Capturing the Economic Impact of the Babraham Institute

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ABBREVIATIONS

3Rs	Replacement, refinement and reduction
AICR	Association for International Cancer Research
AMS	Academy of Medical Sciences
BBSRC	Biotechnology and Biological Sciences Research Council
BBT	Babraham Bioscience Technology
BCS	Babraham Commercial Services
BI	Babraham Institute
BIS	Department of Business Innovation and Skills
BRC	Babraham Research Campus
BSU	Biological Support Unit
BTEC	Business and Technology Education Council
CACHE DCE	CACHE Diploma in Childcare and Education
CLL	Chronic lymphocytic leukaemia
CNS	Central Nervous system
CPD	Continuing professional development
CRT	Cancer Research Technology Limited
CRUK	Cancer Research UK
DEL NI	Department for Employment and Learning Northern Ireland
DNA	Deoxyribonucleic acid
EEDA	East of England Development Agency
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
EMBO	European Molecular Biology Organisation
EU	European Union
FGFR	Fibroblast growth factor receptors
FTE	Full time equivalent
FY	Financial year
GDP	Gross domestic product
GM	Genetically modified
GSK	Glaxo Smith Kline
GVA	Gross value added
HEFCE	Higher Education Funding Council
HEFCW	Higher Education Funding Council for Wales
HEI	Higher Education Institutes
IAT	Institute of Animal Technology
Ig	Immunoglobulin
IP	Intellectual property
IPR	Intellectual property rights
ISP	Institute Strategic Programmes
KEC	Knowledge exchange and commercialisation
LMB	Laboratory of Molecular Biology
Mab	Monoclonal antibody
MEP	Member of the European Parliament
MP	Member of Parliament
NNEB	National Nursery Examination Board
NVQ	National vocational qualification
ONS	Office of National Statistics
PI3K	Pi3 kinase
PLoS	Public library of science
R&D	Research & development
RCUK	Research Councils UK
SFC	Scottish Funding Council
SME	Small and medium-sized enterprises
STEM	Science, Technology, Engineering, and Mathematics
TAP	Transporter for antigen processing
TCR	T cell receptor
TNF	Tumour necrosis factor
UK	United Kingdom

CHAPTER 1. EXECUTIVE SUMMARY

The output from the Babraham Institute has major economic impact through fundamental research underpinning actual and potential health gain via innovative interventions and supporting 'strong and sustained' growth of bio-industry in the UK. World-class research by the Institute and an ecosystem that encourages innovation, enterprise and private sector investment on the Babraham Research Campus has led to high quality business investments by global biopharmaceutical companies (e.g. AstraZeneca), medium-sized biologics companies and start-ups.

The report's main conclusions are:

- The Babraham Institute produces a very high standard of fundamental research with high and increasing Impact. Its epigenetics research has been categorised in the top 10 worldwide.
- Fundamental research over the last two decades has made major scientific contributions leading to commercial development of therapeutics in several important areas. In particular, development of humanised and human monoclonal antibodies, to which Babraham has made a major contribution, has improved, in particular, treatment of cancer and inflammatory and autoimmune disease. Monoclonal antibodies now represent a global industry with sales currently of c. £32 billion. PI3 Kinase inhibitors are promising development-stage targeted therapeutics for treatment of cancer and inflammatory disease, to which Babraham has contributed much of the underlying science. The potential health gain to the UK from successful development of this novel class of therapeutics is conservatively estimated at £92 million pa.
- Inventions have been commercialised through licensing to private companies and through the formation of two new start-up companies.
- Publicly funded research at Babraham is contributing to the productivity of R&D in the private sector through commercial agreements with global biopharmaceutical companies, medium-sized biologics companies and start-ups. It provides national and in some cases, unique scientific facilities (e.g. BSU, Next Generation Sequencing and Mass Spectrometry for lipidomics analysis) that are used by both research and commercial clients.
- Babraham sits at the heart of the Cambridge biomedical cluster encouraging innovation by smaller local high-tech businesses.
- The Babraham Institute produces highly trained scientists, an essential resource for UK companies and foreign companies investing in the UK. It also trains highly skilled technical staff, nursery staff and provides apprenticeships.
- The UK economy is being supported by public investment in scientific research at Babraham and the Babraham Research Campus is a main part of the UK life sciences 'innovation system' making the UK attractive for inward investment by international business and industry.
- The level of public engagement is high and has broadened from student and school engagement to public dialogue.
- The systems in place for knowledge exchange and commercialisation are successful and are taking fundamental discoveries to the market by the most appropriate and sustainable route.

These conclusions are aligned with those of RCUK which recognises that:

- the greatest long-term productivity advances come through breakthroughs in basic knowledge;
- a substantial proportion of the R&D that creates new knowledge and leads to increased productivity is undertaken in universities and other public research institutions; and
- the UK needs to be engaged in frontier research to be able to take advantage of frontier research being done elsewhere.

BIS has an aim of 'promoting impact through excellent research supporting the growth agenda'. The BIS strategy for Knowledge and Innovation is to promote research excellence and to increase business innovation. High quality research at the Babraham Institute and the development of the Babraham Research Campus is successfully delivering these aims and can be considered as an exemplar for the UK. The Bioincubator was one of the earliest established, supported by the UK Government in 1995, and has been fully occupied since 2001, with the demand leading to construction of 80,000 sq ft of purpose-built lab and office space. The case studies of PI3 Kinase and monoclonal antibody technology development leading to biological therapies produced by transgenic mice illustrate the time-lag between research and realisation of economic health benefits of about 15-20 years. However, selling expert services to external clients has very little, if any, time lag between discovery and application.

Many of Babraham's research programme outputs are at too early a stage to identify quantifiable economic impact. However, Babraham's basic biology research programmes in chromatin remodelling, epigenetic and non-coding RNA regulatory mechanisms, and cell signalling address fundamental questions of genome and cellular regulation and lineage specification underpinning human development, immune function, health and disease. Babraham has recently initiated a number of projects addressing changes in cellular function and epigenetic programming related to ageing. As described above, past precedents indicate that the economic impact to be derived from these programmes would be expected to arise in c. 20 years from now.

Investment in the research base at Babraham serves a national purpose. The Babraham Institute undertakes world class life sciences research to generate new knowledge of the biological mechanisms underpinning ageing, development and the maintenance of health. The Institute employs around 335 staff and the research is organised into four Institute Strategic Programmes under 25 Principal Investigators with ~70 Cambridge University PhD students and ~75 postdoctoral researchers, together with support staff, administration staff and visitors, coming from all over the world. About 350 people are employed by 39 companies on the Babraham Research Campus contributing to the Cambridge biomedical cluster. The Cambridge area is the pre-eminent UK biotech/life-sciences research cluster and adult unemployment in the South Cambridgeshire District in which Babraham resides, at 5.4%, is well below the national average.

At an operational level, the economic impact of the Babraham Group in 2011/12 contributed GVA of £41.5 million, supporting 660 jobs nationally. The local economic impact is estimated at GVA of £29.5 million, supporting 477 jobs, directly and indirectly, in the local economy.

CHAPTER 2. BACKGROUND, METHODOLOGY & POLICY CONTEXT

2.1 BIS policy objectives & investment

BIS has a stated aim of "promoting impact through excellent research supporting the growth agenda[1] and stated vision to achieve strong sustained and balanced growth through:

1. An educated workforce
2. Being the best place to start, finance and grow a business
3. Encouraging investment and exports, via
   a) investing further in the UK's world-class research base, and using it to encourage high quality business investment
   b) encouraging innovation, enterprise and private sector investment across the country

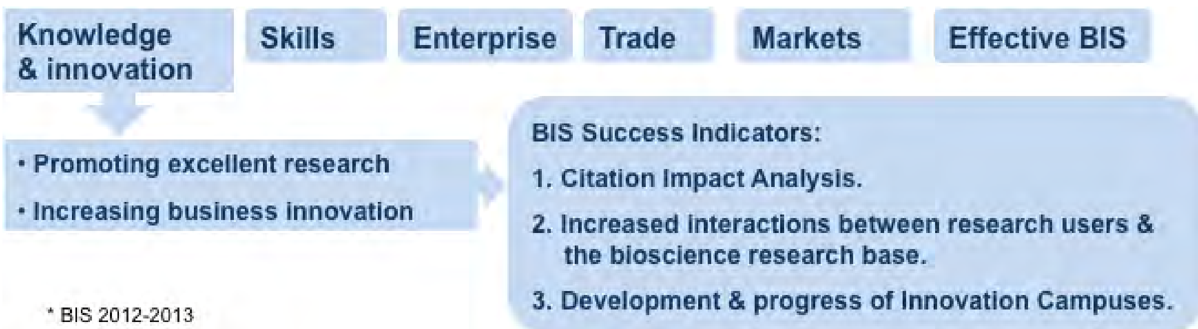


Figure 1 BIS Success Indicators

How does funding from the British Government support the Babraham Institute? In 2012-2013 the BIS budget is £18.1 billion. From this budget £11.8 billion is allocated to Knowledge and Innovation (12% capital), and from this £5.3 billion to Science & Research (11% capital) of which £3.1billion to the Research Councils (12% capital).

Biotechnology and Biological Sciences Research Council (BBSRC) has an annual budget of around £445 million, to support research and training in universities and strategically funded institutes on behalf of the UK tax-payer helping society to meet major challenges, including food security, green energy and healthier, longer lives. BBRSC aims to further scientific knowledge, to promote economic growth, wealth and job creation and to improve quality of life in the UK and beyond. BBSRC investments underpin important UK economic sectors, such as farming, food, industrial biotechnology and pharmaceuticals.

The Babraham Institute received £33.1 million investment from BBSRC in 2011-12. The BBSRC requested that the Institute, in parallel with its other research institutes, undertakes an evaluation of the economic impact of its activities. This is, in part, an update of an evaluation conducted in 2009[2], although the earlier report was more narrowly focussed on the economic impact of the Institute's technology transfer activities. The economic impact of the Institute activities are analysed with respect to the demonstrable excellence of research (in Chapter 4), the translation of the research and newly invented technologies (in Chapter 5) and the development and progress of the Babraham Research Campus (in Chapter 6). These outputs support the key deliverables in Knowledge and Innovation at BIS. The contributions made by the Babraham Institute to developing human capital, policy, knowledge exchange and public engagement are analysed in Chapter 7 using a framework supported by the Research Councils UK (RCUK).

[1] Guide to BIS 2012-2013
[2] The Economic Impact of the Babraham Institute, DTZ, November 2009

2.2 BBSRC policy objectives & investment

Research and training priorities at BBSRC focus on three major economic, policy and societal 'Grand Challenges' facing the UK[3]:

I. Food security - maintaining a safe, affordable and nutritious food supply for UK citizens
II. Sustainable bioenergy - chemicals and renewable materials from bioscience
III. Enhancing lives and improving wellbeing - through fundamental bioscience

Investment in 'healthy ageing' research at the Babraham Institute supports the third Grand Challenge. Fundamental knowledge generation underpins innovations in healthcare, new prevention strategies, new treatments and new pharmaceutical targets. The BBSRC priorities underpin the needs of industry and encourage multiple mechanisms for technology transfer. Thus the economic impact can be demonstrated in the biotechnology and pharmaceutical industries. Fundamental bioscience research at the Babraham Institute focuses on basic molecular and cellular mechanisms responsible for longevity or premature ageing (e.g. triggers of cellular senescence, damage and repair processes) and how these are modulated by diet, exercise and developmental factors.

Transformative changes at BBSRC include increasing integration with Higher Education Institutes (HEIs) and expanding the accessibility of Institute facilities as national resources. To contribute to the UK's 'innovation system' BBSRC supports its Science and Innovation campuses at Babraham and Norwich ensuring that excellent science facilities, accommodation and support for start-up and small companies are developed to enable the companies to benefit from the "low risk" environment, expertise and facilities.

BBSRC views the ultimate demonstration of its impact as being the strength of the UK bio-industry sector, which is the largest contributor to the UK's trade surplus, exceeds other sectors in terms of 'value added' and pursues more research in the UK than any other sector. Whilst there are many aspects to this, the world-class bioscience base is a major contributory factor[4]. The consistent message from the pharmaceuticals and biotechnology sectors is that a substantial contribution to their success, and indeed reason for location in the UK, is access to a world-class bioscience research base and highly-skilled manpower.

2.3 RCUK policy objectives

The investment in science over the last decade by the British Government has been increasing and hence there has been a trend towards analyses that demonstrate and measure economic impact (see Figure 2). The 'Impact Agenda' has been a major, and sometimes controversial, initiative implemented by RCUK over recent years[5], encouraged and supported by HM Government. RCUK defines it thus:

> *"Impact is the demonstrable contribution that excellent research makes to society and the economy. Impact embraces all the extremely diverse ways in which research-related knowledge and skills benefit individual, organisations and nations by:*
>
> - *fostering global economic performance and the economic competitiveness of the UK*
> - *increasing the effectiveness of public services and policy*
> - *enhancing quality of life, health and creative output"*

[3] BBSRC Delivery Plan 2011 - 2015 Maximising Economic Growth in The Age of Bioscience
[4] Research Council's Evidence For The Economic Impact Group – 24 April 2006
[5] See, for example, Research Council's Evidence for the Economic Impact Group, April 2006

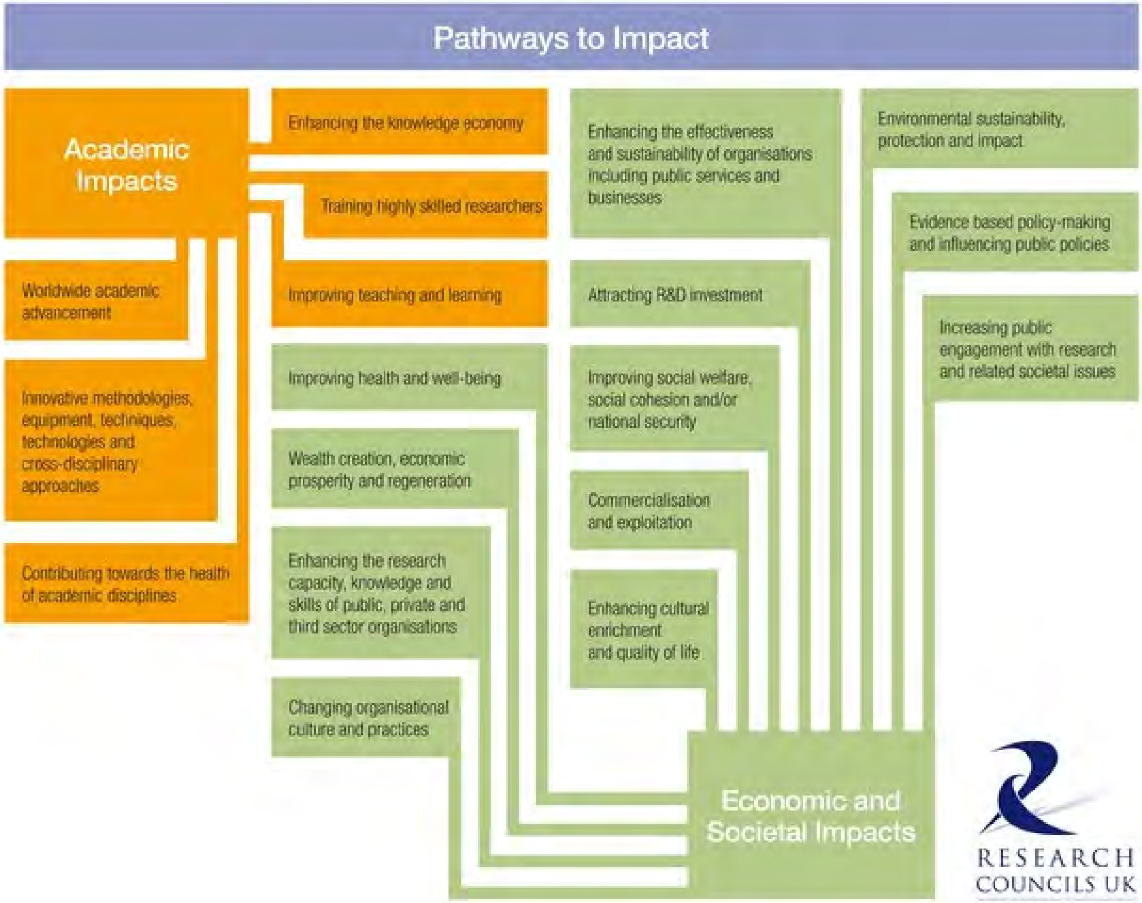


Figure 2 RCUK Pathways to Impact

RCUK is the strategic partnership of the UK's seven Research Councils who annually invest around £3 billion in research. RCUK support excellent research (as judged by peer review) that has an impact on the growth, prosperity and wellbeing of the UK. To maximise the impact of research on economic growth and societal wellbeing RCUK work in partnership with other research funders including the Technology Strategy Board, the UK Higher Education funding bodies, business, government, and charitable organisations. RCUK believe that "research is at the heart of the UK's long-term wellbeing and economic growth.[6]" RCUK developed a framework for measuring impact under four headings:

1. **Development of human capital:** primarily through the acquisition of skills that accompany the research process. Also includes the training and migration of skilled graduates and postgraduates, the movement of skilled researchers into industry and other research organisations. Value measured through additional salary benefits to individuals.
2. **Business and commercial:** commercial adoption of research and exploitation of IP, knowledge transfer through collaboration and creation of clusters and its impact upon inward investment.
3. **Policy:** the impact that research has on government policy, plus research that, over time, challenges conventional wisdom.
4. **Quality of life**: the diverse impacts which manifest themselves in benefits such as improved environment, social welfare, health and cultural advances. Improvement in the delivery of public services which give rise to economic impact through cost savings.

[6] Professor Delphy, RCUK Impact Champion, RCUK Research for our Future 2010

2.4 Research Methodology

The work programme included:

- Consultation with Principal Investigators, senior managers and BBT staff
- Desk review of financial data, mainly from 2006-2012
- Interviews with Babraham Research Campus (BRC) tenant companies (face to face and by telephone)
- Desk research and analysis
- Desk review of impact indicators and other 'comparator' organisations
- Consultation with industrial collaborators.

2.4.1 Research Excellence Analysis

According to RCUK research excellence is judged by peer review. The output of original research papers was measured and the impact factor and the scientific citation rate calculated to illustrate the significance of the research over the last twenty years. Recently, the H Index has come to be the most generally accepted single citation-based measure of a researcher's impact. H Indices were calculated and adjusted for length of career. The economic impact was analysed with reference to the maturity of the research programmes and further illustrated with a case study on PI3 Kinase.

2.4.2 Value chain analysis

The analysis of wealth creation can be mapped onto a value chain. Value chain analysis describes the activities within and around an organisation, and relates them to an analysis of the competitive strength of the organisation[7]. Therefore, it evaluates which value each particular activity adds to the organisations products or services. Some activities are primary activities and some are support activities. The translational activities at the Babraham Institute were mapped onto a value chain and the results described in Chapter 5. The route to market for two technology platforms are illustrated using Crescendo Biologics as a spin out and the licensing strategy for Vectibix.

2.4.3 Business Process Analysis

Business Process Analysis using value chains often stretches beyond the linear workflow processes it was designed for. The activities at the Institute has been mapped onto the 'value chain' in Chapters 5 and 6 to show the commercialisation process for new technologies on their path to generating wealth in the UK. .Pioneering work on Value Chains, Shops and Networks by Stabell and Fieldstad, identified that business value can be generated through business models other than the traditional business process chain. They introduced the concept of the "Value Shop" to cater for expert driven businesses and 'Value Network' for interdependent businesses. An initial analysis has been made for the Institute based upon the relationships to external organisations using the financial data available from 2006-2012; hence the value of the project (current and expired), the physical location of the organisations and the PI involved are shown as a network diagram[8]. Analysis started with random geographical locations but then used a force graph algorithm to cluster the points, so projects that share people and places in common are pulled together. The analyses are shown as screen shots from an interactive display.

2.4.4 RCUK framework

RCUK recognise that the challenge is to identify, and quantify, the economic impact of fundamental research and develop a framework for the analysis (see Table 1). The economic impacts from the Babraham Institute were analysed using this framework in Chapter 7.

[7] Porter, M., "Competitive Advantage: Creating and Sustaining superior Performance" 1985

[8] Analysis using proprietary software, D Burden, www.daeden.com

Framework	Measure of Impact
Business & Commercial	▪ Exploitation of intellectual property ▪ Commercial adoption of research ▪ Creation of clusters ▪ Impact upon inward investment
Development of Human Capital	▪ Acquisition of skills ▪ Training of skilled staff ▪ Movement of skilled researchers into industry
Policy	▪ Impact of research upon government policy ▪ Research that challenges conventional wisdom
Quality of Life	▪ Improved health, environment, social welfare & cultural advances

Table 1 RCUK framework for how research is translated into impact

2.4.5 *Case studies*

The case studies use a bottom up approach to estimating economic impact by taking research outputs and tracking their actual or potential impact. They also illustrate the timescale that the translation of fundamental research/discovery biology takes, over a decade in many cases.

2.4.6 *Modelling economic impact*

A number of methodologies are used depending upon the nature of the evidence that needs to be collected; quantitative evidence from, for example, financial methods, econometrics, network analysis and survey questionnaires or qualitative evidence from case studies, expert judgement and longitudinal studies. The three elements that comprise impact studies were analysed and found to be[9]:

I. Rationale for research funding
II. Analytical frameworks
III. Methodological options

The economic impact of the Babraham Institute, as with most other academic research institutes, accrues in a multiplicity of different ways reflecting their complex public/private ecosystem. These are illustrated in

[9] De Campos, A., A note on the economic impact assessment of the Research Councils 2009

Figure 3, and range from the most immediate and most measurable, in direct, indirect and induced Gross Value Added (GVA) and the associated employment creation (the 'Operating Impact'), to the long-term economic contribution made by academic research to addressing societal needs.

Because of the relative simplicity of measuring the former, compared to the complexity and uncertainty associated with measuring the latter, there is a risk of ignoring or underplaying the economic impact of the research outputs themselves, which are nevertheless, the raison d'être of the Institute. Over the longer term the economic impacts of the research outputs should massively outweigh the Operating Impact. In reality, compared to a baseline ('counterfactual') of alternative investment of equivalent amounts of capital in general employment creation/economic stimulation measures (as opposed to 'do nothing'), the Operating Impact would be very small.

As illustrated in the methodology framework below (Figure 3), the short-term purely economic impact of the Babraham Institute can be readily distinguished from the broader and strategic impact of the Institute's research base and outputs. The analysis is described in Chapter 8.

Figure 3 The components of economic impact

Gross Value Added (GVA) Analysis

GVA is the standard measure of short-term economic impact and is readily derived from the financial information to be collected as described above. The Institute's income and expenditure over the three years since the last Economic Impact assessment has been analysed, applying relevant multipliers to derive indirect and induced impact. Impact at local and national levels to the extent possible with the available spend data have been identified.

Short-term Economic Impact Linked to the Research Base

Short-term economic impacts derived from the Institute's research base include income from scientific consultancy and contract research, which can be valued at cost (as there is an external market and price-setting mechanism). Treatment of collaborative research projects will depend on the length of the project and level of risk-sharing; long-term collaborative projects with industry in which the Institute assumes significant risk should be treated similarly to the IP portfolio (below).

Long-term Economic Impact of the Research Base

Measurement of the economic impact of research outputs, whether patented and immediately commercially exploitable, or 'academic' where the economic and societal benefits accrue in the long-term in an indirect way, is intrinsically difficult, due to a number of factors, including:

- The timescales to realisation of value are long; even for relatively near-market innovations, economic returns usually occur 5 years or more after initial scientific breakthroughs, and may be substantially longer in fundamental research;
- Innovation is usually non-linear and for much academic research inherently unpredictable, with recognition of substantial advances occurring at irregular intervals
- Many innovations represent aggregations of multiple contributions from many, often disparate sources, and identifying respective contributions difficult;
- Development of commercial products particularly in life sciences is subject to a high level of attrition, requiring risk-adjustment to current values of developmental projects.

This study has identified research outputs over the past 10 years and, for the IP portfolio, tracked the commercial development over the period documenting qualitatively, and to the extent possible, quantitatively, the actual and prospective research impact, by Research Theme. The case studies use a bottom up approach to estimating economic impact by taking research outputs and tracking their actual or potential impact.

CHAPTER 3. INTRODUCTION & PROFILE OF THE BABRAHAM INSTITUTE

3.1 Research focus on lifelong wellbeing and healthier ageing

The Babraham Institute undertakes world class life sciences research to generate new knowledge of the biological mechanisms underpinning ageing, development and the maintenance of health. Research focuses on signalling and genome regulation, particularly the interplay between the two and how epigenetic signals can influence important physiological adaptations during the lifespan of an organism. By determining how the body reacts to dietary and environmental stimuli and manages microbial and viral interactions, the Institute aims to improve wellbeing and healthier ageing. For example, in December 2012 the Institute's scientists published new evidence for how cell membranes reassemble after cell division, how heart muscles get remodelled and how DNA in developing egg and sperm are 'reset' in preparation for making an embryo.

