Pharmaceutical Industry)

We can identify the following likely effects on net outputs. A significant additionality effect is identified, based principally on the scheme having achieved its objective of stimulating the pre-competitive networks, often sought between academia and industry. Displacement of existing research programmes of UK based firms or research groups does not appear to have occurred. There has been some leakage of the research outside the UK as a result of a major acquisition by overseas companies, although the companies continue to operate and innovate in the UK. There is also evidence of leverage as some projects have been successful in engaging with and realising long funding commitments from major industry stakeholders.

9.3.2 Case study description

The LINK programme in Applied Genomics was launched in 2000, jointly sponsored by BBSRC, MRC and DTI.

The LINK scheme is a Government initiative for promoting collaboration between industry and academia in pre-competitive research. The scheme focuses on areas of strategic importance for the future of the national economy, and encourages innovative research with good potential for eventual commercial exploitation. The scheme provides up to 50% of the funding for those projects.

Genomics is the study of an organism's entire genome (the hereditary information of an organism encoded in DNA or RNA). At the time of the launch of the Applied Genomics programme, the first "draft" of the human genome had just been announced in June 2000 by the Human Genome Project,⁴⁶³ subsequently published in 2001.^{464,465} This sequencing of the 3.1 billion bases which make up the human genome was achieved through coordinated international collaboration, at 16 centres with thousands of research scientists at a cost of approximately \$300 million.

Applied Genomics aims to increase the understanding of the information contained within the genome and how the resulting proteins function and interact, at the cellular, tissue and organism levels, in humans and other species.

The objective of the LINK Applied Genomics programme is stated as follows: "to encourage research collaborations between industry and academia which will use genome sequence and genetic data to identify new functionalities in biological systems that are capable of exploitation in the healthcare industries."⁴⁶⁶

It was considered important to support and encourage the exchange of knowledge and techniques between the UK healthcare industry and academic research to optimise the exploitation of genomics.

⁴⁶³ See http://www.ornl.gov/sci/techresources/Human_Genome/project/clinton1.shtml

⁴⁶⁴ International Human Genome Sequencing Consortium (2001). "Initial sequencing and analysis of the human genome." *Nature* 409: 860-921

⁴⁶⁵ Venter, JC, et al (2001). "The sequence of the human genome." *Science* 291: 1304-1351

⁴⁶⁶ See the LINK Applied Genomics website: <http://www.appgen.org.uk/index.htm>

Calls for proposals for the programme were announced in July 2000. A permanent programme management committee was responsible for reviewing the proposals and making the decisions. The programme management committee members were appointed by the three sponsors, and were subsequently involved in the monitoring of the projects.

The outline proposals required a joint submission between academia and industry, with the lead Principle Investigator (PI) being from industry. Each was assessed on the following grounds:

- Fit to the remit of the programme
- Eligibility of the company for DTI funding
- Eligibility of the academic for Research Council funding
- Collaborative working
- Scientific excellence.

More than 100 outline proposals were submitted over a period of time, around half of which made it to full submission. These applicants were then visited by the programme coordinator, Dr Celia Caulcott, as part of the assessment process. Following recommendation for full funding, 21 projects were started, representing a total funding of £28 million. All but two of the companies were new to LINK funding.

Each project set out its aims and objectives at the start.⁴⁶⁷ The projects contain a diverse range of research areas under the applied genomics umbrella. These range from the discovery of new antibiotics, diagnostics, drug discovery and modelling of neurodegenerative disease, and technology development.

Throughout the programme, there have been regular formal meetings for each project between the academic and industrial collaborators, held 3-6 monthly and also attended by the programme coordinator. six month reports are also required to be submitted, which contain both scientific and financial data and progress, as well as a final report and a project completion form.

The programme is still ongoing, with 14 of the projects now complete. The last project is due to complete at the end of 2008. two projects were closed or withdrawn before completion. A dissemination event took place in April 2005 at the Royal Society at which eight of the projects presented. A final event is planned for the autumn of 2007.

