Dr Tracey Barrett
Birkbeck College – Senior Lecturer

David Phillips Fellowship – 1997/98

"Structural analysis of the bacterial MutHLS and UvrABC DNA-repair complexes"

Key Research Outcome

Prior to the award of this David Philips Fellowship, little was known about how the bacterial UvrABC pathway functions to correct general DNA damage. A key aim of this Fellowship was to understand this important process in addition to other DNA repair machines at the molecular level. BBSRC support enabled structural studies that culminated in the crystal structure of a trapped complex involving the damage sensor of a general DNA damage mechanism. This structure revealed a molecular "sieve" mechanism where the damage is not explicitly recognised, but excluded from an interface key to translocation of the sensor along DNA when in search of lesions.

Where did this work lead?

This work was pivotal to later studies that addressed the important issue of how repair is exclusively directed to the damaged strand. These studies have informed my current research interests and I now look at genome maturation and host mRNA transcript destruction by the Kaposi's sarcoma-associated herpesvirus (KSHV).

How did the BBSRC Fellowship help you to advance your career?

The David Phillips Fellowship was central to my career advancement. The generous consumables budget meant that I could develop my research over an uninterrupted five year period. The feedback, advice and suggestions from internationally renowned figures in my field were also important. The feedback from the panel at progress meetings held throughout my Fellowship was of great benefit. Having the opportunity to engage with other Fellows to discuss experiences and strategies was also useful. Taken together, these factors were key to my obtaining a lectureship, which would have been significantly more difficult without the Fellowship and BBSRC support.

Professor Dame Ottoline Leyser
University of Cambridge – Director and Professor of Plant Development

Research Development Fellowship – 1999/00

"Molecular markers for axillary meristem development in Arabidopsis"

Key Research Outcome

My research focuses on plant development plasticity, using the control of shoot branching as a model system. The main goal of my BBSRC Research Development Fellowship was to develop gene expression markers for axillary bud activity, and to provide improved temporal resolution in defining bud activity transitions. A key outcome of the Fellowship was that this goal is more technically challenging than anticipated. Nonetheless, I established that live imaging of activating axillary buds on excised nodal segments using confocal microscopy is feasible.

Where did this work lead?

In addition to the work of my Fellowship, I determined that identification of transcripts that truly mark early transitions in bud activity may be impossible because the relationship between bud regulatory checkpoints and transcriptional changes is complex. This was an important finding that informed much of our subsequent work.

How did the BBSRC Fellowship help you to advance your career?

The Research Development Fellowship gave me three years with reduced teaching responsibilities, allowing me to spend more time on my research. The award came at a particularly important time when technologies were rapidly evolving, presenting new opportunities to tackle my research questions in different ways. The Fellowship also allowed me to spend time away at the John Innes Centre and Cal Tech learning techniques and experiencing different research environments. My career goals are to contribute to science, not only through increasing our understanding of plant developmental biology, but also through helping to foster a creative and accessible research system, and to embed science more deeply across society and the public and private sectors. The Fellowship was primarily aimed at supporting my research, but it was also invaluable in providing time to think more widely about science, and to work in different settings.

Professor Giles Oldroyd

John Innes Centre – Group Leader

David Phillips Fellowships – 2001/02

"Genetic dissection of Nod factor signal transduction in Medicago truncatula"

Key Research Outcome

My research focused on how plants perceive symbiotic microorganisms and how this perception leads to the establishment of beneficial associations. When I started my Fellowship we had undertaken a genetic dissection of the symbiosis signalling pathways in legumes, but the genetic identity of the genes discovered had not been demonstrated. The work from my Fellowship highlighted the central importance that calcium played in symbiosis signalling, demonstrating definitively that the calcium signal was not only necessary, but was also sufficient for transduction of symbiotic signals to downstream developmental consequences.

Where did this work lead?

We have since gone on to demonstrate how this calcium-regulated kinase is able to decode the calcium signal. We have also demonstrated how this signal is transduced to gene expression changes.

How did the BBSRC Fellowship help you to advance your career?

I applied for the BBSRC David Phillips Fellowship while a postdoc at Stanford University and it have me a fantastic stepping stone into the UK academic environment. The Fellowship provided me freedom from a number of administrative responsibilities, allowing me to spend more time focussing on my research programme at a critical stage in my scientific career. The discoveries I made as a Fellow provided the building blocks for all of my future research. I used some of these discoveries to justify a large investment into research from the Bill and Melinda Gates Foundation focused on exploring the feasibility of transferring the nitrogen-fixing symbiosis to cereal crops. The years of my Fellowship were exciting, with a number of important discoveries that set me up for many years to come.

Professor Anne Dell

Imperial College London – Head, Department of Life Sciences

Professorial Fellowship – 2001/02

"Structural glycobiology: applications of ultra-high sensitivity mass spectrometry"

Key Research Outcome

My laboratory exploits high sensitivity mass spectrometry to define glycan sequences. I do this in collaboration with hundreds of scientists worldwide, addressing the over-arching question: "What roles do glycans play in cell-cell communication?" Substantial progress towards addressing this question has been achieved through research supported by my Fellowship and associated core grants. Thus, we have made substantial progress in unravelling the glycobiology of mammalian fertilization and reproduction.