3.2 BI Profile

The Institute's scientists aim to understand how normal cellular processes operate and change during development and as we get older. They look to define the underlying mechanisms of cell signalling and gene regulation, focussing on important processes early in development and key functions in the brain, heart and immune system. Knowledge gained from the research may be translated into medicines or therapies for human diseases such as cancer and Alzheimer's disease through strong links with business, industry and the wider community. For example, in December 2012 a new collaboration with Karus Therapeutics was established to characterise novel treatment for inflammatory diseases through the inhibition of phosphatidylinositol-3-kinases (PI3K) - a family of enzymes important to immune cell function.

The Institute's research is organised into four Institute Strategic Programmes under 25 Principal Investigators with ~70 Cambridge University PhD students and ~75 postdoctoral researchers, together with support staff, administration staff and visitors, coming from all over the world:

Epigenetics ISP

The Epigenetics ISP seeks to understand mechanisms involved in establishing, maintaining and reprogramming epigenetic modifications in the genome during key stages in germ cells, embryos and during lineage specification. Developmental decisions in all organisms are accompanied by epigenetic modifications of DNA or chromatin, and by genome regulation through non-coding RNAs and higher order chromatin structure. Epigenetic reprogramming will provide insights into transgenerational effects in mammalian health and ageing, as well as novel approaches to regenerative medicine. The group has expertise in High Throughput Sequencing technologies and developing novel epigenomics computational methods.

Nuclear Dynamics and Function ISP

The Nuclear Dynamics Programme performs basic research to create an integrated understanding of the control of genome function in relation to health and ageing. They use multidisciplinary and systems approaches to assimilate information on the many different genetic, epigenetic, biochemical and structural parameters that affect the behaviour of the genome with a particular emphasis on gene control.

Lymphocyte Signalling and Development ISP

The Lymphocyte Signalling and Development ISP aims to identify the molecular and biochemical mechanisms required for the development and function of lymphocytes using highly purified populations of cells. They study signalling pathways at the molecular level including the PI3K pathway, GTPases, transcription factors, and RNA binding proteins. Understanding the signalling pathways regulating lymphocyte maturation and function translates into improved vaccines, combating autoimmune disease, developing tumour immunotherapy and possibly improving the efficiency of organ transplantation.

Signalling ISP

The Signalling ISP focuses on proteins that play a critical role in controlling communication between and within cells. Signalling information is received at the cell membrane and carried by membrane-captive phospholipids called inositides and membrane-anchored GTPases, which act as molecular switches. These signals are often amplified within cells by cascades of protein kinases. Signalling pathways are the central part of the complex regulatory machinery that organises how cells and organs develop and respond to their environment; indeed, they are vital for maintaining normal cell and organ homeostasis throughout life. In addition to this basic biological research, these signalling pathways often represent targets for therapeutic intervention in a variety of human conditions, including inflammation and cancer.

The Institute conducts basic biological research to understand how cell and organ function is maintained throughout life and how it changes with age. However, many of the biological processes studied are also important in understanding the basis of disease, for example developmental problems before birth and in childhood, cancer, Alzheimer's and other neurodegenerative diseases and in auto-immune diseases. The Institute seeks to develop and maximise the impact of this translational research through collaborations with biotech/pharmaceutical, healthcare and charity sectors. Research highlights in the past have included:

- Major developments in *in-vitro* fertilization and sperm and embryo freezing have been derived from research into sperm and egg function at the Institute.
- Developing the ribosome display technology that helps scientists to look for genes, improve protein modification and refine drug analysis; this has had a growing impact in the biopharmaceutical industry.
- Fundamental research in lipids and membranes led to the development, at Babraham, of liposomes now widely used for drug delivery and by the cosmetics industry.

All of these demonstrate the economic impact of translating fundamental research carried out at the Institute over six decades since 1948 when it was founded as an agricultural institution (the Institute of Animal Physiology, then Institute of Animal Physiology and Genetics Research) that evolved into the current Babraham Institute. Clearly, Babraham has thrived and continues to evolve to address new scientific and societal concerns.

3.3 BBSRC funding for health and wellbeing research

The Babraham Institute is one of eight institutes receiving strategic funding from the Biotechnology & Biological Sciences Research Council (BBSRC). The Institute received £33.1 million investment from BBSRC in 2011-12, including £12.8 million core funding, £7.6 million capital, £2.0 million BBSRC grants and £3.4 million response mode grants from other sources. The Babraham Institute is expected to conduct "innovative, world class bioscience research and training leading to wealth and job creation for the UK economy." In addition, it receives competitive research grants from the MRC, medical charities, industry collaborators and other organisations. The Babraham Institute is a registered charity (registered in England and Wales No. 1053902) and a company limited by guarantee (registered in England and Wales No. 3011737).

The Institute invests ~15% of total annual income in providing cutting-edge core facilities, services and equipment for its scientists. Science services include; bioinformatics, epigenomics, flow cytometry, gene targeting, imaging, lipidomics, proteomics and other specialist equipment. The Institute maintains state-of-the-art research facilities including a £1.6 million Next Generation Sequencing facility and a £1.5million Mass Spectrometry suite with special application for lipidomics analysis. In 2009 the Institute opened a £22 million Barrier Unit, custom-built to support future scientific developments in rodent genetics-based research. The Technology Development Laboratory, managed by BBT Ltd. provides services and expertise to external clients.

In addition to BBSRC strategic funding, the Institute scientists compete for research grants from a wide variety of sources (see Figure 4). The Institute has been successful in diversifying grant funding sources, more than offsetting a real-terms decline in BBSRC funding. Institute scientists work with clinicians or with pharmaceutical and biotechnology companies to translate the research for social and economic benefit, a process managed by Babraham Bioscience Technologies Ltd (BBT), the Institute's wholly-owned trading subsidiary since 1996. BBT had an income of £20.7 million in 2011-12 including £13.3 million capital grants, £3.4 million form rental income from tenants and £2.1 million royalty income from licences.

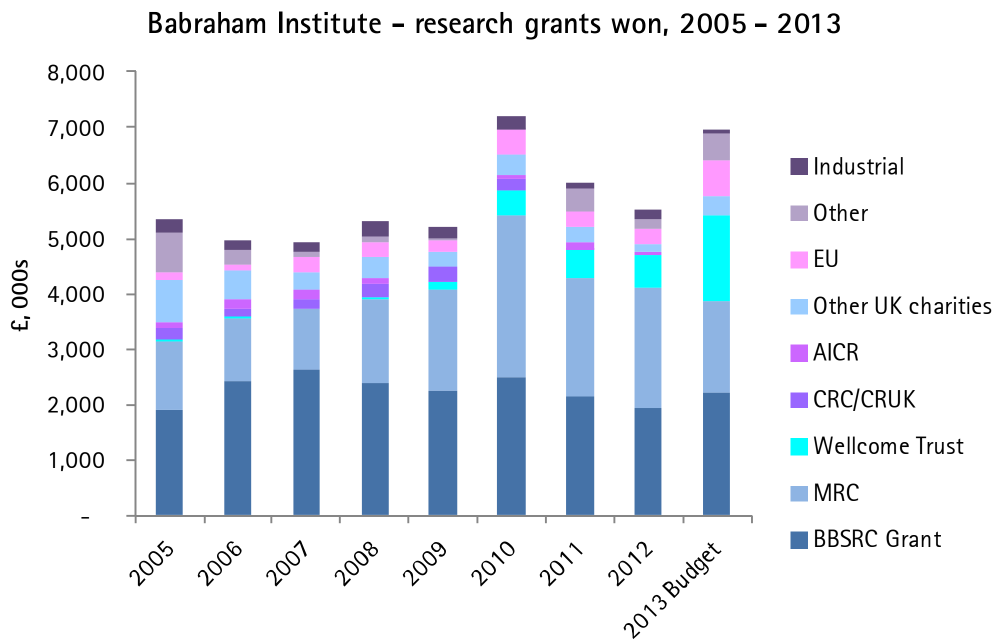


Figure 4 Profile of research grants 2005-2013

3.4 Babraham Research Campus: Discovery Biology for Lifelong Heath

The Babraham Institute sits at the centre of the Cambridge bioscience cluster, close to the Sanger Centre at Hinxton Hall, the rapidly expanding biomedical research campus at Addenbrooke's Hospital and commercial bioscience research parks at Granta Park and Chesterford Research Park. The Babraham Research Campus is home to 39 biomedical SMEs, about half of which have specific links to the research base of the Institute. Babraham Bioscience Technologies Ltd (BBT) promotes knowledge exchange and commercial translation of the Institute's research. BBT actively manages the Institute's intellectual property, negotiates commercial research partnerships and has established spin-out companies, as well as having a management role in the provision of the Institute's bioscience incubator facilities.

The Babraham Bioincubator was opened in 1998 to support spin-out businesses that had scientific specialism linked to the existing animal health research expertise. The Babraham Research Campus now provides ~80,000 sq ft laboratory space in Bioincubator Buildings. In total, 69 companies have graduated through the facilities and these companies have raised over £360 million of investment funding to date. The expanding campus reflects the need for an environment that encourages and nurtures biomedical companies thereby assisting in the process of wealth creation for UK-plc.

About 350 people are employed by companies on site, which when combined with Institute staff, totals around 750 people at the Babraham Research Campus contributing to the Cambridge biomedical cluster. The ultimate aim is to "translate science into biomedical products that will deliver social and economic impact and address global healthcare challenges." The Institute's research provides greater understanding of the biological events that underlie the normal functions of cells and the implication of failure or abnormalities in these processes.

CHAPTER 4. RESEARCH EXCELLENCE & IMPACT AT THE BABRAHAM INSTITUTE

4. 1 The policy context

As discussed in the introductory chapter, BIS has a stated aim of 'promoting impact through excellent research supporting the growth agenda'. The strategy for Knowledge and Innovation is to (i) promote research excellence and (ii) increase business innovation.

> *'The Research Base provides a key underpinning for innovation, enterprise and growth. It generates high level skills, and provides the evidence and innovation needed to develop policy and achieve health and social goals. Research and the creation of new knowledge are also valuable in their own right.'*[10]

The economic rationale for investment in the research base is also made in an RCUK paper[11]. This highlighted the research performance of the UK:

> *'The research base is the most productive among the world's leading economies and its overall quality is second only to the United States. The country ranks high in terms of publications per head of population – about 50 per cent higher than the European Union (EU) average and 16 per cent higher than the United States. In terms of basic research, the UK ranks very highly: second only to the United States in terms of academic citations, accounting for an impressive 11.9 per cent share of total world citations (compared with around 1 per cent of the world's population).'*

The report's main conclusions are:

- Continued public investment in scientific endeavour is essential for the success of the UK economy. Estimates of the impact of Research Council spending on the UK's national output suggest that a cut of £1 billion in annual spending would lead to a fall in GDP of £10 billion;
- The greatest long-term productivity advances come through breakthroughs in basic knowledge – and a substantial proportion of the R&D that creates new knowledge and leads to increased productivity is done in universities and other public research institutions;
- Publicly funded research raises the productivity of R&D in the private sector and encourages companies to do more R&D themselves. It also leads to inventions that can be commercialised through licensing to private companies or via the formation of new start-up companies;
- The UK needs to be doing frontier research to be able to take advantage of frontier research being done elsewhere;
- Alongside new knowledge, universities and research institutes produce highly trained people, an essential resource for UK companies and foreign companies investing in the UK;
- High quality research makes the UK attractive for inward investment by international business and industry through collaborations and siting offices. Universities also encourage innovation by smaller local businesses and, through incubators and science parks, the emergence of new companies.

In recognition of this rationale, BIS identified its success indicators in this area as[10]:

- Expenditure on Research and Development performed in Higher Education;
- UK share of highly cited papers;
- UK's standing in global scientific rankings;
- External income of HEIs – covers engagement with business, charities and Government;

[10] Guide to BIS 2012-2013
[11] RCUK: Research for our Future, 2010

- Positive public attitudes to science and research;
- R&D funding leveraged from abroad as a proportion of GDP compared to other countries

The BBSRC in turn has defined three main success indicators in this area[12]:

- Research impact per unit spend (to be measured by citation impact analysis);
- Increased interactions between research users and the bioscience research base;
- Development and progress of its Research and Innovation Campuses.

The following three chapters demonstrate how the Babraham Institute contributes to these aims.

4.2 Scientific output & impact

Original research, communicated to the broader scientific community and wider world through research publications, is the motive force behind much technological innovation and consequent economic growth, as described above. Babraham's output of original research papers has remained broadly constant at 90 – 95 papers pa over the past 8 years (see Figure 5a). However, the active researcher base has declined over the period, leading to a rise in research output per Principal Investigator (PI) (see Figure 5b).

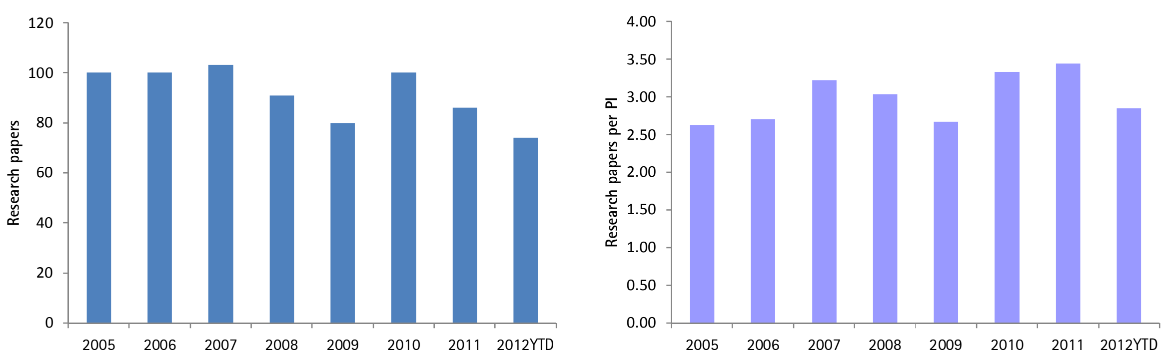


Figure 5 Babraham research productivity, a) total original research papers, and b) research papers per PI from 2005-October 2012.

However, volume of publications is in many ways a misleading and even counter-productive indicator of research performance. BIS, RCUK and the BBSRC all emphasise the importance of excellence in research. The most widely recognised measures of research excellence are the Impact Factor of the publishing journal and the number of scientific citations each paper receives (a measure of the significance of the research results).

The average Impact Factor of Babraham publications has been steadily rising over the past 15 years. Mean Impact Factor fluctuated in the range of 4 to 5 in the early 1990s, and progressively rose to 8.5 at the time of the last Economic Impact report in 2008. Since then, Babraham's average Impact Factor has risen further, to 11.3 in 2012 year-to-date (see Figure 6).

12 BBSRC Delivery Plan 2011-2015

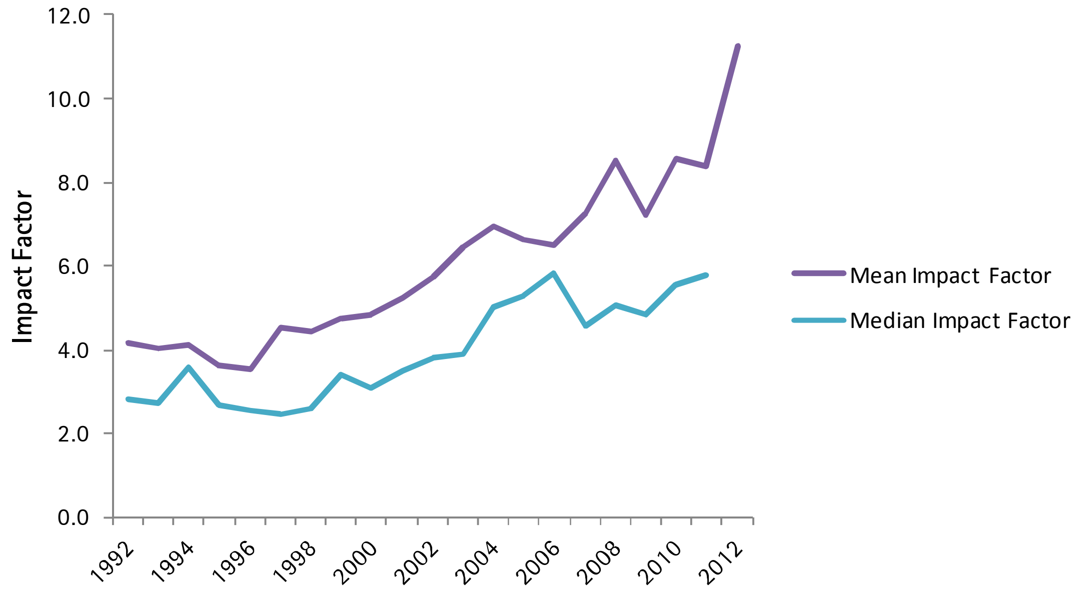


Figure 6 Average Impact Factor of Babraham original research publications 1992-2012

Summing the Impact Factors of all Babraham publications produces a measure of quality-adjusted research productivity, 'Total Impact Factor' (see Figure 7a). This shows a slight rising trend over the 2005 to 2012 period. However, allowing for the decline in the active researcher base, the Total Impact Factor per PI has risen significantly over the period (see Figure 7b).

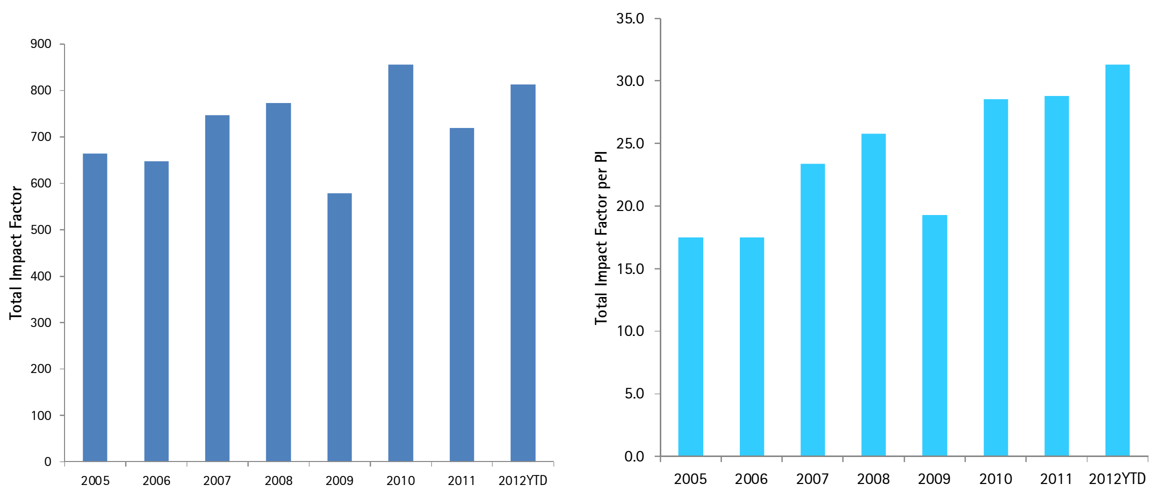


Figure 7 Babraham quality-adjusted research productivity, a) Total Impact Factor, & b) Total Impact Factor per PI

Scientific citations represent an alternative and more direct measure of the scientific impact of a piece of research, being an endorsement of the research by a wider group of the authors' peers in the field. Inevitably, this tends to be a lagging indicator whereas Impact Factor is a more current indicator. However, 'total citations' is generally viewed as a poor measure of scientific impact, being more sensitive to quantity rather than quality of output. Recently, the H Index[13] has come to be the most generally accepted single citation-based measure of a researcher's impact.

[13] JE Hirsch, An index to quantify an individual's scientific research output, Proc. Nat. Acad. Sci., 2005, **102**, 16569-16572

H Indices were calculated[14] for the 23 Principal Investigators at the Institute for whom a sufficiently long publication record was available. These results are shown in Figure 8. These show H Indices ranging from 14 to 76, generally aligned with career experience. The average value for a Babraham PI is 36, and all PIs have an H Index above a reported average for biological sciences of 13.4[15].

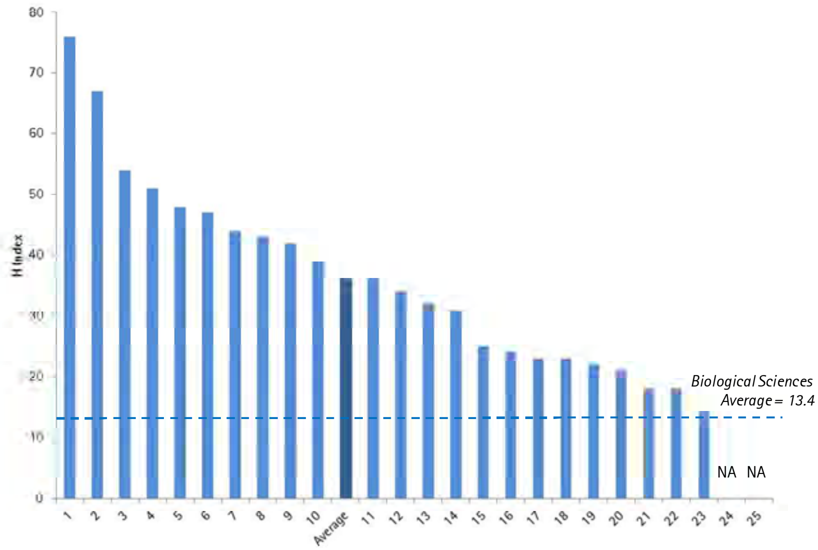


Figure 8 H Indices for the Principal Investigators at the Babraham Institute

An acknowledged weakness of the H Index is its bias towards later career scientists, because of the nature of the accrual rate of citations. Hirsch and others propose use of an additional factor, m, measuring the gradient of the build up of the H Index, which adjusts for the career stage effect. An m value of 1 has been proposed as average, whereas an m value over 2 is proposed as exceptional[16].

The variation of Babraham PIs H indices by career stage is illustrated in Figure 9. All Babraham PIs have an m value in excess of 1, implying above-average scientific impact for their career stage, and 10 out of 23 have an m value in excess of 2.

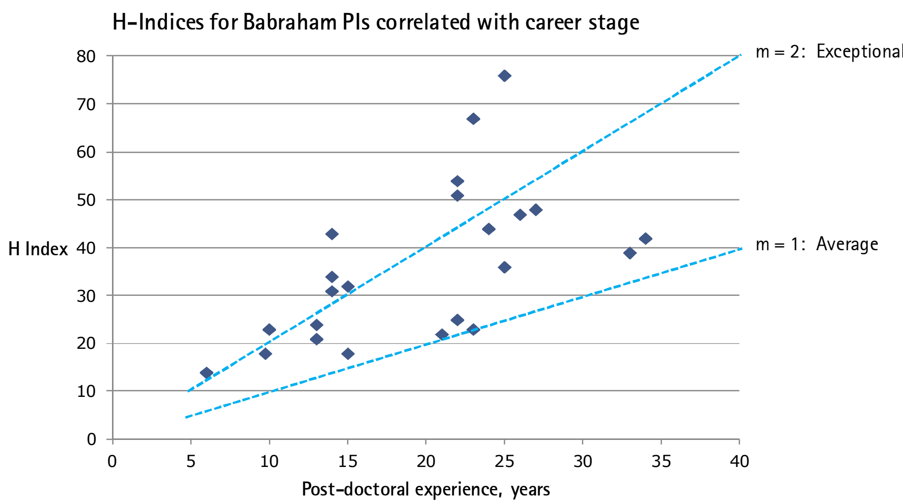


Figure 9 H Indices for Babraham PIs by career stage.

[14] Calculated with Google Scholar
[15] Making Research Count: Analyzing Canadian Academic Publishing Cultures, Higher Education Strategy Associates, June 2012
[16] A Bateman, PLOS Online, Biologue, October 2012

A specific illustration of the high impact of Babraham research was its identification by Science Watch.com as one of the top 10 world leading research centres in epigenetics research[17], out of a pool of 4,877 institutions publishing on this topic, based on an analysis of publications and citations in Thomson Reuters-indexed journal (see Table 2).