9.3.3 Input characteristics

As described in Section 6.2.2, the BBSRC, MRC, DTI as well as the individual companies taking part to the LINK Applied Genomics programme have all contributed to the programme, see Figure 77, representing a total of £28 million.

⁴⁶⁷ Each project objectives are stated on the programme website: <http://www.appgen.org.uk/index.htm>

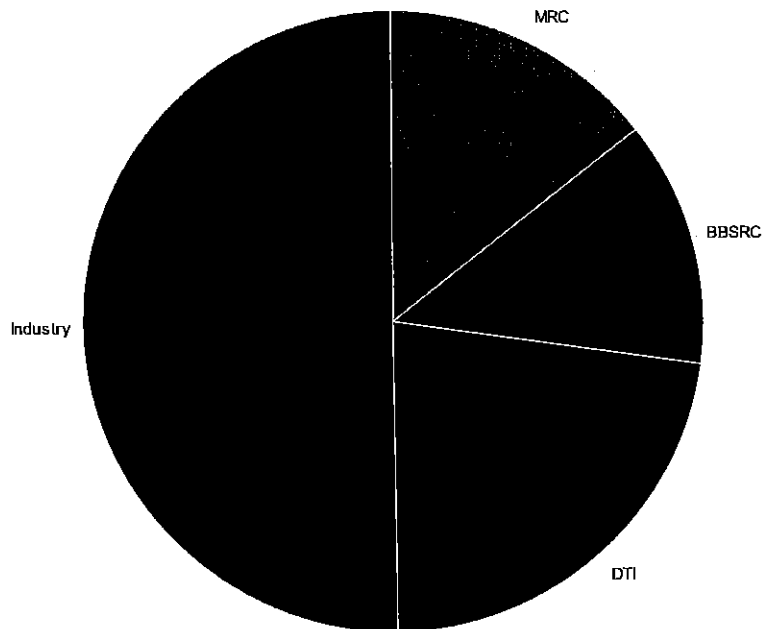
Each academic lab received funding from either the BBSRC, MRC or both, with the associated company receiving DTI funding. The company then contributed an equivalent amount in cash, in kind, or a combination.

In total, 17 different UK universities or research institutes have taken part in the programme, collaborating with 23 companies. 21 of the companies are SMEs (small and medium enterprises). Together, the industrial contribution was almost £14 million.

The total input from the three funding bodies was as follows:

- £3,599,652 from the BBSRC
- £3,990,429 from the MRC
- £6,219,797 from the DTI
- The individual project costs ranged from approx £300k to over £3 million.

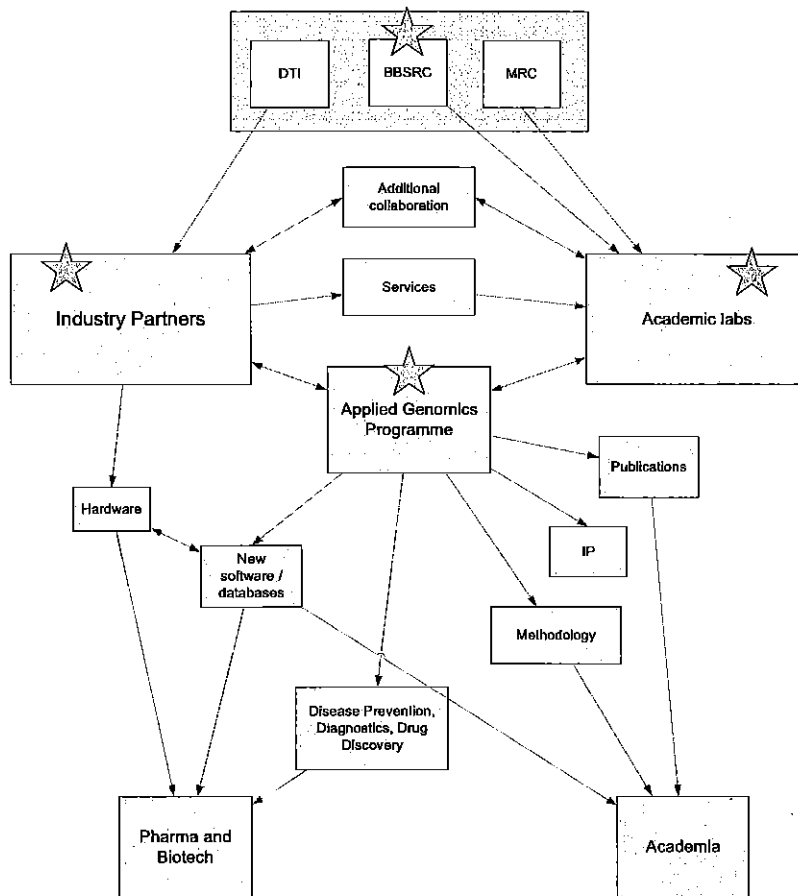
Figure 77: Funding inputs for the LINK Applied Genomics programme⁴⁶⁸