Where did this work lead?

Notably, we have provided rigorous structural evidence to support the Human Foeto-embryonic Defence System (Hu-FEDS) model, proposed by Gary Clark in the mid-1990s. Clark hypothesised that glycans act as functional groups that protect sperm, eggs and foetuses from immune attack. We discovered that human sperm-egg binding is mediated by a Selectin ligand and cancer antigen, which provided key evidence in support of this hypothesis.

How did the BBSRC Fellowship help you to advance your career?

My Fellowship enabled me to engage with dozens of scientists around the world in highly productive consortia and collaborations. Moreover, the award of the Fellowship was a catalyst for additional investment in glycobiology at Imperial, leading to three academic staff appointments and the creation of the Glycobiology Training, Research and Infrastructure Centre (glycoTRIC) which I led from 2004 to 2017. GlycoTRIC is a multi-disciplinary network which facilitates glycobiology research at the interface between the life sciences, the physical sciences and medicine. Since its establishment in 2004, we have provided training for over 100 researchers. The Fellowship gave me the freedom to articulate and implement a vision for collaborative research that has enabled our laboratory to advance its international competitiveness, allowing us to play leading roles in major consortia and networks, such as the Consortium for Functional Glycomics.

Professor Christine Watson
University of Cambridge –Deputy Head School of Biological Science

Research Development Fellowship – 2003/04

"Apoptosis and signalling in 3-dimensional cultures"

Key Research Outcome

During my Fellowship, I learnt how to culture embryonic stem cells and to analyse how they become different cells types when stimulated to differentiate. I established a collaboration with the, then new, Stem Cell Institute in Cambridge to make mice using stem cells that have a gene trap in a gene that was of interest to us, Zfp157. The gene trap produced a knockout/reporter of Zfp157 expression in embryonic and adult tissues.

Where did this work lead?

This was an exciting step forward for my laboratory and allowed us to identify a master regulator of alveolar lineage commitment in the mammary gland. This work has led to several exciting publications and research on this gene is still ongoing in my laboratory.

How did the BBSRC Fellowship help you to advance your career?

The award of the three year Fellowship provided me with the opportunity to undertake research in a new area of biology for me; stem cells. This was facilitated by the proximity of the recently established Stem Cell Institute. I benefitted from being able to interact not only with embryonic stem cell researchers by also those interested in adult tissue stem cells. At the conclusion of my Fellowship, I had established very valuable collaborations with members of the Stem Cell Institute and with mammary gland stem cells biologists. My laboratory has since made a considerable contribution to understanding the regulation of mammary stem and progenitor cell regulation. My career continued on an upward trajectory following my Fellowship and resulted in promotion to a personal Professorship in 2010.

Professor Nicola Stanley-Wall
University of Dundee – Professor of Microbiology

David Phillips Fellowships – 2004/05

"Environmental regulators and the genes required for biofilm formation by Bacillus subtilis"

Key Research Outcome

My research aims to understand complex multicellular behaviours exhibited by single celled bacteria, using the Gram-positive soil bacterium *Bacillus subtilis* as a model system. It is known that many microorganisms are capable of different multicellular behaviour patterns, for example the formation of sessile biofilm communities. During my Fellowship we identified one of the key regulatory mechanisms controlling this lifestyle choice, a finding which laid the foundation for significant changes in our understanding of how two-component regulators function.

Where did this work lead?

During the Fellowship period I also established an interest in the molecules produced by the bacteria that form the extracellular matrix which serves to hold the individual cells in the biofilm together. Through work started in my Fellowship, and with collaborators, we subsequently identified a novel class of surface active protein that is needed to structure the *B. subtilis* biofilm. The theme of understanding the role of the extracellular matrix molecules is on-going in my laboratory.

How did the BBSRC Fellowship help you to advance your career?

The BBSRC David Phillips Fellowship gave me an opportunity; a chance to start my independent research programme and to establish myself in the UK academic system. The Fellowship provided me with time to become comfortable and confident with running a research programme. The funding also allowed me to travel, to get my research known and provided me with opportunities to forge valuable collaborations. Being paired with an experienced academic as a mentor allowed me to access independent advice on diverse topics, something I am still thankful for.

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Associate Professor Andrea Graham

Princeton University – Associate Professor

David Phillips Fellowship – 2005/06

"Cytokine network ecology: towards a dynamic understanding of immune responses to co-infection"

Key Research Outcome

Co-infection of a host by multiple parasite species –e.g. gastrointestinal helminths together with micro parasite species such as malaria – is startlingly common in nature. Prior to my research as a BBSRC Fellow, there was no general framework to explain the variation in the magnitude of effects of co-infection. My work revealed that basic ecological rules predict the outcome of co-infection across a broad spectrum of parasites.

Where did this work lead?

My experimental work confirmed that malaria is most explosive when helminths do not impose resource limitation, but do strongly modulate cytokine interferon (IFN- γ) responses. Through this interdisciplinary lens, predicting the outcome of co-infection therefore becomes tractable.