Rank	Institution	Citations	Papers	Citations Per Paper
1	Johns Hopkins Univ	21385	347	61.63
2	Harvard Univ	10614	307	34.57
3	NCI	8250	284	29.05
4	Univ Southern Calif	7355	114	64.52
5	Univ Virginia	6588	45	146.40
6	Univ Cambridge	5676	155	36.62
7	MIT	5573	87	64.06
8	Vienna Biocentre	5424	25	216.96
9	Univ Calif San Francisco	5286	146	36.21
10	**Babraham Institute**	5285	81	65.25
11	Univ Calif Los Angeles	4907	120	40.89
12	Univ Penn	4835	144	33.58
13	Univ Edinburgh	4763	70	68.04
14	Univ Birmingham	4349	105	41.42
15	Washington Univ	4253	106	40.12
16	Cold Spring Harbor Lab	4226	65	65.02
17	Univ Texas Hlth Sci Ctr Houston	3939	152	25.91
18	Ohio State Univ	3926	152	25.83
19	Univ Washington	3793	104	36.47
20	Ut Southwestern Med Ctr	3298	90	36.64

Table 2 The global top 20 epigenetics institutions

4.3 The economic impact of fundamental research

A recent study conducted by the Russell Group[18] concluded that fundamental, curiosity-driven, research produces the biggest economic returns over the long-term, and that successful commercialisation requires sustained long-term investment in research, often over many years or even decades. An attempt to quantify the economic pay-off of long-term academic research in medical science was investigated in a Wellcome Trust/MRC/AMS report[19]. In a retrospective study in two disease areas as exemplars (cardiovascular and mental health) at 'whole system' level for UK, the report concluded:

- The time-lag between research and health benefits realisation is 17 years;
- The total annual return in health gains from UK public and charitable research is 7-9%;
- Every £1 of extra public/charitable investment in UK medical research yields £2.20–£5.10 of extra industry investment, which taken together earns an extra £1.10–£2.50 GDP per year for the UK economy;

[17] www.sciencewatch.com/inter/ins/09/09marEpigentop20
[18] The economic impact of research conducted in Russell Group universities, Russell Group Papers, 2010
[19] Medical Research: What's it worth?, Estimating the Economic Benefits from Medical Research in the UK, Wellcome Trust, MRC, Academy of Medical Sciences, 2008

- The GDP returns on the investment in medical research are between 20% and 67%, with a best estimate of 30% pa;
- Combining health and GDP returns, the total return from public and charitable medical research is around 39% pa.

However, measurement of the economic impact of research outputs, whether patented and immediately commercially exploitable, or 'academic' where the economic and societal benefits accrue in the long-term in an indirect way, is intrinsically difficult, due to a number of factors, including:

- The timescales to realisation of value are long; even for relatively near-market innovations, economic returns usually occur 5 years or more after initial scientific breakthroughs, and are typically much longer in fundamental research. As Babraham's research portfolio focus is on fundamental biology, the time-lag is likely to be even longer than typical medically oriented research investigated in the Wellcome Trust/MRC/AMS study described above;
- Innovation is usually non-linear and for much academic research inherently unpredictable, with recognition of substantial advances occurring at irregular intervals;
- Many innovations represent aggregations of multiple contributions from many, often disparate sources, and identifying respective contributions difficult;
- Development of commercial products, particularly in life sciences, is subject to a high level of attrition, requiring risk-adjustment to current values of developmental projects.

4.4 Babraham research portfolio evolution

Given the time-lag described above, it is important to recognise that innovations being commercialised now or in translational research and product development phases have their origins in fundamental research typically initiated at least a decade ago. Babraham's research portfolio has evolved significantly over the decades since its foundation, not least over the past few years.

The Babraham Institute was originally founded in 1948 as The Institute of Animal Physiology with a focus on farm animals, recognizing the post-war need to increase food production. However, ground-breaking basic biological research conducted at Babraham since the 1960s has shifted the focus of work towards biochemistry, cellular and molecular biology, molecular immunology and developmental epigenetics. With hindsight the local, national and international economic impact of this work has been enormous and continues today; this was anticipated in 1997 with the founding of the Babraham Research Campus Bioincubator, which is now home to 39 biology-based SMEs. Today the key research programmes (Institute Strategic Programmes or ISPs) continue to conduct world-leading research whilst evolving to incorporate new advances (e.g. systems biology) and to address important scientific and societal concerns, including the biology of normal ageing.

4.4.1 Signalling Programme

The origins of the Signalling Programme lie back in the early 1960s with the discovery and development of liposomes at Babraham, a breakthrough that has since led to numerous applications in fields as diverse as drug and gene delivery through to cosmetics. Babraham's expertise in lipid biochemistry in the 60s and 70s was instrumental in the discovery of inositol lipid signalling including the role of Ins(1,4,5)P3 (inositol trisphosphate) as a calcium ion-mobilising second messenger in the 1980s and the characterisation the PI3 Kinase enzymes in the 1990s; two seminal events in the understanding of cellular signalling.

Since the mid-1990s Babraham's world-renowned signalling laboratory has expanded to include protein kinase-dependent and NAD+-dependent signalling systems that control cell survival, proliferation and longevity. Indeed, PI3K-dependent signalling plays a central and evolutionarily conserved role in the control of ageing in worms, flies and man. Signalling pathways allow cells to sense and respond to their environment and impact on all aspects of cellular function. They continue to be of intense worldwide interest to the biotech/pharmaceutical industry as drug targets for cancer, diabetes, inflammation and cardiovascular disease (investment in the £billions) and BI's Signalling Programme has many industrial collaborations.

4.4.2 Lymphocyte Signalling & Development (Immunology) Programme

Babraham's Immunology Programme emerged from outstanding antibody research begun in the 1960s. Collaborations with Cesar Milstein at the MRC Laboratory of Molecular Biology in Cambridge led to the production of some of the first 'useful' monoclonal antibodies (1978). In the early 1980s the Institute initiated the manipulation of antibody genes in laboratory mice, ultimately leading to the derivation of therapeutic human antibodies from GM rodents; indeed, the Institute receives revenue from companies exploiting this technology (see Chapter 5) and the BRC Bioincubator hosts a number of biotech companies who are using variations on this technology, including Crescendo Biologics Ltd. The use of ribosome display to select antibodies of improved affinity against a particular target was also developed within BI's immunology laboratories and widely taken up by the biotech industry.

Babraham immunologists also identified the transporter for antigen processing (TAP), a key discovery that was fundamental to our understanding of T cell specificity, immune tolerance and autoimmunity. Since 2000 Babraham immunologists have developed a focus on the signalling pathways determining T and B lymphocyte development and behaviour including a highly fruitful, synergistic collaboration between the Signalling and Immunology programmes in the study of PI3 kinase signalling in lymphocytes. This has come to constitute a formidable 'college of expertise', which is widely recognized and frequently accessed by industry.

Today the Lymphocyte Signalling & Development Programme is focused on understanding the molecular determinants of the normal lymphocyte repertoire needed to ensure strong and healthy immune responses throughout life, and trying to understand how lymphocytes communicate with other body systems including the commensal microbiome to maintain normal health.

4.4.3 Epigenetics Programme

The Epigenetics Programme traces its origins back to the 1980s when, as a leading centre in reproductive biology, Babraham pioneered research in developmental epigenetics. Mammalian genomic imprinting – the parent-of-origin dependent monoallelic expression of genes – was discovered by Babraham scientists through elegant nuclear transfer studies in 1984. With the elucidation of the factors involved, imprinting became a paradigm for epigenetic gene regulation; imprinting impacts on many aspects of normal growth and development, is defective in many cancers and may be at risk in assisted reproductive technologies.

Babraham continues to play a world-leading role in epigenetic research, and the current groups in the Epigenetics Programme study epigenetic mechanisms throughout mammalian development, from the specification of germ cells and differentiation of gametes, through the major epigenetic reprogramming events after fertilisation, cell lineage specification in the early embryo, as well as how the epigenome is modified by age and diet. This provides fundamental knowledge underpinning the derivation and maintenance of stem cells, and the Epigenetics Programme has industrial partners to discover factors involved in cellular reprogramming for regenerative medicine. Advances in these areas require continuous technical innovations, and Babraham research has recently identified new epigenetic modifications of DNA and developed methods by which they can be mapped genome-wide at single base resolution.

4.4.4 Nuclear Dynamics & Function Programme

The Nuclear Dynamics & Function Programme began its evolution at the turn of the century focusing initially on chromatin epigenetics at the forefront of the newly emerging field of non-coding RNA transcription and its role in gene control. This work lead to the seminal discoveries of long-range chromatin interactions that control gene expression in 2002 and transcription of co-regulated genes in shared transcription factories. These findings pioneered a new field of functional spatial genome organisation, with major implications for normal and dysfunctional development.

The Programme has taken a leading role in embracing and designing new next generation sequencing technologies and is at the international forefront of research on genome-wide interactions between genes and their regulatory elements and *in-silico* modelling of chromosome architecture. It has complementary interests in key factors that regulate genome organisation and epigenetic maintenance and are currently applying these and other advanced technologies in a systems biology approach to understand ageing in haematopoietic cells, with a focus on identifying key regulatory mechanisms and molecules that underpin age-related frailty in the immune system.

The current focus on research into lifelong health and ageing was established a little over a year ago, so impact generated from new research initiated in the field is unlikely to emerge before 2030.

4.5 The economic impact of fundamental research at the Babraham Institute

As described above, Babraham's current research interests represent a spread of maturities ranging from programmes established almost three decades ago to those established more recently. In consequence, actual or potential economic impact is much more apparent in the well-established programmes. This is illustrated, for a selection of Babraham's research programmes, in Figure 10.

Two well-established programmes have generated demonstrable actual or probable economic impact, through both fundamental and translational research efforts:

- Basic research on methods of modifying and selecting monoclonal antibodies, started in the 1980s, dropped from Babraham's research portfolio a few years ago, but the major economic impact of that research is currently being delivered in the form of therapeutics on the market either directly incorporating Babraham technology or building on Babraham research. In addition, two spin-out companies (Crescendo Biologics and Cambridge Protein Arrays) have been established exploiting different parts of the Babraham Intellectual Property (IP) portfolio in the area, a third SME has licensed further Babraham IP following a substantial collaborative research project and other licence agreements concluded (see separate case studies in Chapter 5).
- Babraham's PI3 Kinase signalling pathway research has its origins in lipid signalling work dating back to the 1960s, and accelerated from the mid- 1980s following the discovery of PI3 Kinase. PI3 Kinase inhibitors are now an area of major pharmaceutical industry research interest, with 20 molecular entities currently in clinical development for anti-cancer or immunology indications. Babraham scientists have engaged in several commercial collaborative research projects and provided scientific consultancy to ten of the companies active in this area. Further commercial collaborative research on the related RAS/RAF/MEK/ERK signalling pathway has generated insights into resistance mechanisms and stimulated evaluation of novel combination therapies (see separate case study on PI3 Kinase inhibitors later in this chapter).

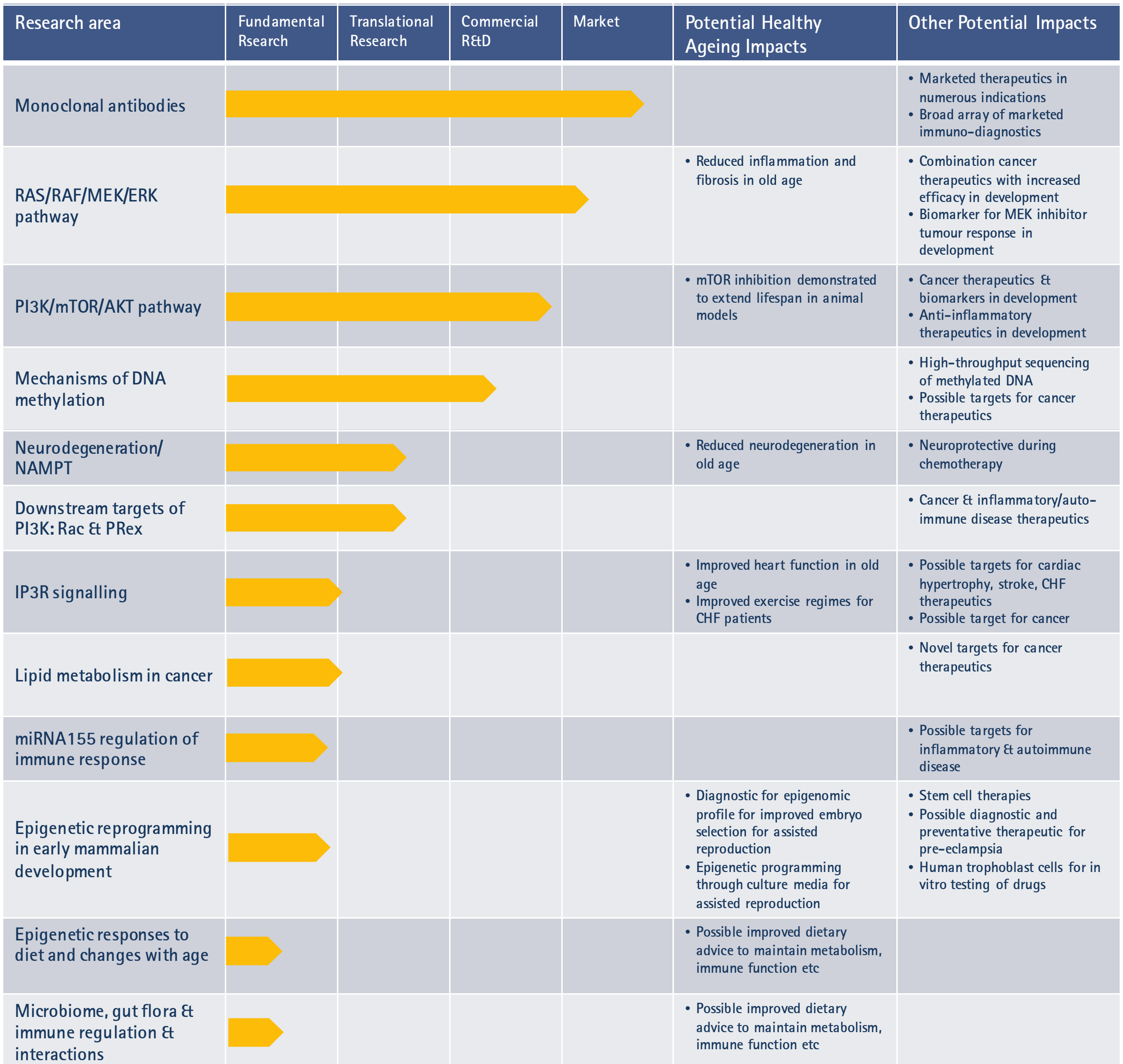


Figure 10 Babraham research portfolio and translational progress towards commercialisation

Several established but earlier stage programmes have reached the point at which directed translational research can progress. However, considerable uncertainty remains regarding potential end-use, utility and value. These include:

- PRex1 inhibitors as prospective therapeutics for inflammatory and autoimmune disease and cancer;
- NAMPT inhibitors as prospective neuroprotectants for use during chemotherapy or to prevent neurodegeneration in old age;
- Development of VDJ-seq, a high-throughput next generation sequencing assay, which provides quantitative characterisation of individual VDJ recombination events, to provide high resolution and high throughput interrogation of antigen receptor repertoires, to assist in screening of transgenic and in vitro antibody platforms.

These and other translational projects are described in the following chapter.

Many of Babraham's research programmes are still too early to identify quantifiable economic impact. However, Babraham research programmes in chromatin remodelling, epigenetic and non-coding RNA regulatory mechanisms, and cell signalling address fundamental questions of genome and cellular regulation and lineage specification underpinning human development, immune function, health and disease. The insights obtained can be predicted to generate novel targets for therapeutic intervention in a variety of human conditions, including cardiovascular, inflammatory, and autoimmune diseases and cancer, provide novel methods for manipulation of stem cells and inform strategies for extending healthspan to an ageing population.

Babraham has recently initiated a number of projects addressing changes in cellular function and epigenetic programming related to ageing. As described above, past precedents indicate that the economic impact to be derived from these programmes would be expected to arise in c. 20 years from now.

Case Study: Bim mimetics and biomarkers

Over a period of almost a decade, Babraham scientists defined the role of the MEK protein kinase signalling pathway in repressing Bim, a pro-apoptotic (i.e. inducing programmed cell death) protein. The discoveries initially made in fibroblasts were then found to be almost ubiquitously operative. This has led to two separate developmental applications. First, because MEK inhibitors increase Bim expression, leading to tumour cell death, Bim is a good biomarker for successful target inhibition. AstraZeneca is using Bim expression as a biomarker for tumour response to MEK inhibitors in clinical development. Separately, Abbott Pharmaceuticals is developing navitoclax (ABT-263) as a therapeutic for both solid tumours and lymphoid malignancies; this in part mimics the action of Bim. Results of a Phase 2 clinical trial of navitoclax in combination with rituxan in Chronic Lymphocytic Leukaemia are promising.

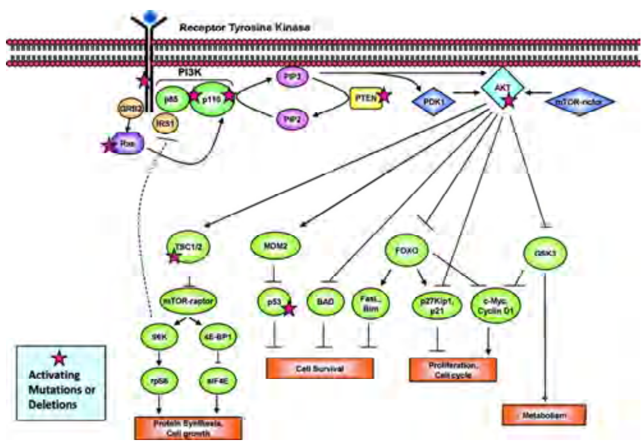
Case study: PI3K pathway

PI3 kinase has over the past decade emerged as a major drug target for cancer and inflammation. The PI3 kinase pathway links insulin signalling and nutrient sensing to cell metabolism, survival, proliferation and migration, and is therefore central to many essential cellular processes.

The Babraham Institute's research activity in the area grew out of its earlier pioneering research on lipids and phosphoinositide signalling, and the Institute has remained one of the world leading research institutes in the area. Other notable UK institutions active in the area include the Ludwig Institute and the Institute of Cancer Research – particularly with regard to PI3 kinase inhibitor development.

During the 1990s and early 2000s, Babraham scientists made major contributions to the fundamental research on the mechanism, function and downstream effectors of PI3 kinase signalling. Key contributions include the identification of the roles of the gamma and delta isoforms of the PI3 kinase P110 catalytic subunit as regulators of inflammatory responses. Babraham has filed two patent applications, with co-applicant Drexel University, on the role of P110delta signalling in influenza virus infection.

PI3 Kinases are implicated in both cancer and immune inflammatory disease. In cancer, up-regulation of the PI3 Kinase pathway is a very common characteristic and several components of the pathway are implicated in the development of cancer. The gamma and delta isoforms of PI3 Kinase are strongly implicated in immune inflammatory disease. Inhibitors of PI3 Kinase gamma and delta down-regulate certain functions of B and T cells, mast cells and neutrophils and have demonstrated significant activity in various experimental models of human immune inflammatory disorders.



The PI3 Kinase pathway

From the late 1990s, PI3 Kinase began to attract industrial interest as a drug target, initially in cancer and later in immunology. In the UK, PIramed, and, later, Karus Therapeutics were spun out to develop PI3 Kinase inhibitors, raising a collective £16 million. Babraham scientists have over the past decade established research collaborations or provided consultancy with 10 companies involved in PI3 Kinase inhibitor research programmes, including AstraZeneca, PIramed and Karus Therapeutics. In addition, the Institute has supplied proprietary animal models to both industrial and academic investigators in the field.

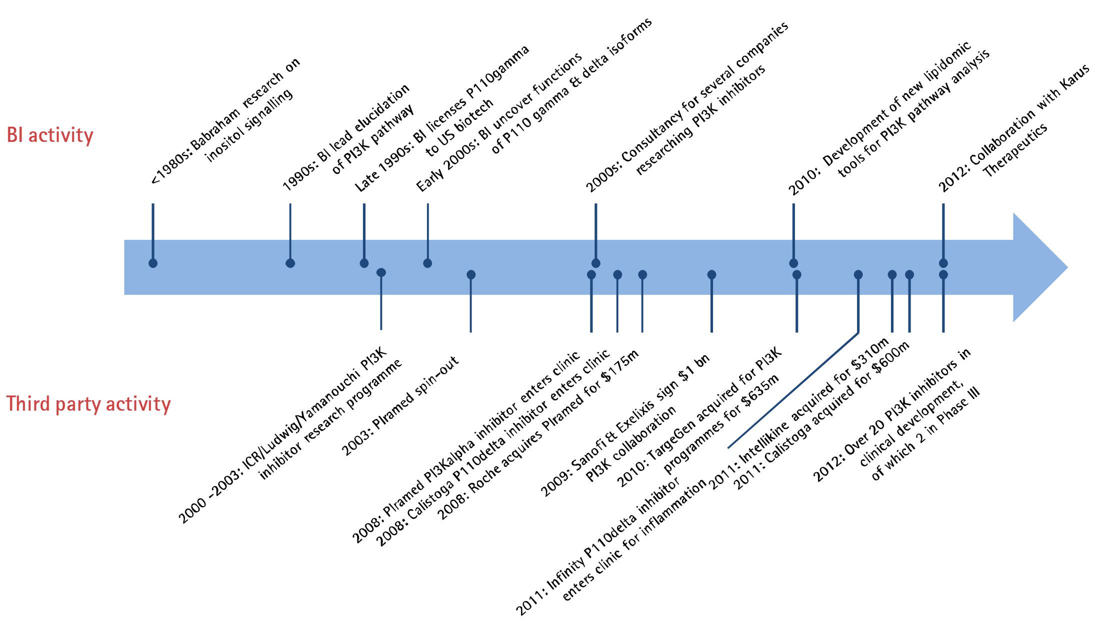
Many major pharmaceutical companies, including Amgen, GSK, Merck, Novartis, Pfizer, Roche and Sanofi, as well as several biotechs, now have clinical stage PI3 Kinase inhibitor programmes. There are over 20 PI3 Kinase inhibitors in clinical development, the two most advanced of which are in Phase III trials, plus many other projects in preclinical or discovery stages. The collective research investment by the industry to date is estimated to be at least £350 million. Mirroring the intense research interest, the aggregate value of acquisitions and licensing deals for PI3 kinase inhibitor programmes to date is in excess of £1.8 billion ($3 billion). These include the acquisition of PIramed by Roche in 2008 for £108 million ($175 million).

It is too early to be certain which therapeutic applications PI3 Kinase inhibitors may eventually serve in either cancer or inflammatory disease. In cancer, clinical trials are on-going in most solid tumour types, including *breast, prostate, head & neck, colorectal, endometrial and non-small cell lung cancers, glioma, glioblastoma and renal cell carcinoma and in lymphoid malignancies including Non-Hodgkins Lymphoma and chronic lymphocytic leukaemia. In inflammatory disease, initial early stage clinical trials have commenced in asthma and rheumatoid arthritis.*

Most cancers still represent areas of major unmet medical need with high levels of mortality and morbidity. Within the UK, the tumour types addressed by the current PI3 Kinase inhibitor clinical programmes alone account for 229,000 new cases and 96,000 deaths per annum[20]. It is probable that further clinical candidates will be forthcoming and that the range of indications will expand. However, on a conservative assumption that 1 in 5 (i.e. 4 of the 20 clinical stage candidates) of the current PI3 Kinase inhibitor clinical pipeline will reach the market in the targeted indications, the potential annual UK patient base will be c. 46,000. Using similarly conservative assumptions that a PI3 Kinase inhibitor is used in 20% of cases and that the average health improvement is an additional 4 months of progression-free survival and overall survival, this represents a health gain amounting to £92 million per annum in the UK alone, applying a figure of £30,000 per QALY[21]. Worldwide, the potential health gain is c. 20 times larger. In addition, PI3 Kinase inhibitors, in common with other targeted therapies, offer improved delivery, safety and tolerability profiles compared to old generation cytotoxic therapies.

These figures take no account of the potential in inflammatory and autoimmune diseases due to the very early stage of clinical trials and consequently lack of any pointers to efficacy or positioning. Although initial trials are underway in asthma and rheumatoid arthritis, it is likely that PI3 Kinase inhibitors will also be investigated in other inflammatory and autoimmune conditions such as lupus, multiple sclerosis, ankylosing spondylitis, psoriasis, Crohn's disease and ulcerative colitis. TNF alpha inhibitors have become the standard of care in severe rheumatoid arthritis and are used in other severe autoimmune conditions, with global sales in excess of £14 billion ($22 billion).

Despite their widespread use, TNF alpha inhibitors have a number of disadvantages including tolerability, adverse event profile and IV delivery. PI3 Kinase inhibitors are viewed as very promising in inflammation and autoimmune indications because they offer a good safety profile and convenient oral dosing.