⁴⁶⁸ Financial details regarding the programme were obtained from LGC Ltd

9.3.4 Stakeholders

Figure 78: Stakeholders in the LINK Applied Genomics case study, with primary category of interviewee shown (blue star)



9.3.5 Gross outputs

The gross outputs from the LINK Applied Genomics programme are expected largely to be in the form of codified knowledge. However, other outputs such as intellectual property, services, skills and networks may emerge and will be considered in this evaluation.

Codified knowledge and Intellectual Property

To date, 70 publications have been produced from the Applied Genomics projects.⁴⁶⁹ Many of these articles have been published in high quality and relevant journals, such as Cell, Nature, and the Journal of Bacteriology.

⁴⁶⁹ Data obtained from LGC Ltd

The quantity is likely to increase by the end of the programme and beyond since it is not unusual for publications to be submitted after a project is complete; for example several interviewees had papers in preparation. Given that the combined input of the BBSRC and MRC to the programme was £7.6 million, this gives a value to the Research Councils of £108k per peer-reviewed paper already published. However, in this case study, it may be that the quantity of publications is not an accurate calculator of the amount and quality of science as an output, given the commercial nature of this programme.

So far, there have been 21 patents filed as direct outputs from the Applied Genomics programme.⁴⁶⁹ As discussed above, this number will possibly increase as the programme is ongoing. This quantity of patents, averaging at one patent per project, confirms the commercial value of the research.

In addition to the intellectual property, outputs that are of direct value to the companies taking part include the development of novel targets, tools and equipment for drug discovery.

Many of the companies involved are small start-ups, and as a result of taking part in the programme, several of the companies have received further investment. For example, one interviewee claimed that the peer-review due diligence and the demonstration that the company had the essential financial know-how through auditing and smooth running of this project enabled the company to receive a further investment of £4.5 million; almost 10 fold the value of the DTI grant.

One of the academic collaborators remarked that their project had been a "resounding success and win-win for every partner".

Services and methodology

Methods have been developed as part of the outputs of some of the projects. For example, the objective of the HUSERMET project is to develop novel methods for the analysis of the human serum metabolome, including an appropriate database and data model, and then to use these methods to make measurements in patient and control populations.

Networks

In terms of the wider networking capability between the project teams, the dissemination events were good opportunities. However, outside of those, there was little communication between the different projects, which is not surprising considering the diverse nature of the different projects.

Application for the LINK funding was required to be a joint submission between the academic and industry investigators. Therefore, to a certain extent, networking was a prerequisite in order to take part in the programme. New collaborations were formed which may not have happened in the absence of the programme, and in other cases the programme has led to improved and closer relationships. These now-established relationships will potentially lead on to further collaboration, but it is too early to see that happen yet.

Therefore, although networking between projects was not a major output, the programme enabled relationships to be created and strengthened between the partners within a project.