How did the BBSRC Fellowship help you to advance your career?

The independence, freedom and flexibility of my BBSRC David Phillips Fellowship offered me the chance to pursue novel, interdisciplinary and even controversial ideas. For an ecological immunologist like me, fellowship support was absolutely crucial to my ability to attain true interdisciplinary insights. My research programme blossomed during my Fellowship, and to this day (over six years after I moved away from the UK), my career trajectory is still reaping the benefits of that. The Fellowship allowed me to fulfil my potential in ways that elevated my publication impact, enhanced my international visibility, landed me a faculty position back in the US, accelerated my promotion here, and firmly established the research agenda that sustains me to this day.

Professor Sivaramesh Wigneshweraraj

Imperial College London –
Head of Section of
Microbiology

David Phillips Fellowship – 2006/07

"Mechanism of action of small-molecule inhibitors of bacterial gene transcription."

Key Research Outcome

We established that viruses that infect bacteria, called phages, have evolved diverse mechanisms to perturb key bacterial processes. The David Phillips Fellowship provided the flexibility in terms of funding, time and mentorship, to exploit the translatable aspects of the research in the space of antibacterial drug discovery with pharmaceutical companies.

Where did this work lead?

The Fellowship allowed me to establish a research niche quickly and conduct research that not only advanced fundamental biology, but also capitalise on the translatable opportunities of the data.

How did the BBSRC Fellowship help you to advance your career?

The Fellowship provided me with the opportunity and support to build a research team quickly and establish independence in a properly managed way. The mentorship provided was invaluable at times because it helped me to decide what is really important when things don't go as planned, or when things turned out better than planned, to pursue a slightly new line of investigation. The latter led to a BBSRC LoLa grant and allowed me to establish a new research stream in my laboratory. All of this catalysed my scientific success and meant that I was offered a Chair in Microbiology at Imperial College. At the end of my Fellowship I was appointed as the Head of Section of Microbiology. BBSRC also provided me with the opportunity to join the Pool of Experts of Responsive Mode Committees and I gained invaluable experience in taking part in grant assessment meetings. I now serve as a permanent member of Committee E, and thus look forward to contributing to the development of the next generation of Fellows.

Professor Chris Bass
University of Exeter- Professor

Institute Career Path Fellowship – 2008/09

"A genomic approach to understanding insecticide resistance in crop pests"

Key Research Outcome

The overarching goal of my BBSRC Fellowship was to understand the evolution of insect resistance to natural and synthetic chemicals such as insecticides. One of the most significant advances made during my Fellowship concerned races of the aphid *Myzus persicae* that have adapted to feed on tobacco and tolerate the natural insecticide, nicotine. We demonstrated that a gene encoding a specific cytochrome P450 enzyme is duplicated many times, allowing these races to detoxify nicotine and therefore feed on this plant.

Where did this work lead?

We were able to translate this fundamental research into tools and strategies for control of this pest. This was achieved by developing molecular diagnostics to monitor field populations of *M. persicae* for the resistance mechanisms we had discovered. We also developed a series of regional recommendations on control targeted at farmers and growers.

How did the BBSRC Fellowship help you to advance your career?

The Fellowship provided time, money and stability to establish myself in my scientific field. The provision of time, and the stability of five years funding, gave me the freedom to learn new cutting-edge approaches without worrying if these would immediately yield a return in terms of publication. The financial resource allowed me to think big, and it was incredibly liberating to be able to plan and execute large scale experiments that while costly, yielded substantial data sets and led to exciting findings. The data generated helped me win significant additional funding during the life of the fellowship, and then provided the preliminary data for a follow on ERC fellowship. The difference the Fellowship has made to my scientific progression has been profound and I will always be grateful for the opportunities it provided.

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Dr Ive De Smet

VIB-UGent Center for Plant Systems Biology – Junior Group Leader

David Philips Fellowship – 2009/10

"Ligand-receptor-like kinase signalling in Arabidopsis root development"

Key Research Outcome

The Fellowship allowed me to further characterise the receptor kinase ACR4, an important regulator of asymmetric cell divisions and cell identity in the root. This led to the identification of an intricate biochemical network involving ACR4 and the phosphatase PP2A. The phosphatase of PP2A is both a target and a positive regulator of the receptor kinase ACR4, thus creating a feed-forward mechanism in regulating cell fates in the root.

Where did this work lead?

We also characterised several small signalling peptides in the context of lateral and primary root development. This work coincided with an increased boost in peptide research in plants, and our work contributed to some extent to this.

How did the BBSRC Fellowship help you to advance your career?

The BBSRC David Phillips Fellowship provided me with the opportunity to establish my own research group at the University of Nottingham. Within a few years, this gave me the basis to apply for other independent research positions, and I was able to consolidate a junior group leader position at VIB-UGent Center for Plant Systems Biology. Beyond this, the Fellowship, and the Fellows conferences, allowed me to perform basic research, to increase my visibility in the scientific community, to train PhD students, and to expand my research and industrial network. Importantly, my stay at the University of Nottingham exposed me to exciting research on wheat, which I am now implementing in my current research on abiotic stress in Arabidopsis and crops.