Case study Figure1: Time line for PI3 Kinase economic impact

[20] CRUK cancer statistics 2010
[21] Recent NICE approvals have applied higher values for a QALY in end-of-life settings

CHAPTER 5. ECONOMIC IMPACT OF TRANSLATIONAL RESEARCH

Bio-industries rely extensively on fundamental research, and in the broader pharmaceuticals and chemicals sectors BBSRC-funded research in basic biology provides essential understanding of basic concepts that can be exploited directly by industry or indirectly through strategic or translational research funded by others, including other Research Councils, research charities and the Technology Strategy Board. At the Babraham Institute basic biological research focuses on signal transduction and genome regulation and how they influence important physiological adaptations to ensure lifelong health and wellbeing. The Institute is committed to knowledge exchange and facilitating academic-commercial links to drive innovation and wealth creation. It has a Knowledge Exchange and Commercialisation (KEC) committee that reports directly to the Director, BI Executive Committee and BI Board.

5.1 Value Chain Analysis

The analysis of wealth creation can be mapped onto a value chain that describes the activities within and around an organisation, and evaluates which value each particular activity adds to the organisation's products or services. The activities at the Babraham Institute have been mapped onto a value chain (see Figure 11). At the start of the value chain, the fundamental research from the four Institute Strategic Programmes generates new discoveries and is the driver of economic impact. Where commercially relevant, patent protection is sought on new intellectual property. Some of this research is of interest to external parties who collaborate on new projects. These external parties may be other academics, NHS clinicians or commercial companies that engage through Industrial Research Collaborations or CASE studentships or by licensing the technology.

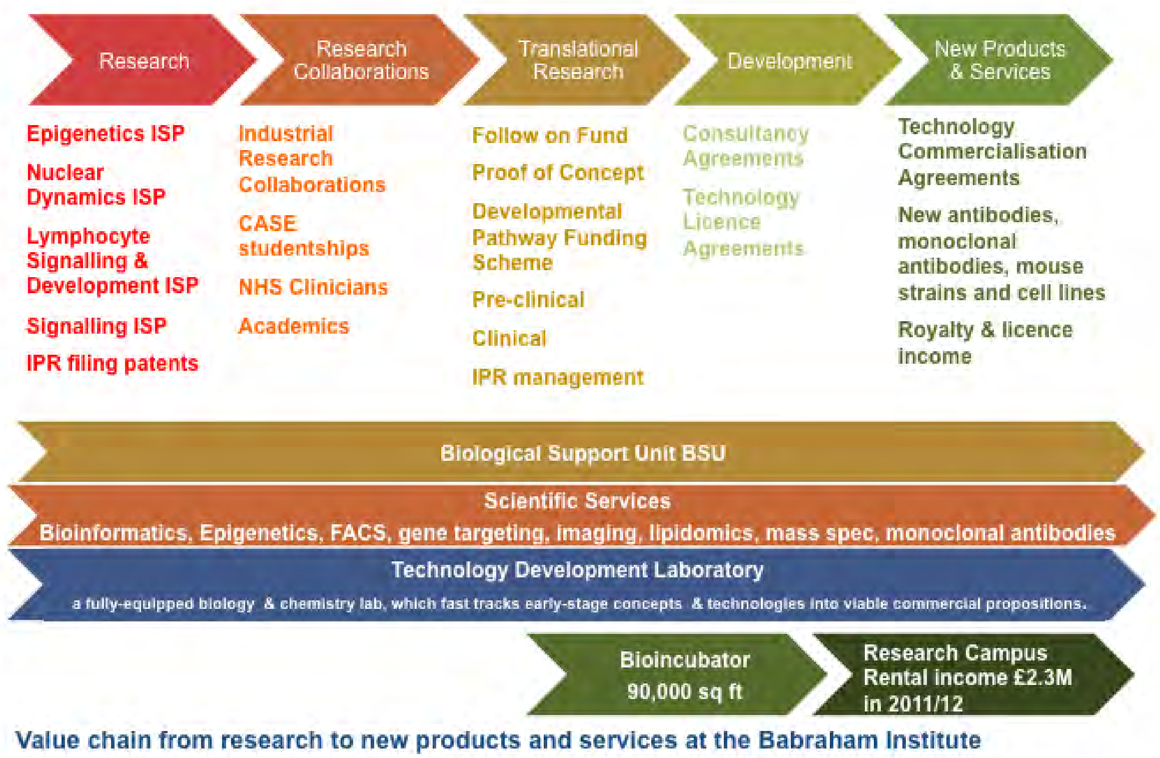


Figure 11 Value chain of fundamental research through to commercialisation

The UK has a range of programmes designed to increase the level and accelerate the rate of commercialisation of research ideas arising from the academic research community. These programmes use the proof-of-concept model where further work on an idea will take it through to the stage at which the route to commercialisation is clear and marketable, to proceed, for example, to a spin-out (using seed or venture finance) or a technology licence. If successful at this stage the idea then requires considerable development work before becoming a new product or service.

All of these activities along the value chain are supported, as required, at the Babraham Institute by a suite of support services for inventing Institute scientists, commercial Campus tenants, other local SMEs and the wider commercial biotech community as required. BBT is the commercial arm of the Babraham Institute which:

- Manages, develops and commercialises Babraham's intellectual property rights (IPR);
- Develops and manages the infrastructure of the Campus to support start-up bioventures. Any spin-out companies, and other SME tenants, can be accommodated in the Bioincubator and as they grow they can 'graduate' into larger premises on the Babraham Research Campus;
- Provides access to scientific services, either from its own laboratory facilities or through the Institute;
- Provides business support services to Campus SME tenants.

The development and economic impact of the BRC is discussed in detail in Chapter 6. In a departure from the traditional industrial collaborative research model, the Babraham Research Campus, Neusentis (Pfizer) and MedImmune (AstraZeneca) have recently established a new open innovation initiative within the Cambridge Bioscience cluster aiming to identify new therapeutic treatments, on the basis that early-stage collaboration maximises success.

5.2 Translational activities leading to economic impact

The economic impact of the Institute's academic research output has been discussed in Chapter 4. Over and above the impact created by advancement of the basic scientific understanding, Babraham has created opportunities to generate direct economic impact through translational and commercial research. Babraham's contributions to these types of project are mapped in Figure 12.

Although the details of these projects differ, two general observations can be made. First, in all cases, these projects are grounded in the fundamental research of the Institute. Second, as is particularly apparent with the more mature research areas, Babraham has in several cases made multiple contributions to specific research areas over many years.

These arise through two routes:

- Identification by Babraham researchers of potentially commercial goal-oriented 'spin-off' translational opportunities arising from insights provided by the basic science. These are typically prefaced by a first patent filing, but commercial exploitation routes can be technology licensing, spin-out company formation or a commercial service offering. ('*Babraham-driven projects'*);
- Requests from external commercial collaborators driven by Babraham's profile and reputation in specific research areas. These are typically embodied in commercial research collaborations or consultancy arrangements, and in some instances, CASE studentships have overtly commercial targets ('*Partner-driven projects*').

	Fundamental research	Translational research	Commercial research	Commercial development	Market Application
Monoclonal antibodies	●	●	●		• Novel transgenic methods of creating humanised & fully human mAb s commercialised by, eg, Abgenix, and products using the technology commercially available • Novel heavy-chain only antibody fragments being commercialised by spin-out Crescendo Biologics • Ribosome display platform for in vitro molecular evolution of antibody fragments also being commercialised by Crescendo Biologics • VDJseq high throughput sequencing tool to assist mAb selection from sequencing data
PI3K/mTOR inhibitors	●	●	●	●	• PI3K inhibitors in late stage clinical development for cancer and inflammatory & autoimmune indications • MEK/mTOR inhibitor combinations in development for cancer
MEK/ERK inhibitors	●		●	●	• MEK/AKT & MEK/RAF inhibitor combinations in development for cancer • BIM companion biomarker for MEK inhibitor tumour response
High throughput sequencing methods for methylated DNA	●	●			• Sequencing technology/kits being commercialised by spin-out Cambridge Epigenetix
PRex inhibitors	●	○			• PRex1 is a potential target in inflammatory diseases • PRex1 & PRex2 are potential cancer targets
NAMPT inhibitors	●	○			• NAMPT is a potential target for neuroprotection
Lipid metabolism	●		○		• Novel targets identified with potential utility in cancer
Lipidomics	●	●			• Lipid analysis by MS techniques
Protein array technology	●	●			• Technology for production of protein microarrays for research use being commercialised by spin-out Cambridge Protein Arrays

Figure 12 Babraham Institute contribution to a range of significant translational and commercial research projects.

Key to Figure 12: (Closed circles = work completed or underway, Open circles = planned activity)

5.3 Babraham-driven projects leading to economic impact

These projects usually involve an early patent filing, as stated above. Babraham has an active IP portfolio of 16 patent families, of which the oldest dates back to 1988 and remains in place due to patent term extension. 12 of the 16 are either licensed or assigned, and the remaining four are at an early stage of prosecution and exploitation.

In two cases, commercial exploitation is through spin-out companies (Crescendo Biologics & Discerna) with the remainder being licensed. Some of these projects are described in the following case studies:

Case study: Vectibix – Licensing as a route to market

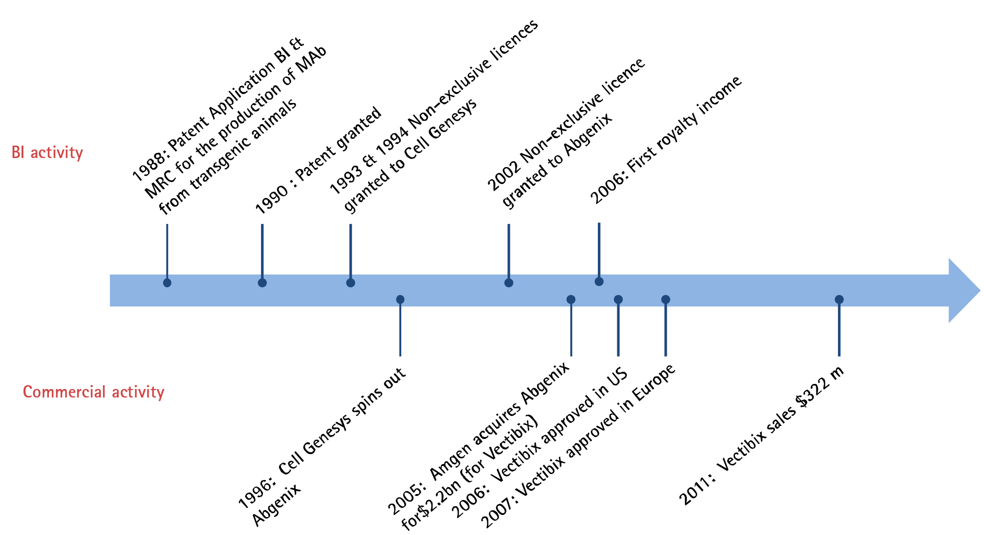
Amgen is the world's largest independent biopharmaceutical company in terms of sales ($15.6 billion in 2011) and R&D expenditure ($3.1 billion) and sells Vectibix®(panitumumab), a fully human IgG2 kappa monoclonal antibody that binds specifically to the human epidermal growth factor receptor (EGFR). Vectibix is approved in 40 countries as a monotherapy for patients with EGFR-expressing, wild-type KRAS, metastatic colorectal carcinoma (mCRC) and in combination with some chemotherapy regimes, as a second line or third line treatment option. Vectibix competes primarily with Eli Lilly/BMS's Erbitux (cetuximab). Global sales of Vectibix were $322 million in 2011 and the current sales forecasts are c. $676 million by 2016.

Colorectal cancer is the 3rd most common cancer worldwide in men and the 2nd most common in women. In 2008, approximately 1.23 million cases of colorectal cancer were diagnosed globally, and an estimated 333,330 in the EU, with UK incidence c. 40,700 pa in 2010. Mortality is c. 40%.

EGF receptors are proteins that play an important role in cancer cell signalling. Although EGF receptors normally help regulate the growth of many different cells in the body, they can also stimulate cancer cells to grow. Vectibix binds to EGF receptors, preventing the natural ligands such as EGF and TGF-alpha from binding and interfering with the signals that might otherwise stimulate growth and survival of the cancer cell. Developing fully human MAbs offers effective targeted therapies with lower risk of immune response against these agents.

Panitumumab is produced in genetically-engineered mammalian cells using technology licensed from the Babraham Institute. It was first approved in the US in 2006 and in Europe in 2007 for use in metastatic colorectal cancer. The Babraham Institute's pioneering research collaboration in the 1980s with César Milstein at the MRC Laboratory of Molecular Biology (MRC-LMB) produced 'the first useful monoclonal antibodies'. The Babraham Institute's pioneering research with the MRC LMB on the production of antibodies from transgenic animals transformed the prospects for monoclonal antibody therapeutics by facilitating the creation of, first, humanised and later fully human MAbs, eliminating most of the immunogenicity associated with the first murine products. Some of the early Babraham-LMB research was patented, and in 1993 & 1994 non-exclusive licences were agreed with Cell Genesys (along with other biologics companies, including Medarex). In 1996, Cell Genesys spun out Abgenix. Ten year later Amgen acquired Abgenix for $2.2 billion.

This successful commercialisation process using the technology to produce human antibodies from transgenic animals invented in the late 1980's and 1990's at the Babraham Institute began generating considerable royalty income in the following decade.



Case Study Figure 2: Timeline of technology licensing for Vectibix commercialisation

Case study: Crescendo Biologics spin-out

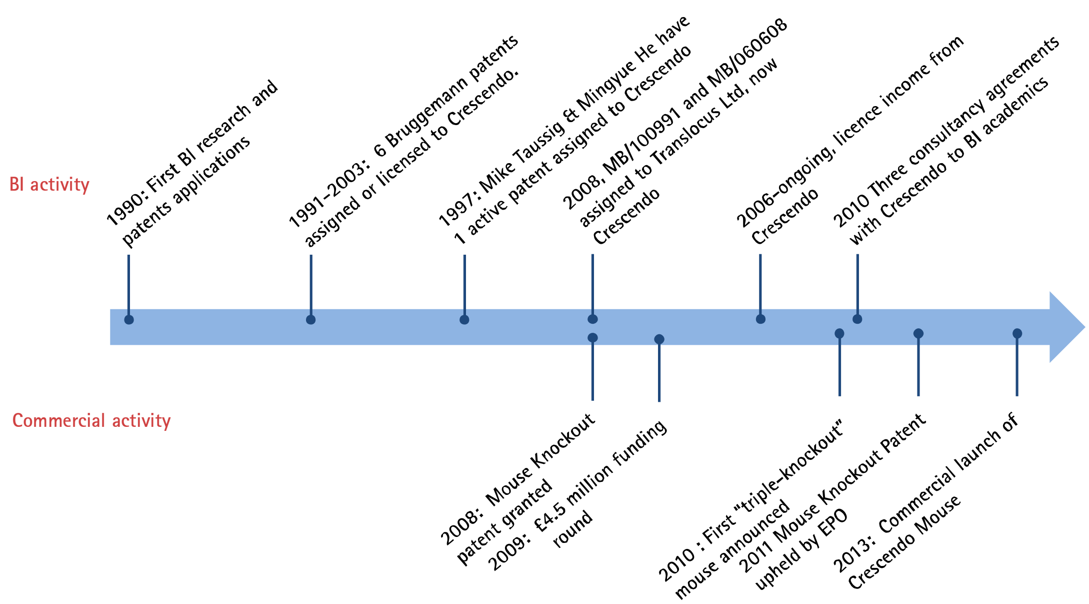
Monoclonal antibodies (MAbs) have over recent years been the strongest performing molecular class across the branded prescription pharmaceutical market, outpacing the growth rates of small molecules, therapeutic proteins and vaccines. The first antibody fragments and antibody-drug conjugates have reached the market. The global market for therapeutic antibodies is now estimated at c. $50 billion (2012).

Further research at Babraham, in the late 1990s and early 2000s, some in collaboration with Professor Michael Neuberger from the MRC-LMB, resulted in the expression of diverse human antibodies, new gene/locus knock-out strategies and, more recently, the development and expression of single chain antibodies. Also in the same decade in vitro ribosome display technology was developed at Babraham. These new inventions arising from the fundamental research were protected by a portfolio of patents.

By combining the innovative in vivo and in vitro technology platforms invented by Babraham scientists, a commercial case was made to create a spin-out company Crescendo Biologics Ltd (formerly Translocus) in 2008. The patent family was assigned to Crescendo Biologics from the Babraham Institute by BBT, the commercial arm of the Institute. In 2008, the Mouse Knock-out patent was granted and upheld by the EPO in 2011, which significantly extends the IP protection for mouse knock-out technology AND transgenic mouse technology.

In October 2009, Crescendo raised £4.5 million to advance the development of its fragment antibody technology platforms from an investment syndicate (including BBT on behalf of the Institute) and led by Sofinnova Partners. In 2010, Crescendo announced the generation of the first "triple-knockout" mouse. Investment in Crescendo Biologics to date totals £7.7 million.

The Crescendo transgenic mouse platform, commercially launched in January 2013, has the potential to generate high-affinity human heavy chain antibodies that, in turn, yield VH fragments. This is combined with a powerful in-vitro ribosome display technology for antibody optimisation. VH fragments provide great flexibility as a starting point for the development of new, targeted therapeutics combining the specificity and binding affinity of antibodies with certain desirable characteristics of small molecules. Crescendo retains strong research links to the scientists at the Institute through consultancy agreements and use of scientific services.



Case Study Figure 3: Timeline of Crescendo Biologics spin-out

Case Study: VDJ-Seq

VDJ recombination, also known as somatic recombination, is a mechanism of genetic recombination in the early stages of immunoglobulin (Ig) and T cell receptor (TCR) production in the immune system. Scientists at the Babraham Institute has developed VDJ-seq, a high-throughput, next generation sequencing method for identifying VDJ recombination products. The method provides unprecedented depth and resolution and a 1,000-fold increase in throughput compared to existing methods.

This technology has been patented and is attracting licensing interest from a number of parties for applications including screening of transgenic and in vitro antibody platforms, for example, for identification and selection of monoclonal antibodies.

Case Study: PRex1 inhibitors

Investigating downstream targets in the PI3 Kinase pathway, Babraham scientists identified two related PI3K-dependent activators of Rac, an intracellular signalling protein, P-Rex1 and P-Rex2. P-Rex1 was shown to be a key pro-inflammatory regulator of leukocyte function, while research in other labs showed P-Rex1 and P-Rex2 control cancer progression and metastasis. P-Rex1 is upregulated in cancers, and therefore is a possible therapeutic target for cancer, while its pro-inflammatory role makes it a potential target for inflammatory and autoimmune diseases.
A collaboration with the Beatson Institute is investigating the role of P-Rex1 in metastasis, but Babraham's main focus has been on the inflammatory indications. Further research under an MRC grant has identified two druggable small molecule inhibitor leads. Work to optimise these leads under a translational research grant is planned.

Case study: NAMPT inhibitors

Every adult loses over two miles of myelinated axon fibres every day, representing a 45% reduction by the age of 80. Despite the survival of most cell bodies, the lack of CNS axon regeneration means this is a largely irreversible loss. The consequences of age-related axon loss arise when numbers fall below a threshold level. We compensate for cognitive decline in middle age by remodelling and using our brains differently. However, limiting axon loss is essential for healthy ageing. A further unmet need is for temporary neuroprotection during chemotherapy with microtubule stabilising agents (such as taxol or vincristine), a common side effect of which is peripheral neuropathy.

Babraham researchers investigating the mechanism of axon loss have identified two enzymes implicated in axonal survival/degeneration. NMNAT2 is essential for axon survival and has a short half-life, so the rapid decline in its level leads to axon degeneration. However, a second enzyme, NAMPT, is required for the toxic effect. A potential therapeutic strategy to increase axon longevity is through inhibition of NAMPT.
Further research at Babraham has identified small molecule inhibitors of NAMPT that show this neuroprotective effect in vitro.

Two patents have been filed by Babraham on inhibitors of NAMPT as neuroprotective agents, and translational research work is planned to further investigate and optimise these small molecule inhibitors.

5.4 Partner-driven projects leading to economic impact

Since 2006, Babraham has been involved in 25 industrial research collaborations worth £2.4 million with a range of major pharmaceutical companies and biotech SMEs, including GSK, AstraZeneca, CellCentric, Karus Therapeutics, and PIramed. In addition to industry funding, grant funding sources have included BBSRC Industrial Partnership Award (IPA), Industry Interchange Programme (IIP) and LINK awards. There have also been 19 CASE studentships with 8 commercial partners. Two examples of partner-driven projects include investigation of acquired resistance to MEK1/2 inhibitors and acquired resistance to FGFR inhibitors, described in the case studies below:

Case Study: Acquired resistance to MEK1/2 Inhibitors

MEK is a key protein kinase in the RAS/RAF/MEK/ERK pathway, which signals cancer cell proliferation and survival. MEK has been shown to be frequently activated in cancer, in particular in tumours that have mutations, including BRAF and KRAS, in the RAS-RAF pathway. AstraZeneca's selumetinib (AZD6244) is a small molecule MEK inhibitor, currently in Phase 2 clinical trials in a range of solid tumour indications either as monotherapy or in combination with other agents. In particular selumetinib has shown promising results in Phase 2 trials against BRAF-mutant melanoma and KRAS-mutant non-small cell lung cancer.

In collaboration with AstraZeneca, Babraham scientists identified tumour resistance mechanisms to selumetinib[22]. The research provided new insight into the signalling pathway, and greater understanding of tumour cells' versatility to overcome therapies targeting this pathway. This also suggested potential therapeutic strategies to overcome the acquired resistance. As a result of this insight, AstraZeneca entered into a pioneering clinical collaboration with Merck to develop a predicted synergistic combination therapy in which selumetinib is partnered with Merck's MK-2206 (an AKT inhibitor, targeting the PI3 Kinase pathway). Further, both GSK and Roche have MEK inhibitor/BRAF inhibitor combination therapies in development, another strategy suggested by the Babraham-AstraZeneca results.

Case Study: Acquired resistance to FGFR Inhibitors

Fibroblast growth factor receptors (FGFRs) can act as driving oncoproteins in certain cancers, making them attractive drug targets. Very recently, scientists at the Babraham Institute, working with collaborators at AstraZeneca, have made a breakthrough in understanding how a particular signalling pathway involving Fibroblast Growth Factor Receptors (FGFRs) can promote aberrant cell growth and pinpointed a mutation that enables tumours to circumvent FGFR inhibitor therapy[23]. This research was funded by AstraZeneca plus a BBSRC CASE-studentship with AstraZeneca.

Babraham's extensive industrial collaborative projects in the field of PI3 Kinase inhibitors over more than a decade were described in the previous chapter. Most recently, Babraham announced a collaboration with Karus Therapeutics to further investigate PI3 Kinase signalling and the immune response, in particular the role of the different isoforms of the PI3K catalytic subunit p110 on neutrophil cell function, and the mechanism by which Karus Therapeutics' PI3 Kinase-p110β and PI3 Kinase-p110δ inhibitors impact on neutrophil function and immune responses, with the aim of developing more effective treatments for inflammatory diseases such as rheumatoid arthritis.

22 Little et Science Signaling 2011
23 Chell, V., & Cook, S Oncogene

5.5 Summary of evidence of value chain

A summary of the translational activities (see Figure 13) shows how the Babraham Institute is active and successful at translating fundamental research.

Research: The excellence of the academic research output has been discussed in Chapter 4. In summary the impact factor of the publications has risen three-fold over 20 years to 11.3 in 2012. All PIs have an above average scientific impact for their career stage and almost half of the PIs have an exceptional scientific impact. The excellence is also recognised by the awards and prizes; 2 FRS, 2 Academia Europaea, 1 EMBO Young Investigator and 2 Welcome Trust Investigator Awards since 2010. In 2009, the Institute was rated as in the top-10 world leading research centres in epigenetics. Any new intellectual property is protected and managed by BBT.

Research Collaborations: PIs are now close to generating as much income from external sources as comes from the strategic BBSRC support. Since 2006, there have been 25 industrial research collaborations worth £2.4 million with a range of commercial companies from large pharmaceuticals to smaller biotechnology start-ups. Sources of funding have included BBSRC Industrial Partnership Award (IPA), Industry Interchange Programme (IIP) and LINK awards. Also since 2006, there have been 19 CASE studentships with 8 commercial partners. Other non-BBSRC funding has originated from 21 charities for 47 projects

Figure 13 Evidence for translational research and increasing interactions in the innovation ecosystem.

Translational Research: In the UK the translation of fundamental discoveries is supported by a suite of funds that aim towards benefits to human health. The technology frequently needs pre-clinical development and early clinical testing if it is related to novel therapeutics and diagnostics. The PIs have translational projects supported by the BBSRC Follow-on Fund, two MRC Developmental Pathway Funding Scheme and two Welcome Trust Seeding Drug Discovery applications. There are 7 pre-clinical collaborations with NHS clinicians. A major contribution to Babraham's royalty income derives from Vectibix sales, based on patents filed and licensed in the late 1980s and early 1990s (described in the Vectibix case study) that graphically illustrates the time lag between fundamental research and economic impact.