Qualifications and skills

Although no formal training, such as PhD studentships, was included in the programme, "on the job" training was provided and skills were gained where the areas of science were different to those carried out in typical research grants. This is also true where extra employment was provided for by the programme. These skills transfers were evident for both the academic and industrial partners, with each benefiting from the other.

9.3.6 Net outputs

On balance, when considering the net outputs from the Applied Genomics programme, we identify the following likely effects that suggest the programme made a significant contribution to the impacts identified:

- A significant additionality effect – based principally on the scheme having achieved its objective of stimulating the pre-competitive networks, sought but not widely realised between academia and industry. Displacement of existing research programmes of UK based firms or research groups does not appear to have occurred
- Significant leverage as some projects have been successful in engaging with and realising long term funding commitments from major industry
- A significant leakage of the research outside the UK as a result a major acquisition by overseas companies, although the companies continue to operate and innovate in the UK, for example the acquisition by Illumina of Solexa, or of Inpharmatica by Galapogas.

To what extent might the programmes have been supported by 'the market' or results obtained from overseas in the absence of Research Council funding?

One can legitimately claim additionality if there is reason to believe that without Research Council funding the particular activities would not have been undertaken.

The Applied Genomics research outputs do indeed have the characteristics of a "public good" in that use by one organisation does not prevent use by another. The additionality provided by public funding is usually stronger where: the research is further from the market and the research outputs are relevant to more than one sector. However, it is difficult to claim that the benefits are non-commercial, given the nature of research and the large number of acquisitions of companies funded by the programme. Furthermore, the displacement of existing activities (one of the determinants of additionality) of existing research programmes of UK based firms or research groups does not appear to have occurred.

Overall the LINK programme seems to have enabled a different type of project to be carried out – too technically risky for many companies but more market relevant with more industry direction than many academic research projects. All types of interviewees found the programme valuable in enabling challenging important research to be carried out that gives both a technical and scientific lead – the programme is very well regarded and has been seen as giving benefit to small businesses. Similar observations have been made by interviewees for many other case studies spanning this type of collaborative DTI led schemes (for example other LINK schemes - see Sections 7.2 and 9.2 - and Foresight Challenge, Section 4.3):

- According to some interviewees, in the absence of the LINK programme, the science could probably have happened and been supported by the BBSRC or MRC in the case of the academic research. Conversely others stated that research would not have happened in the absence of the scheme
- One of the academic interviewees stated that they would not have done this piece of work in the absence of the LINK programme as they deemed it too risky. This was because at the time they didn't know enough about their industrial partner's technology and it would have been challenging applying for a non-LINK grant in this situation. However, the project has been successful and the outputs have given them a lead in their field
- The programme enabled a different type of science to be carried out than would normally be funded by Research Councils – pre-competitive but also market relevant, combining technical risk with an understanding of potential applications. As such the scheme was regarded as valuable and there was general concern that an equivalent scheme does not now exist to enable substantial industry collaboration and funding combined with innovative science. One industrial interviewee commented: "It seems a shame that the Applied Genomics LINK programme has come to an end and that there is no similar vehicle currently in existence provided by the Research Councils or DTI. The situation is very different in other EU countries where government funding is enabling small start-up companies to grow and develop. The Wellcome Trust's "Seeding Drug Discovery" scheme is a good model, and there is room in the UK for the BBSRC and MRC to run an equivalent scheme."
- Furthermore, although it was acknowledged that the academic grant applicants would normally apply to the Research Councils for funding, the size of the grants for this programme were much larger than the BBSRC would typically support.

The question of whether the results could have been obtained from overseas is not really an issue in this case – given an objective of the programme was to bring businesses together with the research and researchers.

In this light, we can suggest that there is likely to have been an additionality effect.

Other effects

There are two other effects which are likely to be significant in the context of the programme, leverage and leakage.

On leverage we have indications of significant leverage as projects have been successful in engaging with and realising long term funding commitments from major industry.

- One of the commercial stakeholders noted that although they had received only a small amount of DTI funding, if the LINK funding had not been available, they would not have been able to leverage the specialist academic technical expertise of the academic groups and a particular aspect of their work would not have occurred. The direct result of this work led to a patent, a publication and a PhD studentship to continue the work in the academic laboratory
- As discussed in detail later, during the scheme at least six of the partner companies received significant further investment or were acquired for their capabilities that were in part developed under the programme. These investments exceed £500 million and helped to retain capability in the UK..

Leakage of the knowledge generated outside the UK is likely to be potentially significant as a result a major acquisition by overseas companies, although the companies continue to operate and innovate in the UK:

- One of the projects resulted in an achievement that had previously been unsuccessfully attempted by other groups. The academic partner attributed their success to the focussed, goal-orientated, specific and systematic approach taken by their participation in this programme, and the resources being provided to carry out this approach. This end-result is in the process of being written up for publication and has already been requested by several other academic groups. The partner company has benefited by having expanded their tool set to offer their customers
- As noted above several parties were acquired, some by international companies during the course of the programme which is expected to result in leakage of the expertise and knowledge.

9.3.7 Economic impacts

The programme has been considered a success by many; success being defined as giving benefits to both the academic and industrial communities.

With 2002 revenues at around \$ 940 million, the functional genomics market is forecast to become more dominant in the future and increase to around \$2.2 billion by 2007. A report in 2002 estimated a grow rate of around 18% per annum for the short to medium term.⁴⁷⁰

Many of the outputs of these projects have direct or indirect application in the fields of disease prevention, diagnostics and drug discovery, and as such, the final products remain several years from reaching the market. However, the value of this early stage research can be seen by the acquisition of six of the companies taking part in this programme, totalling well over £500 million. Further investment in several others also reinforces the value of this research.

⁴⁷⁰ The Global Functional Genomics Industry, Scope Marketing & Information Solutions (P) Ltd, Nov 2002

New products, processes or services

One participating company fulfilled its aim on this programme of developing a novel chip based high throughput instrument, and has gone on to partner with another company and received £465k of further investment to further develop their drug discovery instrument. This new instrument is said to be "... based on a prototype successfully constructed under the highly effective 'Applied Genomics' programme. This programme was led by deltaDOT and Imperial College".⁴⁷¹ One of the academic interviewees stated that the outputs of their project had given them a significant boost and placed them three years ahead of the competition. It had enabled them early access to certain data, and the partnership had accelerated the work which was placed in the public domain.

Increased or retained investment in the UK

A major output of the programme for Prolysis Ltd was a £4.5 million investment from US venture capital, to whom the Prolysis could point their thorough peer-review assessment and due diligence to become involved in this LINK programme; a demonstration of the "softer" benefits, other than funding, that the programme brought. The further development of technology and tools from the Applied Genomics programme enabled a total of £10 million investment. Many of the small start-up companies involved in the programme have gone on to receive further rounds of investment, some of whom attribute that success to having taken part in this programme.

Several of the participating companies have been acquired since the programme began, as detailed in Table 26, further attributing value to the type of research funded by the LINK Applied Genomics programme. Note that due to the overlap in subject areas, both Solexa and Inpharmatica were formed on the basis of research conducted on the back of BMS Committee grants and are also discussed in the BMS case study.

Table 26: Recent acquisitions of participating programme companies

SME	Acquired by	Value of Acquisition	Date
Solexa ⁴⁷²	Illumina	Approx. \$600 m	January 2007
KuDOS Pharmaceuticals ⁴⁷³	AstraZeneca	\$210 million	December 2005
Arrow Therapeutics ⁴⁷⁴	AstraZeneca	\$150 million	February 2007
DanioLabs ⁴⁷⁵	VASTox Plc	£15 million	March 2007
Lorantis Ltd ⁴⁷⁶	Celldex Therapeutics	unknown	October 2005
Inpharmatica ⁴⁷⁷	Galapagos	€12.5 million	December 2006