Development: Many translational projects require expertise from Babraham academics and so they act as consultants to a range of commercial companies. There are currently 6 active consultancy agreements. From 2006-2012, 20 new consultancies were started, in which Institute staff advised 14 different companies. In addition, 6 existing consultancies with 5 companies were renewed.

New Products and Services: The Institute sells products and services through its commercial trading company BBT. These are discussed in detail in the next chapter as part of the development of the Babraham Research Campus.

CHAPTER 6. ECONOMIC IMPACT OF THE BABRAHAM RESEARCH CAMPUS

6.1 BBT economic impact created through new products and services

BBT sells products and services developed by the Babraham Institute and these have been increasing steadily as shown in Figure 14. Income has increased five-fold from just over £500k in 2006/7 to over £2.5 million in 2011/12 (excluding rental income). Since 2006, 110 organisations have purchased antibodies, 58 companies and external organisations have purchased Scientific Services and 18 companies have used the Technology Development Laboratory. There are currently 22 Technology Commercialisation Agreements for new antibodies, monoclonal antibodies, mouse strains and cell lines. The advances in lipid analysis by MS techniques has led to a new service offered by Scientific Services and used by two pharmaceutical companies as an outsourced technique too specialised for in-house research.

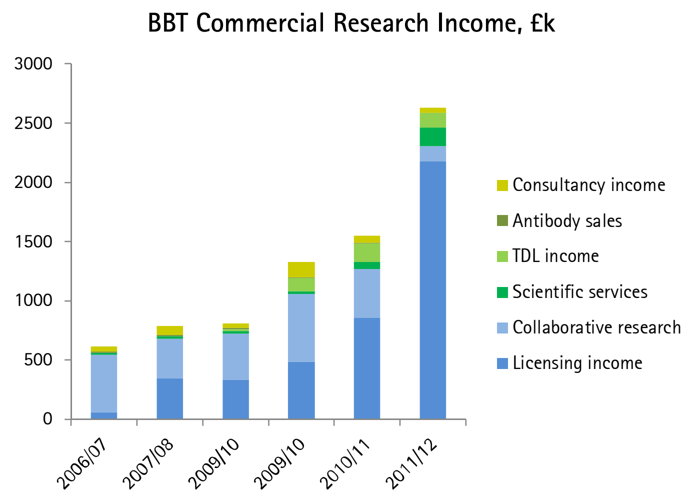


Figure 14 Increased interactions between research users & the bioscience research base from 2006-2012

The direct economic impact of the translational research activities can be measured by the income generated. BBT commercial income has risen from £2 million in 2006 to £5million in 2012 (see Figure 15).

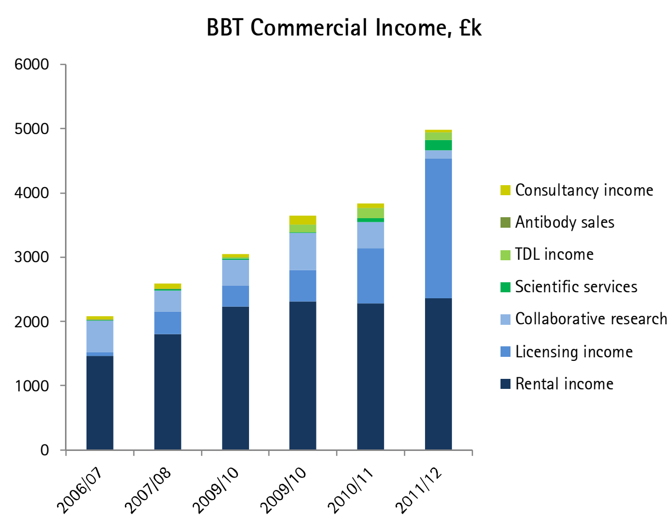


Figure 15 BBT Commercial Income 2006-2012

6.2 Development of the Babraham Bioincubator & BRC

The economic impact of the Babraham Institute cannot be considered in isolation. The development of the Babraham Research Campus has been an integral part of the expansion of the site since the opening of the Babraham Bioincubator in 1998 funded by the Department of Trade and Industry. In the 1980's the UK Government recognised that the private sector would not build and equip the specialist premises required by early stage bioscience companies nor offer short-term, flexible leases. The DTI Biotechnology and Incubator Challenge offered modest grants to support business mentoring linked to a source of research that could be patented and commercialised by licensing to commercial companies or by creating spin-out businesses.

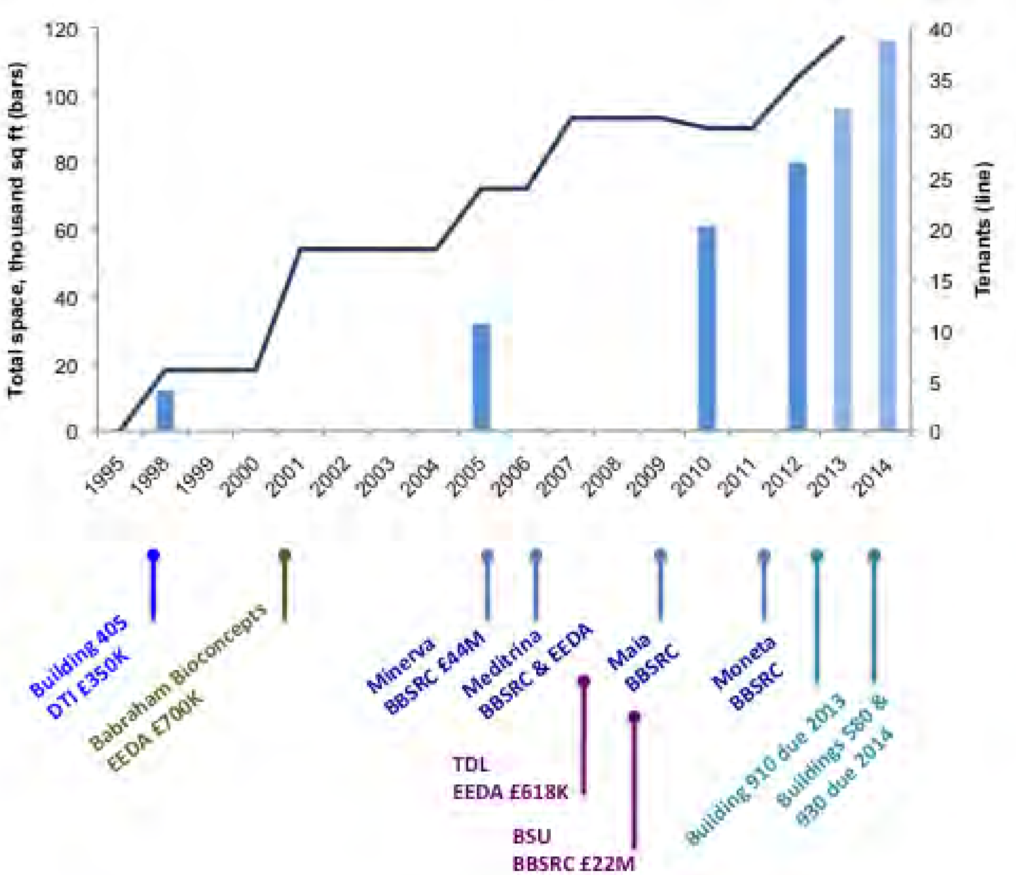


Figure 16 Development and growth of the Babraham Research Campus – Bioincubator, TDL and BSU.

The Babraham Institute developed the under-utilised Building 405 as a bioincubator and by 2001 it was fully occupied. By 2005 there were 24 tenants and 6 businesses had graduated out of the incubator. The need for grow-on space and a proven demand led to three new commercial buildings. Minerva, opened in 2005 funded by BBT through a commercial loan, Meditrina opened in 2007 and Maia in 2010 resulting in 60,000 sq ft of incubator and 'grow-on' space within the Babraham Research Campus (see Figure 16).

In May 2012, Moneta was opened by David Willetts, the Minister of State for Universities and Science bringing the total space (laboratory and office) available to life science companies to 80,000 sq ft. This new research facility has been funded through the £44 million capital development project, for four new buildings, awarded to the BBSRC, which was announced by the Chancellor in 2011. The second facility, Building 910, is due for completion in April 2013. Cancer

Research Technology (CRT) has taken a lease on half of this building, which will accommodate up to 30 of their researchers working in the area of cancer therapeutics (both bioscience and chemistry)[24]. Building 580 will provide central scientific services from the Babraham Institute and the Technology Development Laboratory. Construction of Building 930 will begin in May 2013. Building 910 and 930 are designed to accommodate growing rather than early-stage companies.

> *BBSRC is playing a key role in leading the developments at both campuses. Going forward at Babraham, we will build on our current strengths in research and innovation, and initiate further infrastructure and facilities which will help create and support exciting new companies and jobs based on world-leading bioscience.*

6.3 Economic Impact of the BRC

In 2002/3 the rental income was £0.4 million but this has risen steadily to £2.4 million in 2011/12 reflecting the increasing space available (see Figure 17).

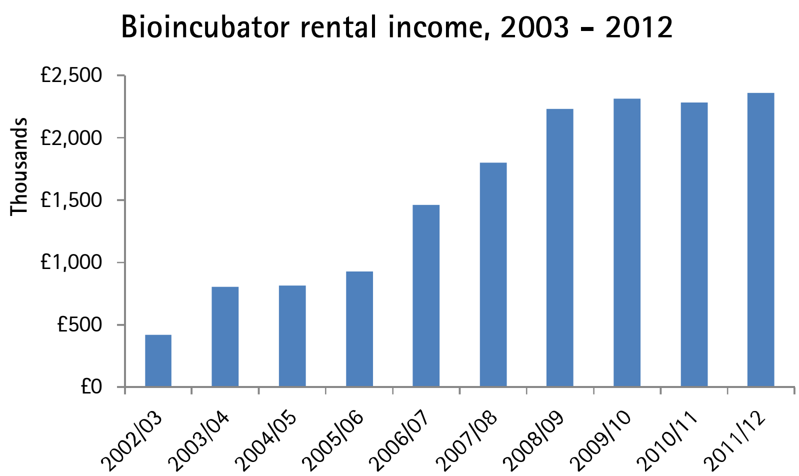


Figure 17 Total rental Income from 2002/3 to 2011/12

Most importantly the space has, on the whole, been fully occupied with a void rate of about 5% since 2009 (see Table 3). The average void rate rose in 2012 when Moneta opened. It is now 70% occupied with half of the tenants being new to the BRC and the other half graduating from other buildings.

Financial Year	Bioincubator space sq ft	Average void %	Total Staff number	Number of Companies
2009/10	61,000	6%	230	31
2010/11	61,000	4%	287	30
2011/12	63,500	4%	299	31
2012/13	80,500	13%	350	39

Table 3 The Bioincubator occupancy rates 2009 – January 2013.

[24] www.cancertechnology.com/news/single/crt_babraham_research_campus/

At a local level, the investments at BRC have a huge economic impact and shows how important South Cambridgeshire science and innovation businesses are nationally. At present around 700 people work on site, 350 for the 39 BRC companies (see Appendix 5) and the potential is there to create a further 400 new jobs following the £44 million strategic investment into four new buildings. For two decades the Institute has worked closely with the South Cambridgeshire District Council and the Parish Council to ensure that the planning process supports the developments within the region.

The Babraham Research Campus has been developed as an innovation campus, with research and development focused on biomedical science and technologies. BBT fostered a culture and environment that promotes interaction and two-way knowledge-flow from fundamental research to technology translation and on to near-market product development. As shown in Figure 18, 76% of BRC companies have interactions with the Babraham Institute. The majority of interactions are purchasing Scientific Services followed by CASE awards, consultancy, antibody sales, IP licences and collaborative research.

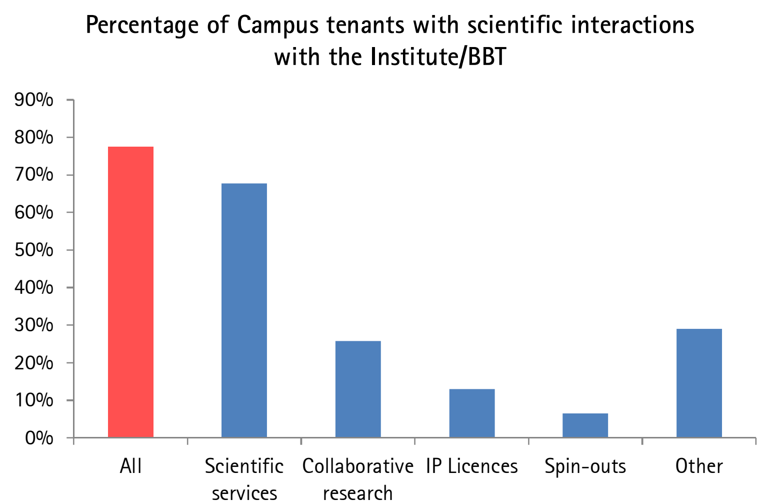


Figure 18 Interactions with campus companies

6.4 The Babraham Research Campus Ecosystem

Synergy between the Institute's science base and the companies is key to the Bioincubator concept; ventures must be developing services or products that are of relevance to human healthcare and the biotechnology or pharmaceutical sectors. The juxtaposition of companies with the Babraham Institute on the campus allows synergistic relationships to flourish between the academic and business communities. This promotes the translation of scientific advances to commercial reality and complements the internationally-competitive research of the Institute.

We interviewed CEOs, Chairman or other Board level executives of a sample of the SME tenants to identify specific attractions of the Babraham Research Campus as a location for their businesses. A large majority of them viewed the Campus as offering substantially more than a commercial property rental proposition. The key attractions identified were:

- *Scientific services:* Two thirds of the SMEs on Campus have made use of at least some of the scientific services made available through BBT. Whilst some of the services provided (such as flow cytometry or plate-readers) are relatively generic and survey respondents made use of them primarily because of the convenience of working on Campus, several respondents highlighted specific offerings as being either relatively unique (the BSU represents a Nationally unique transgenic research facility accessible on a partnering basis, and was a major attraction in coming to the site) or of exceptional quality (Bioinformatics);
- *Flexible space:* A major attraction for almost all SMEs interviewed was the flexibility with respect to leasing space, providing small office/lab space for embryonic companies, and allowing early-stage companies to expand without moving off-site. This flexibility was viewed as unobtainable in commercial research parks in the area;
- *Support services:* BBT through the Bioincubator makes available a range of basic office and laboratory services (e.g. health & safety, waste disposal, lab supplies, telecoms, IP advice) which would otherwise be a distraction in the early stages of setting up a company;
- *Campus interactions:* Most interviewees have, post-arrival, found the interactions on Campus, primarily between Campus tenants and to a lesser extent with scientists in the Institute, to be beneficial;
- *Prestige:* An important consideration for many of the SME senior executives spoken to was the importance of creating the right impression with both prospective investors and pharmaceutical industry collaborators, and enticing them to visit. The prestige of the Babraham Institute, and by association the Babraham Research Campus, was a significant factor in their decision-making;
- *Logistics:* The location of the Babraham Research Campus on the South side of Cambridge, providing easy access to other bioscience research facilities locally and good road, rail and air transport links, was also a consideration in the location decision.

The integration of the right people, the right skills and the right facilities in the BRC innovation ecosystem is shown in Figure 19.

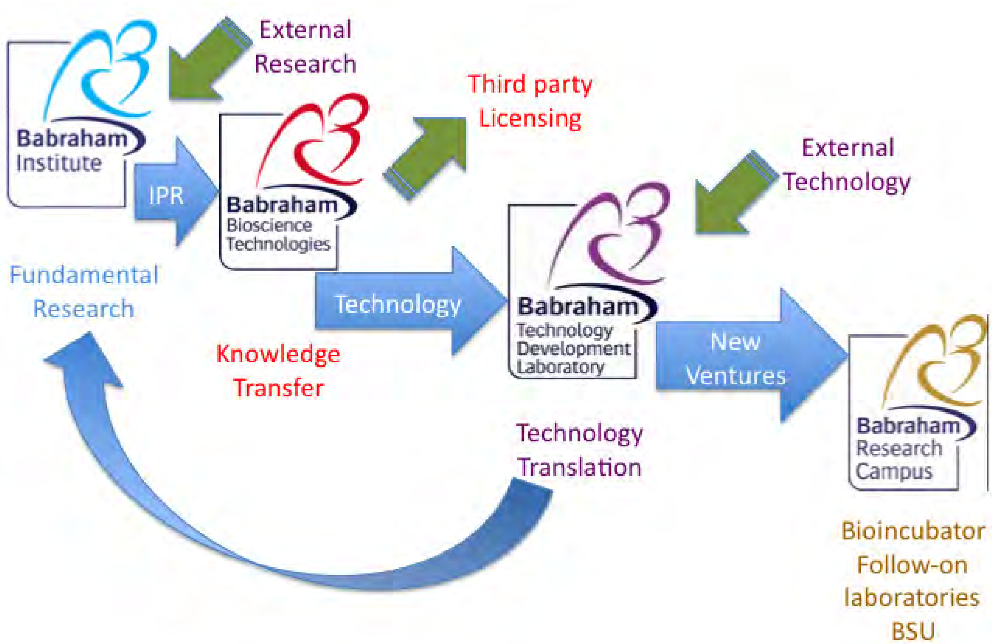


Figure 19 The BRC ecosystem that supports Innovation In life sciences.

In 2012 BBT, MedImmune (Astra Zeneca) and Neusentis (Pfizer) established an 'open innovation' partnership. There is an increasing global trend towards 'open innovation' with public/private partnerships and recent examples from November and December 2012 include:

- Neomed Institute, $100m biotech Hub AstraZeneca/Pfizer/Quebec Government for pre-competitive, early stage collaboration across disciplines; expertise, funding and easy access to specialised expensive equipment.
- Campus Biotech SA, a new company that intends to transform the Merck Serono's facility in Geneva into a public/private research centre focused on healthcare and biotech.

Also in 2012, BRC and The University of Cambridge's ideaSpace entered into a strategic relationship through which early-stage ventures will have dual access to the 'plug and play' laboratory facilities at Babraham and the co-working community at the ideaSpace in the Hauser Forum. ideaSpace is a co-working community space offering 'hot desks', coaching and mentoring support to around 70 members, most of whom represent early-stage ventures looking to develop and accelerate their business idea. Partnerships such as these will remove any potential barriers to new businesses, such as an inability to access wet-laboratory space or technical equipment.

Babraham Bioscience Technologies Limited, One Nucleus, ideaSpace and Cambridge Enterprise organise the annual Biotechnology Investment Forum that facilitates putting new and early-stage biomedical companies in front of Venture Capital and Business Angel investor groups interested in biotechnology.

> *"I found it stimulating and I am following up a number of companies for potential investments" Dr Hermann Hauser of Amadeus Capital Partners*

The Campus is home to a growing number of companies aiming to commercialise novel antibody therapeutics. Three examples of biologics spin-out companies that have moved onto the Campus are Recombinant Antibody Technology, Kymab and Bicycle Therapeutics, commercialising technology licensed from the Babraham Institute, the Wellcome Trust Sanger Institute and the MRC-LMB respectively. Other tenants with a biologics focus include F-star and MRC ARES. The Babraham therapeutic antibody company cluster now comprises:

- Recombinant Antibody Technology Ltd (wholly owned subsidiary of HCOantibody): the generation of recombinant immunoglobulin loci for the generation of genetically engineered rats expressing antibodies with fully human idiotypes;
- Kymab: optimised monoclonal antibody biopharmaceuticals from the genomically-engineered mouse, the Kymouse™;
- Bicycle Therapeutics: creation of novel molecules that combine the desirable features of small molecules and biopharmaceuticals;
- Crescendo Biologics: building a pipeline of novel medicines based on its highly innovative VH antibody fragment platform; and
- F-star: therapeutic antibodies and antibody fragments based on a unique Modular Antibody Technology.

> *"The opening of new research facilities at Babraham for early stage companies is very good news for the development of the antibodies of the future" Sir Gregory Winter, FRS*[25]

[25] BBSRC Impact Report 2011

In addition to the support provided to these new companies, Babraham Bioscience Technologies draws upon the Institute's capability to produce antibody products for both research and commercial organisations through the Technology Development Laboratory.

6.5 BRC position in the UK economy

The BRC contributes to the strength of the life sciences and pharmaceutical sectors in the UK. As of 2012, the outlook for biotechnology in the UK and Europe may appear less than secure. Overall employment in UK biotech has remained static for nearly ten years[26]. Some regions have experienced declines in biotechnology-related employment, usually due to the loss of a single significant organisation, e.g. Pfizer from Kent, Merck from central Scotland. Broad economic trends aside, there are indications of support for the industry from the UK government. In the 2011/12 budget, Chancellor George Osborne announced:

- £500 million of extra spending in capital for science
- an increase in R&D tax credits from 100% to 225% for science-based firms
- a decrease in corporation tax from 28% to 23%
- an increase in the tax-free allowance to angel investors in scientific companies from £2 million to £10 million.

Such measures are likely to increase access to resources for the development of the UK biotechnology industry. In a speech to the Royal Society in November 2012 Chancellor Osborne praised the Babraham Institute:

> *".....additional investment, adding £500million of extra spending in capital for science. It helps that our excellent research institutions have projects that are well-managed and ready to roll. A new building with labs and offices at the Babraham Institute was built, fitted-out, and occupied by new spin-out companies all within twelve months of the funding being announced in the 2011 Budget. That is the kind of flexibility we all like.[27]"*

In May 2012, while visiting the BRC, the Minister of State for Universities and Science highlighted £250 million funding into the UK's bioscience research base to ensure that it remains globally competitive and at the forefront of meeting the grand challenges faced by society in the coming decades. The BBSRC allocated the strategic investment, to eight of the UK's world-leading bioscience research institutes and their university partners with 26 strategic science programmes and 14 key national research capabilities. £37 million has been allocated to the Babraham Institute, including a Strategic Programme Grant to improve understanding of immunology by sustaining an excellent fundamental research base. The economic impact will be long-term supporting healthy, longer lives as the population ages.

In conclusion, BBT has established a reputation for successfully translating excellent science and technology into sound business opportunities through developing partnerships for wealth creation. As part of the UK Science Base, the Babraham Research Campus

[26] Bock, AJ., Beyond the Magic Beanstalk: A study of life science ecosystem formation at the university-industry boundary, Centre for Entrepreneurship Research, University of Edinburgh 2012

[27] Chancellor Osborne Nov 2012 Royal Society

contributes to the wealth creation, quality of life and public understanding of science objectives of Government. BBT has created the opportunity for commercial science to stimulate curiosity driven research to the benefit of the Babraham Institute's user communities. All these achievements directly meet Governmental, regional and science sector economic impact targets.

6.6 Value network analysis

Although the commercial interactions have been analysed using the "value chain" model, more recent analyses of 'expert-driven' businesses (e.g. medical centres, law firms, engineering consultancies and research institutes) have used 'social network analysis' to recognise that not all activities are linear sequential processes[28]. Value network analysis exposes the interdependence of organisations and the value that flows between them. A value network can be defined as[29]:

" any web of relationships that generates tangible and intangible value through complex dynamic exchanges between two or more individuals, groups or organisations"

Using the available financial data on the commercial interactions at the Babraham Institute a network diagram has been developed (see Figure 20).

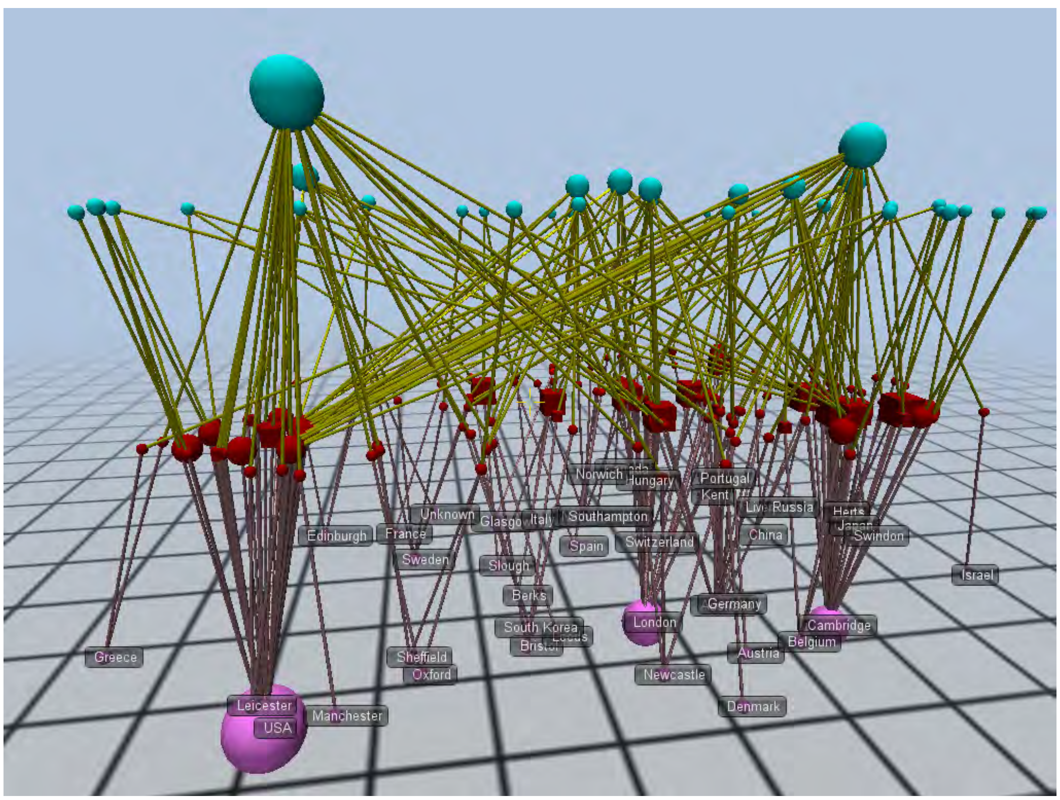


Figure 20 Value network analysis for Babraham Institute commercial interactions 2006-2012.

Key to Figure 20. Top blue layer represents PIs, the middle red layer represents projects (sphere = current projects & cube = completed projects) and the bottom purple layer represents geographical location.

The sizes of the red objects are related to the value of the project (log scale). The size of the sphere for PIs (blue, top) or geography (purple, bottom) relates to the number of interactions.

[28] Stabell, C. and Fjeldstad, O., (1998) "Configuring Value for Competitive Advantage: on Chains, Shops and Networks." Strategic Management Journal 19, 413-437.

[29] Allee,V. (2008) Value network analysis for accelerating conversion of intangibles. J.Intellectual Capital, 9(1), 5-24.

Social network analysis will recognise that the relationships between individuals, the rest of the organisation and external organisations connect in a variety of ways and these can reveal where most interactions occur and potentially where the most impact happens.

This analysis is limited to the commercial transactions over a 7-year period and shows that interactions with Cambridge, London and the US are dominant but also that there is a spread across the globe and throughout the UK. This is a screen shot from the analysis that if viewed using the software programme can be navigated through and the data held in the 'nodes' (spheres and cubes) interrogated.

If the PIs are removed from the analysis the data reveal the value, spread and scale of the commercial interactions (see Figure 21). There are three geographical clusters (green spheres) and these represent the dominance of interactions with global biopharmaceutical companies in the US (Amgen) and Cheshire (Astra Zeneca) and Cambridgeshire (biotechnology and pharmaceutical companies).

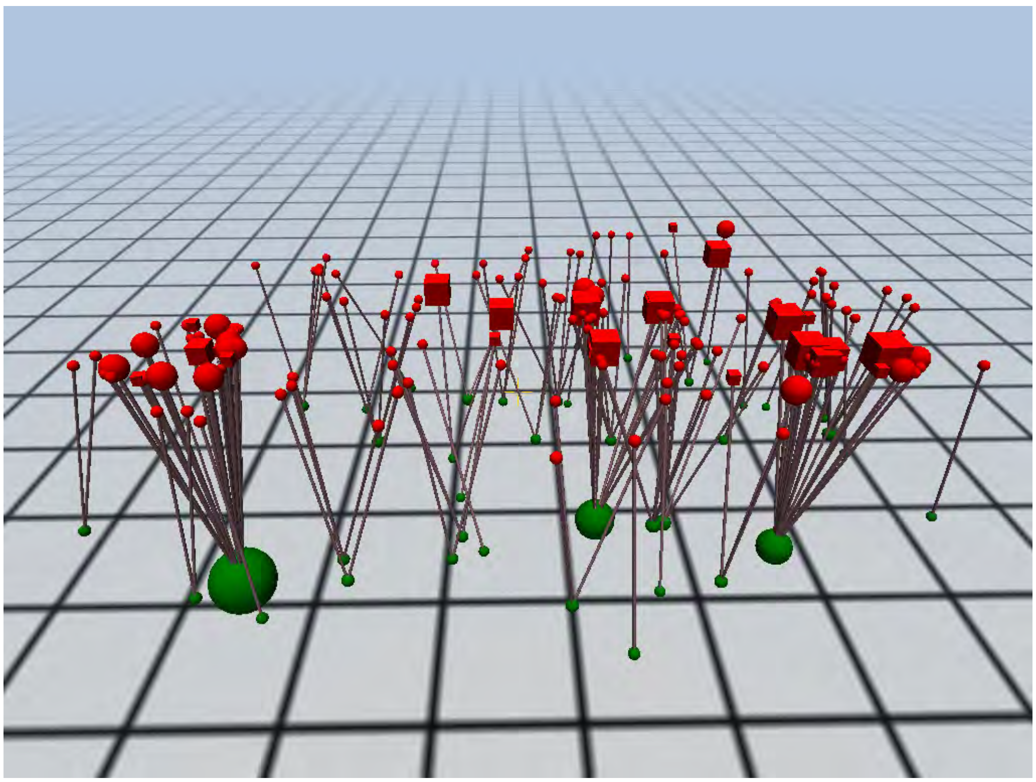


Figure 21 Value network analysis without PIs from 2006-2012.

Key to Figure 21. Top red layer represents projects (a sphere for current projects and a cube for completed projects) and the bottom green layer represents geographical location.

This network analysis approach would show a much greater and vastly expanded global network if the academic-to-academic relationships were mapped (e.g. using grants, published papers, journal referees etc). This was outside the scope of this economic impact report.

CHAPTER 7. PATHWAYS TO IMPACT AS SET OUT BY THE RESEARCH COUNCILS UK

7.1 UK business success through public investment in research

RCUK recognise that research has both academic, and economic and societal impacts described as the demonstrable contribution that excellent research makes to society and the economy. Impact embraces all the extremely diverse ways in which research-related knowledge and skills benefit individuals, organisations and nations by fostering global economic performance, and specifically the economic competitiveness of the UK, increasing the effectiveness of public services and policy and enhancing quality of life, health and creative output. RCUK developed a framework for how research is translated into impact as shown in Figure 22.

Business & commercial	Development of human capital	Policy	Quality of life
• Exploitation of intellectual property • Commercial adoption of research • Creation of clusters • Impact upon inward investment	• Acquisition of skills • Training of skilled staff • Movement of skilled researchers into industry	• Impact of research upon government policy • Research that challenges conventional wisdom	• Improved health, environment, social welfare & cultural advances

Figure 22 RCUK framework for how research is translated into impact

7.2 How research is translated into business & commercial impact

Many of the illustrations of how excellent fundamental and translational research at the Babraham Institute have resulted in an economic impact been discussed in detail in Chapter 5 and Chapter 6. This analysis will summarise the relevant business and commercial evidence with respect to the RCUK framework and discuss the contributions through the development of human capital, to policy and quality of life.

7.2.1. Exploitation of IP

BBT is the commercial arm of the Babraham Institute and they manage, develop and commercialise the intellectual property rights (IPR) as part of the Knowledge Exchange and Commercialisation (KEC) remit. IPR are assigned, licensed (exclusive and non-exclusively) or are under option agreements and significant income is generated (see Figure 14). The IPR portfolio includes antibodies, monoclonal antibodies, mouse strains and cell lines, small molecule lead series and software.

The Institute has 22 active Technology Commercialisation agreements with a range of commercial companies, large and small.

7.2.2. Commercial Adoption of Research

Scientists at the Babraham Institute have had Industrial Research Collaborations with companies in the life sciences sector worth £2.4 million since 2006. New collaborations with NHS in 2012 include Addenbrooke's and Papworth hospitals for potential new clinical tests in immunology and haematology.

In addition to the scientific facilities and services available through the Babraham Institute, a unique offering of the Babraham Research Campus is BBT's Technology Development Laboratory (TDL), a fully equipped biology and chemistry laboratory, which is accessible by companies both on and off site. It was established to support innovation in biotechnology and biomedical fields. Translational research is also supported by a suite of Scientific Services including Bioinformatics, Epigenomics, FACS analysis, Gene Targeting, Imaging, Lipidomics and Monoclonal Antibody production. The Biological Support Unit is developing transgenic rodents for research into healthy-ageing. The facilities are used by Institute staff and external companies.

The commercialisation and exploitation of scientific knowledge, has led to spin out companies and the creation of new processes (e.g. lipid analysis), products and services. In 2012, 14 mouse lines were exported to other researchers.

Case Study: 5-hydroxymethylcytosine

Following the prior identification of 5-hydroxymethylcytosine as a novel DNA modification, Babraham scientists developed novel antibodies to document its presence in several mammalian species, revealed the underlying molecular mechanisms and linked its role to epigenetic reprogramming. These antibodies have been licensed to several companies. Babraham scientists in the Epigenetics Programme have also collaborated with the Department of Chemistry, Cambridge University in development of a technique for high-throughput sequencing of methylated and hydroxymethylated DNA. The oxidative bisulfite sequencing (oxBS-Seq) technology enables quantitative sequencing of 5-methylcytosine and 5-hydroxymethylcytosine at single-base resolution.

This methodology has potentially important clinical and non-clinical applications in the rapidly expanding field of epigenomic sequencing and will dramatically change the way in which epigenetics research is conducted. A University of Cambridge spin-out company, Cambridge Epigenetix, has been established to exploit the oxBS-Seq technology.

7.2.3. Creation of clusters

The development and success of the BRC campus since the early 1980s has been discussed in Chapter 6 from an internal perspective. The BRC is a significant part of the 'Cambridge Cluster'[30],[31]. The County of Cambridgeshire has 1,400 high tech firms employing 48,000 people with an economic output (GVA) of almost £7.5billion and the GVA per job is well above the national average (see Table 4). There are about 70 staff employed on the BRC in total. Babraham is located in the South Cambridgeshire District and this along with the City of Cambridge has 900 high tech businesses employing 37,000 people. While the impact of a major research institution should not be underestimated, rigorous research has repeatedly demonstrated that organisational

[30] 'The Cambridge Phenomenon Revisited',SQW. 2000 http://www.sqw.co.uk/special- feature/cambridge-phenomenon

3 'Cambridge Cluster at 50: the Cambridge economy, retrospect and prospect'. SQW 2011 http://www.sqw.co.uk/file_download/284

heterogeneity and broadly based absorptive capacity in the form of extensive and dense networks of technologists, industrialists, financiers, and entrepreneurs are essential to cluster formation[32].

	1984	1998	2008
Number of High Tech Firms	300	1,250	1,400
Number of high tech Employees	15,000	32,500	48,100

Table 4 The Growth of the High Tech Cluster in Cambridgeshire over Three Decades[33].

In 1985, the SQW analysis of the Cambridge Phenomenon put the University of Cambridge at the centre of its cluster diagram but by 2000, the high tech firms were at the centre of the cluster with the four elements of Intellectual Capital, People, Money and Expertise, and Land, Property and Infrastructure as the supporting elements. Cambridgeshire has an active and integrated biotech networking community, making it a stimulating environment in which to develop new bioventures. BBT is an active member of One Nucleus, the Cambridge Network and the UK Bioincubator Forum. It also plays an active role in organising events to bring together diverse stakeholders.

7.2.4. Impact upon inward investment

The Institute is successful at attracting R&D investment from global business, as shown by the range of Industrial Research collaborations described above. The new open innovation initiative launched by BBT, MedImmune and Neusentis 2012 is in the vanguard of global trends involving public and private sector partners. International companies such as StemCells Sciences, F-star and NorayBio have chosen to locate an office in Cambridgeshire at the BRC and likewise investment firms see value in co-location, e.g. Imperial Innovations Ltd and Midven Ltd.

7.3 Development of human capital

In some analyses training highly skilled researchers is classified as 'academic' impact whilst training of skilled people for non-academic professions is classified as 'economic and societal' impact. This study analysed staff training across the Institute. With around 330 people working at the Institute; 25 Principal Investigators, ~70 Cambridge University PhD students, ~75 postdoctoral researchers, together with support staff, administration staff and visitors, there is a vast range of skills and levels of experience, hence a range of training courses and programmes offered to the staff.

7.3.1. Training of skilled staff & acquisition of skills (value measured by additional salary benefits)

The Institute regards itself as an exemplar in the training of scientists at all stages of their careers, from PhD to the Post-Doctoral Career Progression Fellowships (CPF) awarded by the Institute. The majority of UK and EU students are supported by studentships from the Institute quota Departmental Training Awards provided by the BBSRC and MRC. Babraham has the status of a recognised postgraduate institution within the University of Cambridge where students are registered within the Faculty of Biology for the PhD degree. Babraham students account for almost 6% of the total postgraduate population in the Faculty of Biology at the University. Project Leaders are full University supervisors and the Institute Director acts as a 'Head of Department'. Institute scientists examined more than 20 PhD theses in 2012. The UK is ahead of

[32] Zucker, L. G., Darby, M. R., & Armstrong, J. (1998). Geographically localized knowledge: Spillovers or markets? Economic Inquiry, 36(1), 65-86.
[33] Cambridge Phenomenon Changing Perspectives, SQW July 2011

other countries in its extension of researcher career development to postdoctoral research staff, particularly through the implementation of the 'Concordat to Support the Career Development of Researchers' and the activities of Vitae in this area[34].

The Babraham Institute Graduate Programme has been described as a 'model of best practice' and has averaged 15 PhD students per year (range 11-20) over the last 11 years, the majority funded by Research Councils (BBSRC). However, the number of RCUK-funded PhD studentships awarded to Babraham has reduced drastically in 2012 as a result of BBSRC's decision to cease directly funding the BI Graduate Programme as part of a national reorganisation of graduate student funding into fewer, larger, centres (as shown in Figure 23) The PhD cohort since 2004 has always included a CASE award student. The Institute has held 15 CASE studentships since 2005 and currently 8 are active.

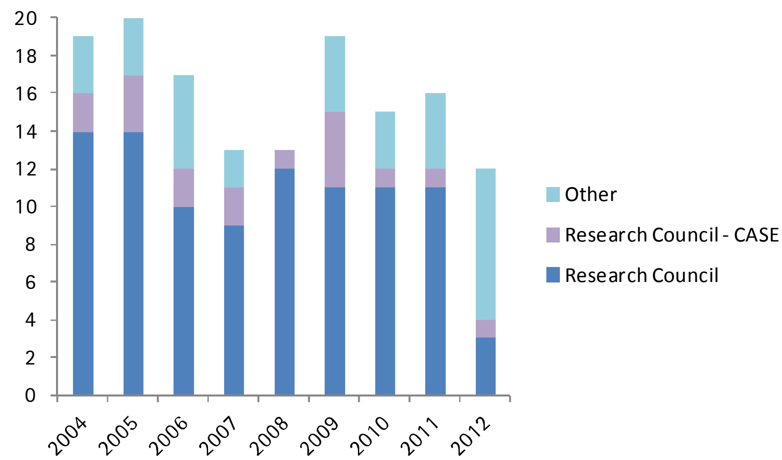


Figure 23 PhD students at the Babraham Institute

The Industrial CASE schemes provide training grants for PhD studentships that are supervised jointly by academic and industrial partners. As well as providing high-quality training for students, the Industrial CASE scheme helps to foster links between students, academia and industry. An independent evaluation has found that the BBSRC Industrial CASE schemes provide high quality training for students, helping them to develop a broad range of both research and professional skills. The majority of CASE students undertake a placement with their industrial supervisor and these, the evaluation concluded, were a major strength of the scheme delivering real 'added-value' for students and partners.

The Institute's Graduate Committee provides a training credit system to ensure that students accumulate the level of transferable skills training required by the Research Councils. The training meets the Joint Research Councils' Skills training Requirements and the level of training recommended by the Roberts' Review[35]. Babraham's students currently exceed the target 10-days per annum training recommended by the Research Councils at this level. The following are some of the courses available to students[36]:

- Experimental design and data management (Good Laboratory Practice, Home Office courses)
- Research environment: ethics, funding, health and safety

34 www.vitae.ac.uk/policy-practice/505181/Concordat-to-Support-the-Career-Development-of-Researchers.html
35 SET for Success: the supply of people with science, technology, engineering and mathematic skills, Roberts 2002
36 www.babraham.ac.uk/graduate/formal.html

- Communication skills: oral presentation, effective poster production and presentation, scientific writing, team working and leadership skills
- Interpersonal skills: career, networking, time management
- IT skills: Microsoft Office software, www, e-mail, bioinformatics, reference management
- Science in the commercial environment: intellectual property, entrepreneurship and business planning; Careers Research Advisory Centre courses

Students are also encouraged to enter the BBSRC Biotechnology YES (Young Entrepreneurs Scheme) an innovative competition developed to raise awareness of the commercialisation of bioscience ideas among postgraduate students and postdoctoral scientists.

The high level skills developed through research careers are deemed to be essential by David Willetts, Minister for Universities and Science, Research Councils UK, for the sustainability of the UK research base which in turn drives growth of the UK economy as well as bringing many broader benefits for society. To strengthen the support for developing of world-class skills amongst research staff in 2012 RCUK and HEFCE, both sides of the dual support system, formed a new partnership[37]. However, assessing the economic impact of PhD graduates is the topic of a new study in 2013. The study has been commissioned by RCUK and the five UK funding bodies (RCUK, HEFCE, SFC, DEL NI, HEFCW). Collectively, they share an interest in demonstrating the impact of these investments. Assessing the economic impact of PhD graduates is a key objective that will help to establish the extent to which doctoral training drives innovation and growth. However, this is not new, as long ago as the Warry Report in 2006 continued to stress the need for the Research Councils to demonstrate the impact of their investments in both research and researcher training, particularly to be able to quantify the economic, social and cultural impact of their funded postgraduate researchers[38]. A common metric to assess economic impact of education is to show an increase in salary with an increase in qualifications. However this has been shown not to be true for many PhD scientists as a significant proportion stay in research and in teaching in universities and because these are relatively poorly paid, there is no salary advantage[26].

Training of skilled staff includes graduate students from the Universities of Otago, Auckland, Maastrict, Nottingham, Newcastle, Cancer Research UK in 2012. Summer undergraduate research placements are competitively funded by the BBSRC Research Experience Placements, Wellcome Trust Biomedical Vacation Scholarships, Society of Biology Undergraduate Research Bursaries, Amgen Scholars Programme, the Biochemical Society, British Society for Cell Biology, Genetics Society, British Society for Immunology and Physiological Society. The Institute has hosted up to 6 Nuffield Bursary summer students each year from local 6th forms since 2006.Since a partnership with the University of Rome began in 2006, Group Leaders have supported the training of over two dozen Master's students from Italy, selected through the Da Vinci UniPharma Graduates Project[39]. The scheme provides 6 month's training and several of these students have continued with further degrees either at Babraham or in Italy.

Besides delivering training to Babraham researchers, Principal Investigators have delivered bespoke training courses for MedImmune, Institute of Cancer Research and Centre for Trophoblast Research, University of Cambridge staff in 2012.

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[37] RCUK and HEFCE join forces on researcher skills development 30 May 2012 www.hefce.ac.uk/news/newsarchive/2012
[38] Warry Report: Increasing the Economic impact of the Research Councils (2006)
[39] www.unipharmagraduates.it

7.3.2. Training of skilled people for non-academic professions.

With over 700 staff on site there is scope for training at all levels in many occupations. Three examples of vocational skills training have been identified:

- BSU staff: Four out of five senior managers in the BSU joined after school and have progressed up the career ladder by working for vocational qualifications offered by the Institute of Animal Technology (IAT) while employed at Babraham. The 'Understanding Animals in Research' Workshop, developed by the Public Engagement team, has been presented to 350 Year 10/11 pupils since 2007 and includes career options for working with animals in a research environment. Technical staff attend 6 seminars per year as part of their CPD training and staff gain qualifications thought the IAT the Awarding Body under the Qualification and Credit Framework) as shown in Table 5. Institute staff have repeatedly been the top student in these national exams.

	IAT First Diploma (Level 2)	IAT National Diploma (Level 3)	IAT Higher National Diploma (Level 4)	IAT Membership
2009	x 1 staff			
2010	x 3 staff			
2011	x 1 staff	x 4 staff	x 1 staff	x 4 staff
2012	x 3 staff			
2013		2 x staff ongoing		
2014			1 x staff ongoing	

Table 5 Qualifications and training of the BSU staff

- Nursery staff: There is a body of evidence which has found that the qualification levels of staff within early years settings can be directly linked to the quality of provision provided by the setting. Furthermore longitudinal studies have linked high quality pre-school to improved outcomes for children into their Primary and Secondary years[40, 41]. Therefore there has been a drive within government to increase the qualification levels of staff. The Babraham Institute Nursery has been graded as 'Outstanding' by Ofsted in every area in its most recent two consecutive inspections in 2007 and 2011. The staffs' commitment to continual professional development enables the Nursery to continue to improve and develop. The staff at the Nursery hold a range of qualifications, as shown in Table 6.

Qualification Level	Type of Qualification	Number of staff
7	Master's Degree in Early Years Education	1 ongoing
6	BA Hons and Early Years Professional Status	2
4	NVQ's, working towards Foundation Degree	5
3	NVQ, BTEC, NNEB, CACHE DCE	18
2	NVQ	3 + 2 ongoing
None	None	1

Table 6 Qualifications and Training by the Babraham Nursery Staff

[40] www.education.gov.uk/nutbrownreview
[41] www.education.gov.uk/tickellreview

- The overall qualification level of the staff team exceeds the Statutory Legal Requirements set by the Department for Education. There are 31 staff currently employed to work directly with children, as well as support staff including 2 cooks and an Administrator. 20 of these staff gained their highest level of qualification with the Babraham Institute and Cambridgeshire County Council. The Nursery now accommodates 75 children aged from 6 weeks to 5 years and 15 older children during school holidays. Since 1990, the Nursery has allowed Institute staff to fully participate in the workplace by providing care for their children[42]. The manager is currently working towards a Masters degree in Early Years Education.
- Apprenticeships: In 2001, Babraham introduced an apprenticeship scheme with training in carpentry, electric and plumbing[43].

Research organisations have a responsibility to support the professional development of all their staff members and as such, staff development practices and quality of management should be a normal part of research organisations' human resources policies, according to RCUK[44]. The Babraham Institute is fully engaged with the professional development of all their staff at all levels.

7.3.3. Movement of Skilled Researchers into Industry

Destinations of PhD graduates: Of 16 postgraduate scientists who left the Institute from 2000[45], 64% remained in academia, 30% went to industry and the remaining 6% had another career destination (see Figure 24).

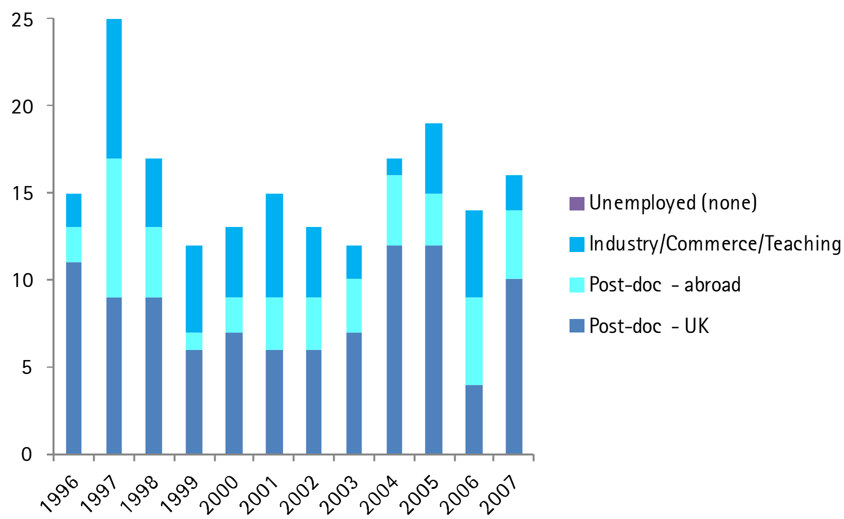

Figure 24 First destination after PhD 1996-2007

No one was recorded as unemployed. These statistics align with the employment outcomes recorded by a series of surveys since the turn of the century, that there is a low level of unemployment, 3.2%, among PhD graduates across all disciplines, and that they tend to go into research and education[46]. First-degree graduates were twice as likely to be unemployed, 6.6%. Of all graduates, PhD graduates are more likely to move overseas, either for employment or further study.