⁴⁷¹ See website: http://www.deltadot.com/downloads/news/04_June_2007.pdf

⁴⁷² See: http://www.forbes.com/2006/11/13/illumina-pharmaceuticals-earnings-markets-equity-cx_rs_1113markets10_print.html

⁴⁷³ See: <http://www.astrazeneca.com/pressrelease/5207.aspx>

⁴⁷⁴ See: <http://www.astrazeneca.com/pressrelease/5298.aspx>

⁴⁷⁵ See: http://www.vastox.com/news/press/20070322_acquisitions.pdf

⁴⁷⁶ See: http://www.celldextherapeutics.com/wt/page/pr_1162507676

Other, quality of life and social impacts

Most of the outputs of the projects have direct or indirect application in improving the prevention, diagnosis and treatment of disease.

Without exception, all of the interviewees commended the contribution that Dr. Celia Caulcott made as programme coordinator. As such, she was actively engaged in every project, gave good advice at the relevant level, and facilitated all parties throughout the process.

⁴⁷⁷ See: <http://www.glbq.com/press/2006/26.pdf>



LINK Applied Genomics

[Home](#)[Funded Projects](#)[Event](#)

A success story

[Objectives](#)

This LINK programme has, by any measure, been one of the most successful LINK schemes ever. One of the reasons for the success of the programme has been the varied and high quality projects which have been supported. Most of the projects funded by the sponsors of the LINK Applied Genomics Programme, on the recommendation of the Programme Management Committee are described in the following pages.

[PMC](#)[Projects](#)[Completion](#)

[The Link Applied Genomics Booklet](#) (pdf, 1.5Mb) describes some of the projects in more detail

[Contact](#)

Projects

[The Use of Differential Proteomics to Identify Markers for Active DNA Repair Pathways](#)

[Genome wide identification of proteins essential for cell cycle progression in Drosophila](#)

[Prototype systems development for protein expression profiling and novel antibody selection](#)

[Capturing Protein Functional Information from Structural Data: 3D templates and genomic annotation](#)

[Identification and Validation of Novel Protease Genes of Pathogens as Therapeutic Targets](#)

[Development of a Protein Folding Chip](#)

[A partnership to help build verified human protein-protein interaction maps](#)

[Genomic differences between human acute and chronic wounds](#)

[Novel anti-microbial target identification and exploitation](#)

[Neuroregeneration Genomics](#)

[Pathogenomics, a novel genome-wide strategy for the construction and evaluation of mutants in *Salmonella enterica* serovar Typhimurium: application to drug discovery and vaccine development.](#)

[Generation of new natural and non-natural antibiotics by genome mining and pathway engineering](#)

[DNA Diagnostics for analytical microbiology](#)

The *Bacillus* Cell Factory: a new tool for the biomanufacturing industry

Bioinformatics for the Analysis and Exploitation of Re-sequenced Genomes

Differential Display proteomics for drug discovery and diagnostics for Alzheimer's Disease

Zebrafish models of Parkinson's and Alzheimer's Disease - novel tools for identifying pathways and drugs that modulate disease

The Human Serum metabolome in health and disease

Canine population genetics and study design for linkage disequilibrium gene mapping

A genomic and genetic analysis of Notch signalling as a modulator of immune response

New Expression systems for polyketide antibiotics

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Home**Neuroregeneration Genomics****Event**

Dr Liang-Fong Wong, [Oxford BioMedica](#), Professor Malcolm Maden and Dr Jonathan Corcoran, [MRC Centre for Developmental Neurobiology](#), King's College, London and Prof Steve McMahon, [Centre for Neuroscience Research](#), King's College, London.