42 www.thenursery.babraham.org.uk/index.html
43 Babraham Group Corporate Report 2001-2005
44 www.rcuk.ac.uk/documents/researchcareers/RobertReport2011.pdf
45 Babraham Institute Corporate Plan 2001-5
46 The Career Choices and Impact of PhD Graduates in the UK: A Synthesis Review for ESRC & RCUK. January 2009, Raddon, A. and Sung, J., Centre for Labour Market Studies (CLMS), University of Leicester

Destinations of Postdoctoral Researchers: Of 66 postdoctoral scientists who left the institute from 2000-2004[47], 56% remained in the UK as postdoctoral researchers, 13% went overseas for postdoctoral research and 31% moved into industry and commerce.

7.4. Policy

7.4.1. Impact of Research on Government Policy

Institute staff have been contributing towards evidence based policy-making and influencing public policies and legislation at a local, regional, national and international level. At Director level, there have been meetings with David Willets Minister for Universities and Science, Research Councils UK, Andrew Lansley MP, local MEPs, BIS and extensive meetings with BBSRC plus meeting the Head EU science over the Horizon 2020 proposal (European Commission proposal for a €80billion (£65billion) research and innovation funding programme for 2014-2020).

The most extensive policy activity has been from the Veterinary Services Manager, as a past President and Senior Vice President of the Laboratory Animals Veterinary Association, a Division of the British Veterinary Association. He has provided Institute feedback to BBSRC and to Science/Industry Coalition informing their responses to Home Office on the transposition of EU Directive 2010/63/EU on the protection of animals used for scientific purposes into UK law in January 2013. The Directive is largely based upon the 1986 UK Act since this legislation was 'fit-for-purpose' and acted as an exemplar showing how the UK is leading the EU in the treatment of animals in research. As a British Veterinary Association Animal Welfare Foundation member he has attended at House of Commons meetings on animal welfare and discussed 'Animal Experimentation: are EU Regulations adequate?' in the Parliamentary and Scientific Committee meetings. The Veterinary Services Manager has contributed to forming British Veterinary Association policy on ethical matters as diverse as laboratory animal usage to dog breeding as part of the British Veterinary Association Ethics and Welfare Group.

Other parliamentary work has included a submission to the House of Lords Committee report on the 'Future of Genomic Medicine", a House of Commons 'Defeating Dementia' report and contribution to the House of Commons Commercialisation of Science meeting. Contributions were made to the BIS 'Science for All' working party[48] to develop a new set of BIS objectives and programme of activity which complement and add value to the broader science and society endeavour in the UK.

7.4.2. Research that Challenges Conventional Wisdom

Perhaps the most high profile example of research at Babraham that challenges conventional wisdom is epigenetics since this is a relatively new concept in the public domain. Similarly, the development of monoclonal antibodies would have challenged conventional wisdom in the 1980s, as would cell signalling in the 1980s and 1990s.

7.5 Quality of life, knowledge exchange and public engagement

Quality of life impacts include improvement in the delivery of public services that give rise to economic impact through cost savings. The Institute promotes "discovery biology - for lifelong health" and their focus on ageing research that ultimately will support a healthy lifespan, will in turn keep people in work and avoid healthcare costs.

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[47] BI corporate plan 2001-5

[48] http://scienceandsociety.bis.gov.uk

7.5.1. Knowledge Exchange

Institute researchers contribute to knowledge exchange through peer review of papers and grants for UK and overseas agencies, being members of expert panels and other professional responsibilities in the academic community:

Expert participation in international panels includes Evaluation of Immunology Frontier Research Center (IFReC) of Japan as part of Japan's World Premier International Research Center Initiative; tenure decision panel for Department of Cell Biology, UC Berkeley, Scientific Advisory Board, Centre for Genomic Regulation, Barcelona; Keystone Symposia Scientific Advisory Board; Scientific Advisory Board, Institut Curie Developmental Biology and Genetics Unit, Paris, the Portuguese Foundation for Science and Technology Panel Member for the sub-area Immunology and Inflammation in the Immunology and Infection panel, ERC, Genetics, Genomics and Systems Biology Committee, grant reviews for Israel Science Foundation, AFM (France), DFG (Germany), FCT (Portugal), DTG (German 'research Council') e:Bio grant panel member; Scientific Advisory Board EraSysBio (European systems biology initiative which is subscribed to by the BBSRC), external panel member for University of Otago animal facilities review and Royal Society sponsored knowledge exchange event in Bangalore, India.

Expertise provided for UK panels including Wellbeing of Women Research Advisory Board, Leukaemia and Lymphoma Research (LLR) grant review panel. LLR site visit chair. BBSRC, Tools and Resources Development Fund Panel, BBSRC Systems Biology Panel, BBSRC Ageing Working Group. External panel member for professorial appointments Imperial College London, member of Biochemical Society Signalling Theme Panel, Assessment of Quinquennial Review papers for PIs at CRUK LRI; grants for BBSRC, CRUK, MRC, AICR, Wellcome Trust Translation Awards, and Investigator awards, Laboratory Animals Ltd Council of Management, Deputy Chair of Cambridge MRC Centre/LMB Ethical Review Committee,

Scientists at the Institute are on the Editorial Board for Journal of Molecular Biology, Cell, Cell Reports, Journal of Biological Chemistry, Biochemical Journal, Journal of Clinical Investigation, Current Biology, Placenta, Scientific Reports Stem Cells and Development, Reproductive BioMedicine Online, PLoS Genetics, Human Molecular Genetics, Open Biology, Nongenetic Inheritance, Epigenetics and Chromatin, International Journal of Developmental Biology, Frontiers in Immunology volume on PI3K in lymphocytes (open access), Frontiers in Pro-Inflammatory Cytokines (open access), Epigenetics and Chromatin, Nucleus, Genes Chromosomes and Cancer, Genome Biology, BMC Neuroscience, Experimental Neurology, Biochimica et Biophysica Acta Lipids and Lipid Metabolism and Laboratory Animals.

Scientists at the Institute referee articles for a range of scientific journals including Bioinformatics, Nature Methods, Nature Communications, Nature Reviews Genetics, PLoS One, PLoS Biology, PLoS Genetics, Journal of Neuroscience, Biochemical Journal, Cell Death & Differentiation, Journal of Cell Science, EMBO and Science Signalling.

Open access publishing is fully supported by the scientists at the Institute allowing more people and organisations in the UK to have access to more of the published findings of research than ever before. More research will be accessible immediately upon publication, and free at the point of use. In June 2012 the RCUK Working Group on Expanding Access to Published Research Findings (the 'Finch Group', chaired by Dame Janet Finch) published their report 'Accessibility, sustainability, excellence: how to expand access to research publications', which sets out a road map to improve open access to scholarly literature[49]. The aim is to bring substantial benefits in

[49] www.researchinfonet.org/publish/finch/

transparency and accountability, engagement with research and its findings, closer linkages between research and innovation, and improved efficiency in the research process itself.

The Bioinformatics group support the online SeqAnswers[50] community forum providing help and assistance to anyone asking questions about bioinformatics. In 2012 two new software products were launched, HiCUP and Trim Galore!; and updated versions of several existing products including ASAP, Bismark, FastQC, FastQ Screen, SeqMonk, Sierra and Sherman were released by the Bioinformatics group:

Case Study: Babraham Bioinformatics group

Software packages derived from code developed by the Bioinformatics group for in-house use are made available, with free-informal support, to any interested parties, thus facilitating knowledge exchange to a wide community. Formal support for these packages is available via a consultancy service. The latest range of packages covers many applications:

- ***ASAP*** *is a program to align a sequencing file to two genomes at the same time.*
- ***Bareback*** *processing allows 'movement' of raw images acquired by the Illumina Genome Analyser.*
- ***Bismark*** *is a program to align bisulfite treated sequencing reads (BS-Seq) to a reference genome.*
- ***Difference tracker*** *is a set of two ImageJ plugins which can be used to track a large number of faint moving particles in a noisy environment.*
- ***FastQC*** *is a quality control application for high throughput sequence data.*
- ***FocalPoint*** *is an image browser which provides enhanced functionality for images with multiple frames or channels.*
- ***FastQ Screen*** *is an application which allows you to search a FastQ sequence file against a set of sequence databases and summarises the results. It is useful for incorporating into a sequencing pipeline to identify sources of contamination or mislabeled samples.*
- ***FocalPoint*** *is an image browser which provides enhanced functionality for images with multiple frames or channels.*
- ***FRETSaw*** *is a specialised image browser that creates a colourised image showing the differences between the source images.*
- ***HiCUP*** *is a bioinformatics pipeline for processing Hi-C data.*
- ***SeqMonk*** *is a program to enable the visualisation and analysis of mapped sequence data. It was written for use with mapped next generation sequence data.*
- ***Sierra*** *is a web based LIMS system designed for use by small sequencing facilities.*
- ***Sherman*** *is a script to simulate high-throughput sequencing data.*
- ***Trim Galore*** *is a wrapper for the stand-alone tools Cutadapt and FastQC, which is designed to enable consistent quality control and quality/adapter trimming for Next-Gen sequencing applications.*

[50] www.seqanswers.com a discussion forum and information source for next generation sequencing.

7.5.2. Public engagement[51]

Public engagement describes the myriad of ways in which the activity and benefits of higher education and research can be shared with the public according to the National Co-ordinating Centre for Public Engagement. Engagement is by definition a two-way process, involving interaction and listening, with the goal of generating mutual benefit. At the Institute about 90 scientists, staff and students annually undertake public engagement work, supporting the External Relations team.

An ageing population presents interesting scientific, social and economic issues for debate. As life science research becomes more prominent in the UK, there is an increasing need for effective communication by scientists and their engagement with society. Babraham Institute events are designed to provide both a greater understanding of the biological mechanisms underpinning the determinants and the maintenance of lifelong health, together with opportunities to discuss the applications and ethical implications these advances hold for society. They also provide a forum to engage with the public and listen to their concerns about breakthroughs in bioscience research. As such they are successfully continuing to deliver public engagement at an impressive level.

The Institute now delivers 15-20 events annually to over 40 secondary schools/6th forms across the East of England, London and nationally. About 40 academics are STEM Ambassadors (a scheme coordinated nationally by STEMNET and locally by STEMTEAM-Cambridgeshire to inspire children and young people in STEM subjects) or 'Researchers in Residence' (ended 2012), acting as role models to inspire an interest in science.

The public engagement programme provides access to real science in a research environment and positive role models to raise interest in science-based careers. Speakers from both BBT and Babraham's Bioincubator companies demonstrate the process through which science is commercialised and delivered to society. The general public is engaged at Science Festivals and at local dialogue events introduced in 2012. These events support the BBSRC Science in Society programme that aims to enable informed debate with public groups about challenges in the 'Basic Bioscience Underpinning Health' strategic priority and, in turn, ensure broad input into strategic decision-making[52].

Within Babraham's research laboratories a culture of public engagement with support, reward and recognition is firmly embedded as scientists and PhD students develop communication skills and confidence as they engage with the public both at a local and national level. All group leaders do at least two days per year. PhD students earn credits towards their 'transferable skills' portfolio and are encouraged to participate in the HEFCE-funded 'Rising Stars' course at the University of Cambridge to develop the communication skills required to become ambassadors for their subjects[53].

The Institute's Public Engagement work from 2005-2010 aimed to increase the number and range of activities to enthuse young people about bioscience, to inspire them to consider science careers and nurture scientific talent. This has been achieved with support from the Institute, competitive grants from BBSRC (Science in Society Awards, PE Awards), RCUK National Science Week Awards.

Public engagement with school students is longstanding and includes the:

[51] Babraham Institute KE Impacts Submission Sept 2012.xls
[52] www.bbsrc.ac.uk/society/pe-strategy-and-funding.aspx
[53] www.publicengagement.ac.uk/how/case-studies/rising-stars

- **Schools Day Project,** during National Science Week, has been the Institute's flagship public engagement event for 16 years and recently CREST-accredited[54]. Around 140 GCSE/6th form students spend the day alongside 'real scientists' immersed in research using techniques like microscopy, PCR, cloning and DNA digestion and discussing the societal impact of research. Evaluation conducted at Schools' Day 2006 indicated that students valued further lab experience and opportunities to interact with researchers to assist career decisions. In 2009 this included 15 students from Finland. *"The impact of one day like this is something that hours spent in the classroom cannot replicate!" Janet Holden, Head of Biology, CATS.*

- **Bioscience Boot Camp**, (since 2007) is a one-week programme of scientific seminars, lab work, a science-ethics workshop and careers guidance concluding with a Bioenterprise Masterclass illustrating the processes through which science becomes a commercial reality growing from a pilot with fifteen 6th formers to an annual 25 students. *"Boot Camp confirmed my decision to do a scientific degree and gave me the opportunity to see what real scientists do." 6th-form student.*
- **6th Form Conferences** (2007 & 2010) on ethics and stem cells to broaden awareness of socio-ethical issues in contemporary science, contribute to teachers' CPD and, by engaging with researchers, inspire the next generation to consider science careers. Similar events were organised for 45 students from the London International Youth Science Forum in 2010.
- **Animals in Research** annual ½ day workshop explores the scientific and ethical issues of using animals. Since 2007 around 350 key-stage 4 students have taken part. A highlight is to emphasise the excellent vocational training that animal technology careers offer, breaking down preconceptions about the role and contributing to the skills training agenda. *"Allowed me to explore ethical issues surrounding topics. Brilliant." Local school student.*
- **Primary School and Pre-school 'Real Life, Real Science'** and 'Science Saturday.' Scientists', from PhD students to the Director, deliver activities to around 3,500 individuals/year, two-thirds of whom experience more than one activity; equating to over 200 visits to 60 different primary schools and nurseries since 2005.
- **Hard-to-reach Students** in schools that were identified as disengaged from science, had no prior STEM enrichment or had high social/economic deprivation; unemployment and diverse ethnicity were visited for a half-day of talks and experiments. Since 2010, a total of 12 such schools were included and 89 Year 6 pupils from six Hackney primary schools visited the campus.
- **After-School Science Clubs** were piloted in 2009/10 as part of the strategy to maintain interest in science at the primary/secondary transition.
- **Researcher in Residence** at Netherhall Comprehensive school in 2011. 'Researchers in Residence' has been a nationwide scheme, funded by Research Councils UK and supported by the Wellcome Trust, which aims to bring schools into closer contact with scientific researchers and, through young positive role models passionate about their science, help to make science more stimulating.
- BI Principal Investigators and other staff serve as school governors.

[54] www.britishscienceassociation.org/crest-awards

Public engagement at the national level includes:

- Royal Society Summer Science Exhibitions 2010 & 2012 including, 'Calcium signalling' (2010) and 'DNA is not your only destiny: Epigenetics behind the scenes' (2012) attracted around 46,000 visitors online (2012) with about 7000 visitors to the Institute's contribution during the 7 days, with several hundred children doing hands-on activities/quiz at the weekends. *"Amazing staff. Fantastic , the best stand at the event." Isabella's mother*
- Cambridge Science Festival, since 2006, now attracts over 35,000 visitors from across the UK - around 2000 visitors to The Biology Zone (one day). Through partnerships with MRC, Wellcome Trust Sanger Institute, CRUK, University Departments and local BRC companies, the Babraham Institute has developed an exciting 'science trail' through the Biology Zone, with a quiz and feedback forms.
- 'Bioscience of Ageing' 6th-form conference was delivered during the Institute's 60th Anniversary.
- 'Science in the Grafton Shopping Centre' in 2010 with colleagues from BBSRC Rothamsted Research, on evolution, genetics and diversity.
- Night at the Natural History Museum 2012

Other engagements in 2012 ranged from interactions with lay members of ethical review committees to explain science and debate cost:benefit aspects of animal research.

Since 2010, fewer external funds have been available and so core Institute funding has sustained school activities where impact has been demonstrated in line with RCUK's Concordat for Engaging the Public with Research. From 2011-2015 the remit will continue to enrich schools and include an expanded dialogue with adults. Activities include:

- Public discussion event 'A Question of Ageing' – which was attended by over 100 people – included listening and responding to people's views.
- Annual Science Festivals/Royal Society Summer Science Exhibition/Society for Biology Big Bang.
- An annual Schools' Day and annual Bioscience Bootcamp.
- Deliver to additional schools with little STEM curriculum enrichment and engage particularly 'hard-to-reach' pupils following successful pilots with inner city primary schools.
- Sustaining delivery of after-school science clubs and to evaluate effectiveness by monitoring cohorts from primary to primary-secondary transition and into secondary education.
- An annual 6th form conferences involving the wider campus and companies for up to 150 students on themes within the Institute Strategic Programmes e.g. 'Nutrition and healthy ageing process', 'Stem Cells and Epigenetics in Regenerative Medicine', and 'Bioinnovation: from molecules to medicines' (using topics like vaccines or MAbs to show how science is commercialised into therapies to improve lifelong health and wellbeing).
- To contribute to Teachers' Continuing Professional Development (CPD).

7.6. National facilities

Biological Support Unit

In 2009, Lord Drayson, then Minister for Science and Innovation, opened a £12 million state-of-the-art BSU Barrier Unit, custom-built to support future scientific developments in rodent genetics-based research. It is considered to be a unique national facility since it was established to support collaborative research using transgenic animals. The BSU provides exceptional facilities for research that will: improve understanding of human development and conditions such as obesity and disease; investigate responses to infections and study the processes governing healthy ageing. The high health status and experimental facilities in the BSU are ideally suited to aid research into healthy ageing using mouse models - it is vital that animals are completely disease free for up to two years for this purpose and the BSU sets a new gold standard for the biomedical research community. It is currently delivering the first colonies of healthy ageing mice.

Universities often have an 'ad hoc' arrangement of dispersed animal units based upon historical needs by Departments. The BSU facility has been designed to provide a consistent and quantifiable environment, with the highest consideration for animal welfare, which will provide reliable data with reduced variability or experimental artefacts, both within experimental groups and over time. This ultimately means that fewer animals will be needed in research to show a statistical effect supporting the 3Rs - Replacement, Refinement and Reduction – ethical framework in the UK[55].

[55] www.nc3rs.org.uk

CHAPTER 8. OPERATING IMPACT

As discussed in an earlier section, although the strategic rationale for funding research at Babraham, as with other early stage research, is based on the long-term economic value of the research outputs and the broader contribution to the scientific research base, the operational activities of Babraham nevertheless generate a current operating economic impact. This section develops an estimate of the economic impact of these operating activities. This includes the activities of the Babraham Institute itself and BBT.

The economic impact of the private companies located on the Babraham Research Campus is **not** included in this calculation. Nevertheless, a part of the wider impact of the Babraham Institute is in providing a favourable environment for life-science research-based SMEs located on site. This is addressed in a separate section.

Economic impact in this study is calculated at UK national level. Investment in the research base at Babraham serves a national imperative. There is no significant local economic development rationale or agenda to consider. The Cambridge area is the pre-eminent UK biotech/life-sciences research cluster and adult unemployment in the South Cambridgeshire District in which Babraham resides, and in the adjacent districts of Cambridge, Huntingdonshire and Uttlesford, are well below the national average, at 5.4%, 5.7% and 4.7% and 4.4%[56] respectively. However, an estimate is made for economic impact at the local level.

8.1 Methodology

Economic impact is quantified in two ways:

- Gross Value Added (GVA), which measures the monetary contribution of the organisation and individual to the economy; and
- Employment, measured in terms of full time equivalent (FTE) jobs supported.

The economic impact of operating the Babraham Institute (including BBT) derives from the activities of running the Institute, principally employment of staff and expenditure incurred (such as laboratory consumables, equipment, utilities etc) and also the knock-on effects of the spending of the supplier base and the staff within the UK economy.

There are three types of quantifiable economic impact considered in this assessment:

- Direct impact: economic activity directly supported by the organisation or individual, including economic output (i.e. the turnover of Babraham) and employment (i.e. staff employed by Babraham);
- Indirect (or supplier) impact: the output generated and employment created in the businesses within Babraham's supplier base through the purchase of supplies and services and all the consequent purchases of supplies and services down the supply chain that have occurred because of the original purchase; and
- Induced (or income multiplier) impact: the output generated and employment created when workers employed directly or indirectly spend their incomes in the economy.

This is illustrated in Figure 25 below.

[56] Office of National Statistics, Regional Labour Market Statistics, June 2012, from NOMIS database

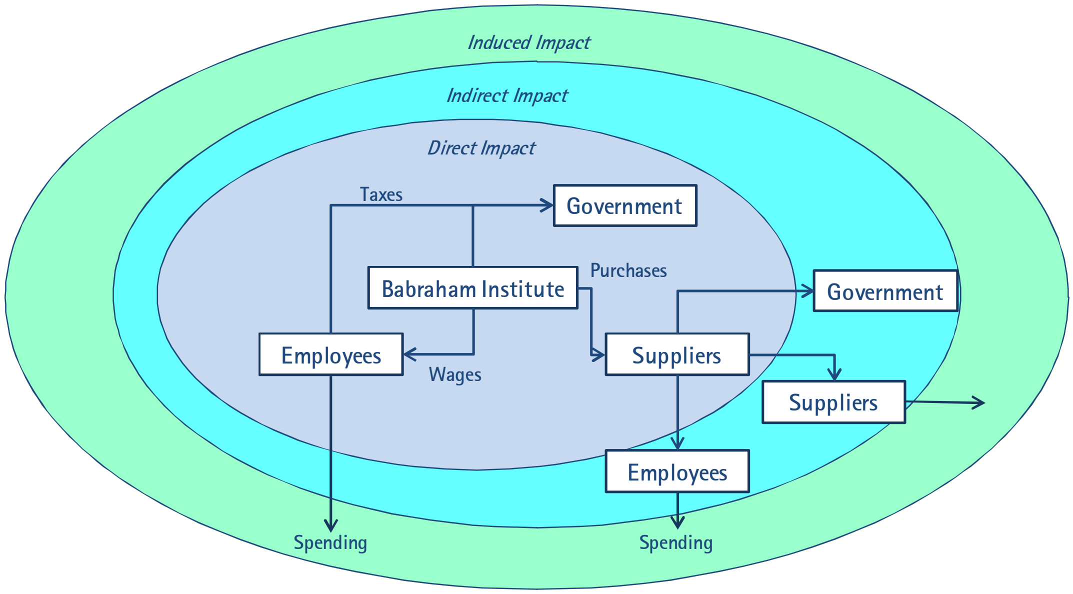


Figure 25 Schematic map of the Babraham Institute's economic footprint

The total of these effects is the gross economic impact. Consideration needs to be given to whether the net economic impact should be adjusted for the following factors:

- Leakage: Leakage allows for any element of the economic activity which occurs outside the study area. In this case, a calculation is performed at the whole UK level, so leakage is incorporated into the industry multipliers used to estimate the indirect and induced effects; and
- Displacement: Displacement allows for whether the activity of the Institute results in the reduction of activity elsewhere. The unique nature of the research base of the Babraham Institute means that displacement is not an issue for the majority of its activity; one possible exception is with respect to the leasing of laboratory space in the BRC bioincubator. There are a number of alternative sites for life-science research companies in the Cambridge area, such as Granta Park and Chesterford Research Park. However, the Babraham Research Campus is relatively unique in the facilities it makes available to its tenant companies, and these are a major attraction for the site (see discussion on wider impacts). For this reason displacement can be ignored.

These estimates have been developed in accordance with relevant HM Treasury Green & Magenta Book and Office of National Statistics[57] guidance. Data on the direct impact and expenditure profile was provided by the Institute, and relevant multipliers have been obtained from the Office of National Statistics or derived from UK National Accounts Input-Output tables.

8.2 Income analysis

The total consolidated income for the Babraham Group (the Babraham Institute and its subsidiary entities) for the financial year April 2011 to March 2012 (FY2011/12) was £50.4 million, after elimination of intra-group cross-charging (see Figure in Appendices). This comprises BBSRC and other grants funding the Institute's operations and core research activities, and commercial revenues generated by BBT.

[57] Office of National Statistics: Measuring the economic impact of an intervention or investment, December 2010

Income for FY2011/12 is enlarged by substantial capital grant income to the Institute for the construction of a new laboratory building (Building 570) and to BBT for the construction of new bioincubator facilities (notably Moneta). Income for the Babraham Institute itself was £33.1 million whilst that of BBT was £20.7 million.

The composition of the Institute's income is shown in Figure 26 whilst that of BBT is shown in Figure 27.

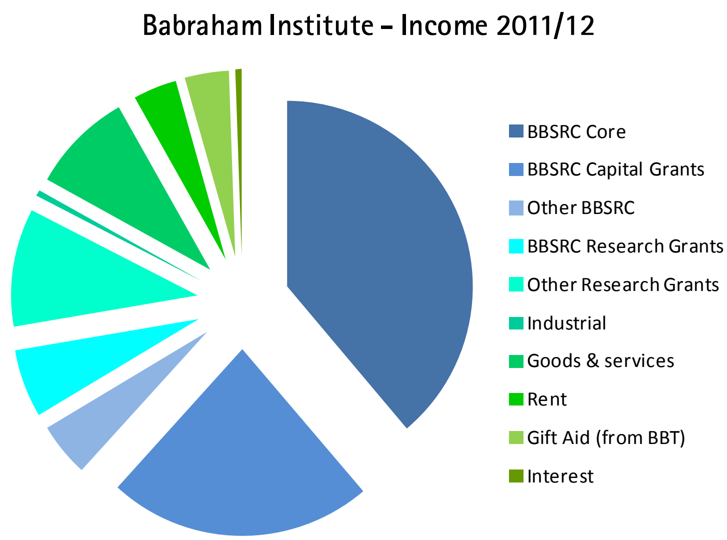


Figure 26 Composition of Babraham Institute Income FY2011/12

The BBSRC Core Grant represents the largest single element of Babraham Institute income, in total £12.8 million, while BBSRC capital grant income contributed a further £7.6 million. Project grant funding from the BBSRC and other public sector/charitable funding sources represented a further £2.0 million and £3.4 million respectively.

Because of the building programme, capital grants (£13.3 million) account for almost two thirds of BBT's income in 2011/12. Incubator tenant income accounted for almost half (£3.4 million) of BBT's £7.4 million operational income, whilst licensing income grew strongly to £2.1 million, driven principally by royalties on sales of a monoclonal antibody therapeutic. Commercial income from scientific supplies and services and collaborative research and consultancy represent the majority of the remainder.

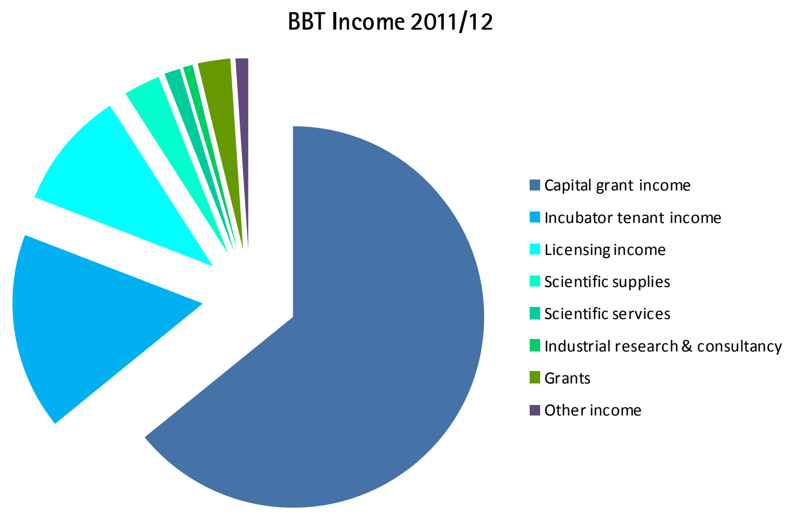


Figure 27 Composition of BBT Income FY2011/12

8.3 Expenditure analysis

The total consolidated expenditure (excluding staff costs) for the Babraham Group in FY2011/12 was £31.3 million. The composition of that spend is shown in Figure 28 below.

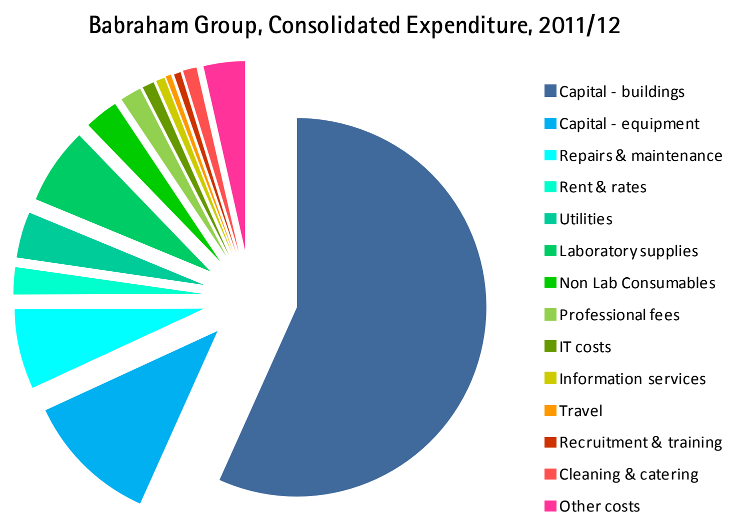


Figure 28 Composition of Babraham Institute consolidated expenditure FY2011/12

As is the case with income, the Babraham Group's expenditure is expanded by the capital costs of the Building 570 & Building 910 construction projects, representing £17.7 million (56.7%) of the total. A further £3.5 million (11.4%) represented capital investment in scientific equipment. A review of the asset purchase list reveals that most of this will have been imported, through UK national distribution operations, from abroad; this is generally the case with life science research equipment. The remaining £10 million represents the operating expenditure of the Institute and is typical for life sciences research organisations (e.g. laboratory supplies, IT and information services, utilities and property-related costs).

8.4 Direct Impact

The direct GVA of the Babraham Group is estimated by subtracting the value of supplies and services from its income. The Institute's income for 2011/12 was £50.4 million and expenditure on supplies, after adjusting for non-cash items, was £31.3 million, giving direct GVA of £19.2 million. Full time equivalent employment for 2011/12 was 335. This is summarised in Table 7 below.

	Source	Amount, £ million
Institute income	BI Accounting	50.44
Expenditure on supplies & services	BI Accounting	31.25
GVA	Calculated	19.19
Employees (FTE)	BI Accounting	335

Table 7 Direct impact of Babraham's operational activity

8.5 Indirect impact

As described above, the indirect impact of the Institute's activity relates to the downstream effect of its supply chain expenditure. However, calculation of indirect impact is complicated by the Institute's construction programme, requiring an adjustment to the multipliers applied. At the national level, indirect effects of the research operational element of the Institute's activities have been calculated using output, GVA and employment multipliers derived from ONS data for Research & Development activities. For the construction element, an output multiplier has been applied to derive the indirect output, and GVA and employment effects calculated using sector-wide turnover/GVA and GVA/sales ratios from ONS data. The resulting indirect impacts are shown in Table 8 below.

	Output, £ million	GVA, £ million	Employment
Direct (Babraham)	50.44	19.19	335
Indirect (supply chain)	32.98	14.39	230

Table 8 Indirect impact of Babraham's operational activity

8.6. Induced impact

Induced impacts arise from the expenditure of Babraham staff plus jobs supported indirectly in the supply chain. Induced impacts have been calculated in a similar manner to indirect impacts, using relevant multipliers. The resulting induced impacts are shown in Table 9.

	Output, £ million	GVA, £ million	Employment
Direct (Babraham)	50.44	19.19	335
Induced (wage spend)	21.40	7.88	95

Table 9 Induced impact of Babraham's operational activity

8.7 Overall operational impact

A summary of the overall operational impact of the Institute at national level is shown in Table 10 below. In addition to the direct economic impact producing £19.2 million in GVA and employment of 335 FTEs, indirect and induced effects add a further £22.3 million GVA and support an additional 325 jobs. Total GVA is therefore estimated at £41.5 million that supports a total of 660 jobs. GVA-per-worker in 2011/12 was £57,300, a ~20% increase on the reported GVA-per-worker in 2008/09 in cash terms. A major contributor to the increase is the rise in royalty income received by the Institute. This compares with a national average GVA-per-worker for R&D on natural sciences and engineering of £41.9k in the latest reported year (2008) in the ONS Annual Business Survey, and an average GVA-per-job for the East of England of £42.3k (2009)[58].

	Output, £ million	GVA, £ million	Employment
Direct (Babraham)	50.44	19.19	335
Indirect (supply chain)	32.98	14.39	230
Induced (wage spend)	21.40	7.88	95
Total	104.82	41.46	660

Table 10 Total operational economic impact

8.8 Estimated local impact

Local economic impact is determined by retention of economic activity (i.e. net of leakage) within the local area. For the purposes of an estimate of local economic impact of Babraham, the local area is taken to be the travel-to-work area. A full analysis of local economic impact is beyond the scope of this report but assumptions with respect to the proportion of expenditure retained in the local area can be made to generate an estimate, summarised below in Table 11.

	Basis	% in local area
Direct (Institute income)	Definition	100%
Indirect (supply chain)	Estimates, adjusted for high equipment spend	34%
Induced (wages spend)	Comparator studies	70%

Table 11 Assumptions made for operational economic analysis

Applying these factors to the national level economic impact statistics produces the following estimate of local level economic impact (see Table 12).

	Output, £ million	GVA, £ million	Employment
Direct (Babraham)	50.44	19.19	335
Indirect (supply chain)	10.88	4.75	76
Induced (wage spend)	14.98	5.52	66
Total	**76.30**	**29.45**	**477**

Table 12 Total local level operational economic impact

[58] ONS Sub-regional productivity, March 2012 and other ONS data. Note, this is different from the regularly reported GVA-per-head (of population) in ONS regional labour productivity statistics

CONCLUSIONS

The report's main conclusions are:

- The Babraham Institute produces a very high standard of fundamental research with high and increasing Impact. Its epigenetics research has been categorised in the top 10 worldwide.
- Fundamental research over the last two decades has made major scientific contributions leading to commercial development of therapeutics in several important areas. In particular, development of humanised and human monoclonal antibodies and PI3 Kinase inhibitors as development-stage targeted therapeutics have the potential for huge economic impact (described in detail in case studies).
- Inventions have been commercialised through licensing to private companies and through the formation of two new start-up companies.
- Publicly funded research at Babraham is contributing to the productivity of R&D in the private sector through commercial agreements with global biopharmaceutical companies, medium-sized biologics companies and start-ups. It provides national and in some cases, unique scientific facilities (e.g. BSU, Next Generation Sequencing and Mass Spectrometry for lipidomics analysis) that are used by both research and commercial clients.
- Babraham sits at the heart of the Cambridge biomedical cluster encouraging innovation by smaller local high-tech businesses.
- The Babraham Institute produces highly trained scientists, an essential resource for UK companies and foreign companies investing in the UK. It also trains highly skilled technical staff, nursery staff and provides apprenticeships.
- The UK economy is being supported by public investment in scientific research at Babraham and the Babraham Research Campus is a main part of the UK life sciences 'innovation system' making the UK attractive for inward investment by international business and industry.
- The level of public engagement is high and has broadened from student and school engagement to public dialogue.
- The systems in place for knowledge exchange and commercialisation are taking fundamental discoveries to the market by the most appropriate and sustainable route.

High quality research at the Babraham Institute and the development of the Babraham Research Campus is successfully delivering these aims and can be considered as an exemplar for the UK. The Proven demand for bioincubator facilities has led to the development of 80,000 sq ft of purpose-built lab and office space.

Many of Babraham's research programme outputs are at too early a stage to identify quantifiable economic impact. Babraham has recently initiated a number of projects addressing changes in cellular function and epigenetic programming related to ageing. As described above, past precedents indicate that the economic impact to be derived from these programmes would be expected to arise in c. 20 years from now.

At an operational level, the economic impact of the Babraham Group in 2011/12 contributed GVA of £41.5 million, supporting 660 jobs nationally. The local economic impact is estimated at GVA of £29.5 million, supporting 477 jobs, directly and indirectly, in the local economy.

APPENDICES

Appendix 1. Annual incidence and mortality of most common cancers, UK 2010

	Incidence			Mortality			Mortality %		
Cancer Site	Male	Female	Persons	Male	Female	Persons	Male	Female	Persons
Breast	397	49564	49961	77	11556	11633	19.4%	23.3%	23.3%
Lung	23175	18851	42026	19410	15449	34859	83.8%	82.0%	82.9%
Prostate	40975		40975	10721		10721	26.2%		26.2%
Bowel	22834	17861	40695	8705	7308	16013	38.1%	40.9%	39.3%
Malignant Melanoma	6201	6617	12818	1266	937	2203	20.4%	14.2%	17.2%
Non-Hodgkin Lymphoma	6538	5642	12180	2402	2050	4452	36.7%	36.3%	36.6%
Bladder	7416	2908	10324	3294	1613	4907	44.4%	55.5%	47.5%
Kidney	5906	3733	9639	2451	1611	4062	41.5%	43.2%	42.1%
Oesophagus	5637	2840	8477	5105	2505	7610	90.6%	88.2%	89.8%
Pancreas	4189	4274	8463	3872	4029	7901	92.4%	94.3%	93.4%
Uterus		8288	8288		1937	1937		23.4%	23.4%
Leukaemia	4816	3441	8257	2526	1978	4504	52.5%	57.5%	54.5%
Stomach	4641	2625	7266	3102	1858	4960	66.8%	70.8%	68.3%
Ovary		7011	7011		4295	4295		61.3%	61.3%
Oral	4307	2232	6539	1323	662	1985	30.7%	29.7%	30.4%
Brain and CNS, Invasive	2831	2086	4917	2253	1636	3889	79.6%	78.4%	79.1%
Myeloma	2570	2102	4672	1355	1278	2633	52.7%	60.8%	56.4%
Liver	2672	1569	4241	2249	1540	3789	84.2%	98.2%	89.3%
Cervix	0	2851	2851					0.0%	0.0%
Thyroid	748	1906	2654				0.0%	0.0%	0.0%
Other Sites*	18799	16180	34979	12370	12552	24922	65.8%	77.6%	71.2%
All Cancers Excluding Non-Melanoma Skin Cancer	164652	162581	327233	82481	74794	157275	50.1%	46.0%	48.1%

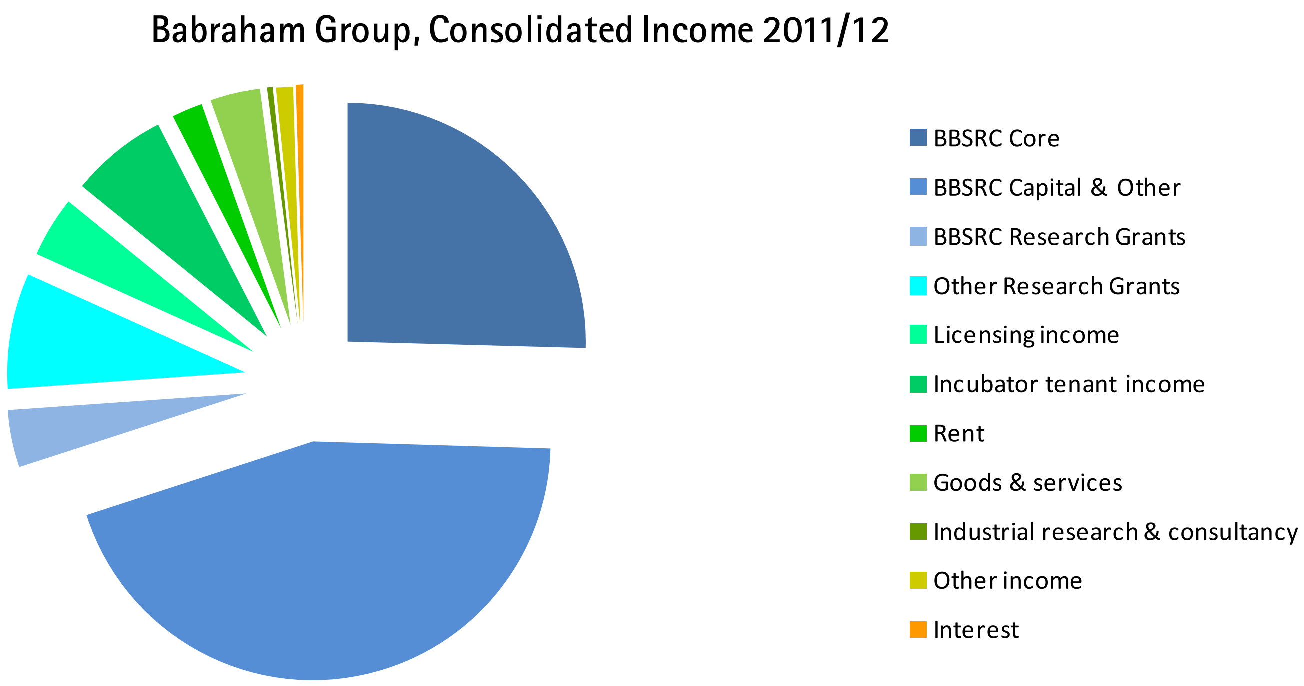
*3% of all male and female cancer cases are registered without specification of the primary site

alacrita

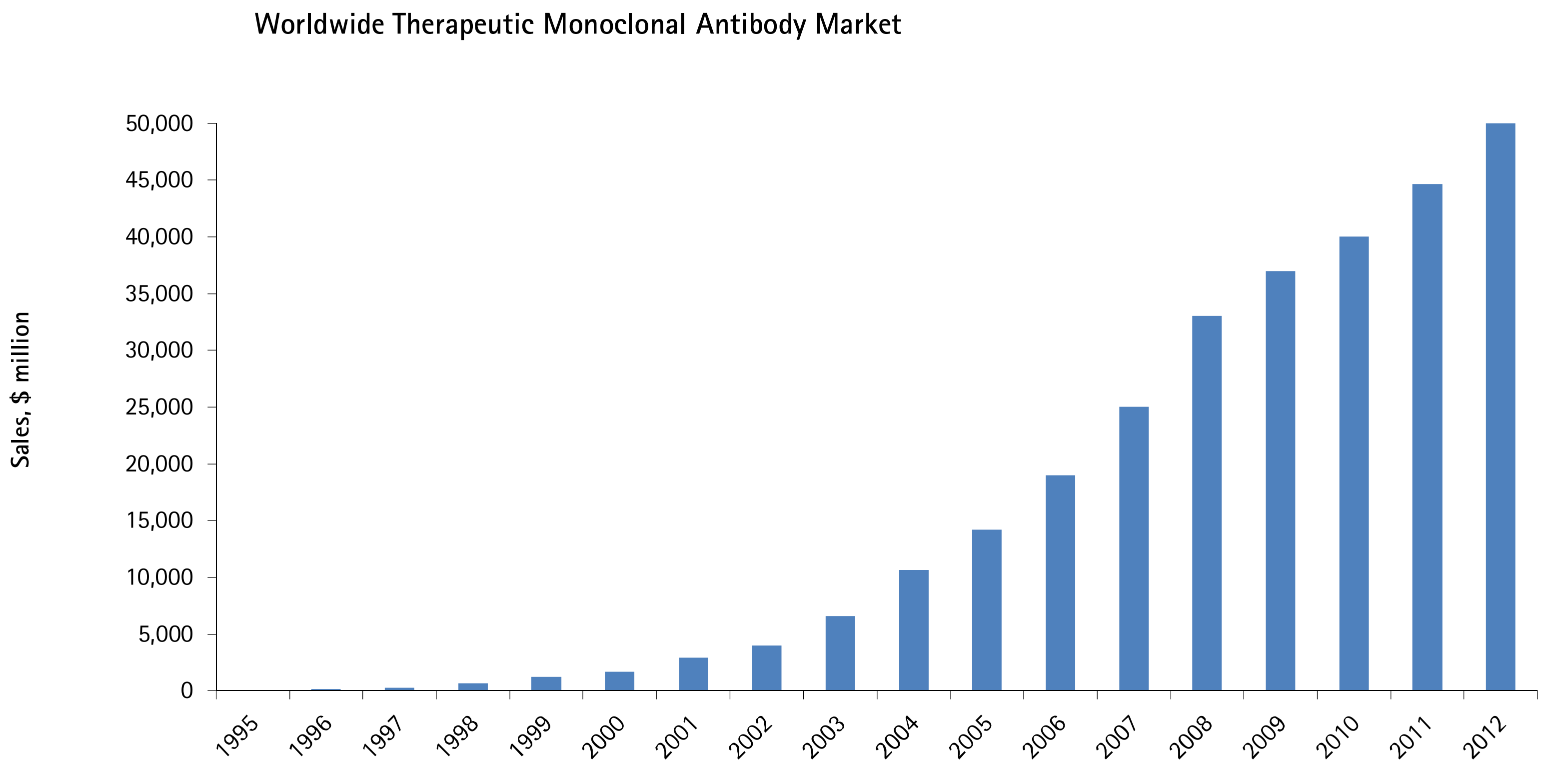
Appendix 2. PI3 Kinase (and related mTOR Kinase) inhibitors in clinical development

Agent	Company	Selectivity	Status	Comments
AMG319	Amgen	PI3K delta isoform	Phase I	Lymphoid malignancies
AZD8055	AstraZeneca	Dual mTOR	Phase I/II	Solid tumours, lymphoma
BAY806946	Bayer	Class I PI3K	Phase I	
BEZ235	Novartis	Dual PI3K/mTOR	Phase I/II	Solid tumours, advanced breast cancer
BGT226	Novartis	Dual PI3K/mTOR	Abandoned	Terminated in Phase II
BKM120 (buparlisib)	Novartis	Pan PI3K	Phase III	In Phase III single agent & combination trials in breast, prostate, HNC, GBM, RCC, colorectal & endometrial cancers
BYL719	Novartis	Isoform-specific PI3K	Phase I	Solid tumours
CAL-101/GS-1101	Gilead	PI3K delta isoform	Phase III	CLL & indolent NHL
Certican/Afinitor (everolimus)	Novartis	mTOR 1 rapalog	Marketed	
GDC0941/RG7321	Roche/Genentech	Class I PI3K	Phase II	ex-Piramed
GDC0980/RG7422	Roche/Genentech	Dual PI3K/mTOR	Phase II	Solid tumours, NHL
GDC0084/RG7666	Roche/Genentech		Phase I	Glioma
GSK-1059615	GSK		Abandoned	Stopped in Phase I due to poor pharmacological profile
GSK-2126458	GSK	Dual PI3K/mTOR	Phase I	Solid tumours
IC87114	Lilly	PI3K delta isoform	Abandoned	ex-ICOS
INK-1117	Takeda	PI3K alpha isoform	Phase I	Solid tumours. Intellkine acquired by Takeda
INK-128	Takeda	Dual mTOR	Phase I	Solid tumours. Intellkine acquired by Takeda
IPI145	Infinity	PI3K delta & gamma isoforms	Phase II	Licensed from Intellikine. Targeted at inflammation - asthma trial commenced, RA trial to start
LY294002	Lilly		Abandoned	
OSI-027	Astellas	Dual mTOR	Phase I	Solid tumours. Ex-OSI
PF04691502	Pfizer	Dual PI3K/mTOR	Phase II	Endometrial cancer, solid tumours, and in combination with MEK inhibitor PD-0325901
PKI-587/PF05212384	Pfizer	Dual PI3K/mTOR	Phase II	Endometrial cancer
PX866	Oncothyreon	Class I PI3K	Phase II	Single agent & combination trials in HNC, prostate, NSCLC, glioblastoma
Rapamune (sirolimus)	Pfizer	mTOR 1 rapalog	Marketed	
ridaforolimus	Merck	mTOR 1 rapalog	Phase III	Initial NDA rejected by FDA and EMEA; continuing in combination therapy trials
SF1126	Semafore	Pan PI3K	Phase I	Prodrug of LY294002
TG100-115	Sanofi	PI3K delta & gamma isoforms		Ex-TargeGen
Torisel (temsirolimus)	Pfizer	mTOR 1 rapalog	Marketed	
XL147/SAR245408	Exelixis/Sanofi	Class I PI3K	Phase II	Endometrial, breast cancer
XL499	Exelixis/Merck	PI3K delta isoform	Preclinical	Targeted at inflammation
XL765/SAR245409	Exelixis/Sanofi	Class I PI3K/mTOR	Phase II	CLL, NHL, breast cancer

Appendix 3. Babraham Group, Consolidated Income 2011/12



Appendix 4. Worldwide Therapeutic Monoclonal Antibody Market



Appendix 5. Babraham Research Campus Commercial Tenants 2013

Aitua Ltd	Eagle Genomics Ltd	Phico Therapeutics Ltd
AImagen Ltd	Epsilon-3 Bio	Population Genetics Technologies Ltd
Antitope Ltd	F-Star	Proximagen Ltd
Bicycle Therapeutics Ltd	Helminthic Therapy Research Ltd	Rapid Biosensor Systems Ltd
Cambivac Ltd	Immunobiology Ltd	Recombinant Antibody Technology Ltd
Cambridge Protein Array Ltd	Imperial Innovations Ltd	Stem Cell Sciences
Cell Guidance Systems Ltd	Innova Bioscience Ltd	Synome Ltd
Convergence Pharmaceuticals Ltd	Kymab Ltd	TCP Innovations Ltd
Crescendo Biologics Ltd	Life Biomedical Ltd	Total Scientific Ltd
DefiniGEN Ltd	MidVen Ltd	Twist Dx Ltd
DiagNodus Ltd	Mission Therapeutics Ltd	Urosens Ltd
Discerna Ltd	NorayBio	

Note: 4 new companies expected in Q1 2013