Objectives**PMC****Projects****Completion****Contact**

There are very few therapeutic options for spinal cord injuries as, unlike embryonic central nervous systems (CNS), adult CNS has limited regenerative capacity. There is research evidence that this is due to intrinsic differences in the regenerative capacity of adult and embryonic neurones, in part at least due to the presence, during regeneration of embryonic neurones, or absence, during failure of regeneration of adult neurones, of retinoic acid receptor 2 (RAR 2). Using the various expertise of the partners, the project aims to discover downstream targets of RAR 2 and identify further target genes which will be of direct clinical relevance for the treatment of spinal cord injury. This will be based on differential gene expression profiling between embryonic and adult spinal cord and between lentiviral vector RAR 2 transduced and untransduced adult spinal cord. Identified candidate genes will be tested for their ability to induce neurite outgrowth when transfected into adult spinal cords and other appropriate models.

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Home**DNA diagnostics for clinical microbiology****Event**

Dr John Clarkson, Molecular Sensing plc, Dr Toby Jenkins University of Bath, Prof Jon Cooper, Univ of Glasgow and Dr Giles Edwards, Stobhill Hospital

Objectives**PMC**

This project aims to develop a novel platform technology for use in exploitation of genomic data from clinically important bacterial pathogens. The principal objectives are:

Projects

- Optimisation of electrochemical DNA assays for selected bacteria
- Characterisation of appropriate electrode materials, sensor geometries and surface functionalisations to enhance detection sensitivity and specificity

Completion**Contact**

- Incorporation of microsystems technology with DNA amplification and detection protocols

The outcome of the project will be an initial prototype microsystem.

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[Home](#)

Bioinformatics for the Analysis and Exploitation of Re-sequenced Genomes

[Event](#)

[Objectives](#)

Clive Brown, Solexa Ltd., Dr Richard Durbin, The Wellcome Trust Sanger Institute, Professor David Balding, Imperial College and Dr Ewan Birney, EBI.

[PMC](#)

[Projects](#)

[Completion](#)

[Contact](#)

The overall aim of this project is to accelerate the development of software infrastructure and analysis methods to exploit multiple whole-genome sequences of humans and other organisms. In parallel with this, the Ensemble system is to be extended and advanced so as to enable the management, data visualisation and querying of output from whole-genome sequencing technologies. The project will develop statistical methods and tools which exploit total genome data to localise genes involved in disease causation and drug metabolism. It is planned to develop whole-population simulations under more realistic assumptions than have previously been employed and to use these simulations to investigate the performance of the statistical methods, leading to the development of software implementing the most effective statistical procedures for whole-genome data.

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Home**Canine population genetics and study design for linkage disequilibrium gene mapping****Event****Objectives**

Dr Neale Fretwell, Masterfoods, Prof David Balding, Imperial College and Dr Jeff Sampson, The Kennel Club

PMC**Projects****Completion****Contact**

Dogs are of interest for commercial, social and scientific reasons. In particular they provide promising models for many human diseases because: a) the canine genome is very similar to that of humans and dogs suffer many diseases that are very similar to human diseases; b) the small effective population sizes in many breeds and the fact that certain diseases are particularly prevalent in certain dog breeds, means that it is likely that genes for many diseases will be much easier to find in dogs than in humans.

The project brings together the three applicant groups with the aim of developing an understanding of canine genetics relevant to disease. Canine population genetics will be studied through Kennel Club records, and a genetic pilot study will be undertaken in order to design the best possible studies to identify disease genes in dogs.

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Home**Genomic differences between human acute and chronic wounds****Event**

Dr Sharon O'Kane, [Renovo Ltd](#), Professor Charles McCollum (Dept of Surgery) and Professor Andrew Boulton (Dept of Medicine), [University of Manchester](#).

Objectives

The principal aims of this project are:

PMC**Projects****Completion****Contact**

- Identification of gene expression differences linked to healing /non-healing status of chronic wounds (venous and diabetic ulcers)
- Identification of gene expression differences specific to healing/non-healing status of venous or diabetic ulcers
- Identification of genes involved in acute healing in patients with both conditions
- Identification of differences in gene expression between acute healing in patients with chronic wounds and acute healing in patients without chronic wounds.

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