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Building on a legacy in antibody research

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With world-class facilities and a vibrant research community, the Babraham Research Campus has recently attracted some of the most exciting new generation antibody companies in Europe. This cluster of commercial excellence complements expertise at the Babraham Institute, an institute of BBSRC, where fundamental research is driving new technologies and innovation.

Therapeutic antibodies have become best selling pharmaceutical drugs, with the global monoclonal antibody market currently valued at around $40 billion. Cambridge-based scientists, institutions and companies have played a major role in this success, from early invention to product development. In the 1980s, Jonathan Howard and Geoff Butcher from the Babraham Institute collaborated closely with Nobel Prize winner César Milstein and colleagues at the Medical Research Council's Laboratory of Molecular Biology (MRC-LMB) to produce, what were described as, 'the first useful monoclonal antibodies'. Later pioneering work by Babraham's Marianne Brüggemann, using transgenic methods to manipulate human antibody genes, has led to exciting approaches for the production of therapeutic antibodies.

Babraham Institute Director Professor Michael Wakelam explains, "Much of the pioneering work on monoclonal antibodies was carried out at the Institute and in the Cambridge area, so it is particularly thrilling to see so much commercial expertise gravitating to Babraham. Today the Campus is a hub of biomedical innovation in the heart of the Cambridge cluster."

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Even in the current economic climate, the campus is expanding. November last year saw the opening of the fourth bioincubator building, Maia, named after the Roman goddess of growth. Constructed with financial support from BBSRC, Maia provides seven early-stage biomedical companies with flexible lab and office space, cell culture and high-class level 2 containment facilities as well as access to the Institute's world-class animal facilities, next generation sequencing, mass spectrometry, cell sorting and imaging services. In total the campus provides around 70,000 sq ft lab space to 28 early-stage biomedical companies.

"There's a real hub of monoclonal antibody expertise that's coming together here," commented Mark Doran, Director of process development and manufacturing at Alpha Biologics, which has just expanded with a move into Maia, "More and more companies have come on site over the past few years because Babraham is getting recognised as the place to be. There's a real sense of community here - and the practical and technical support is exceptional."

Four biologics spin out companies have recently moved to campus: Kymab, a spin out from the Wellcome Trust Sanger Institute, Bicycle Therapeutics from the MRC-LMB, Recombinant Antibody Technologies, and Crescendo Biologics, whose technology is derived from BBSRC-funded research. Andrew Sandham (note 1), Chairman and CEO of Kymab said, "We evaluated many locations in the Cambridge area to found our business. We chose the Babraham Research Campus because of the high quality of research laboratories, its proximity to academic centres of excellence and its flexibility in providing the capacity and services we will need as we expand our R&D operations."

Fostering partnerships

One of the attractions to prospective companies is the opportunity to interact with academics at the Institute, where BBSRC-funded research is directed towards understanding the basic bioscience underpinning health (see 'Immunology research points to new therapies' below). The Institute is committed to knowledge exchange and facilitating academic-commercial links to drive innovation and wealth creation. For example, Crescendo Biologics, established in 2008, brings together highly innovative *in vivo* and *in vitro* technology platforms invented by Babraham scientists, including Dr Brüggemann, who recently joined Recombinant Antibody Technology Ltd, also based on campus, and Dr Mike Taussig, an expert in protein display and array systems.

In October 2009, Crescendo raised £4.5 million to advance the development of its fragment antibody technology platforms. The company is in the process of producing heavy-chain-only human antibodies in transgenic mice. Brüggemann's discovery stage research, some in collaboration with Professor Michael Neuberger from the MRC-LMB, has 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. Funded by MRC, BBSRC, the Wellcome Trust and other organisations, this has led to several major patents and considerable royalty income.

The future's bright

At the official opening of Maia, therapeutic antibody pioneer Sir Gregory Winter, FRS, Deputy Director of the MRC-LMB, delivered the 2010 Bioenterprise Lecture, explaining the importance of 'biologicals', including antibodies, as future medicines. Sir Greg is also a founder of Bicycle Therapeutics Ltd, which has just moved onto campus.

"Modern antibodies can tackle serious diseases in ways that chemical drugs cannot. In the future we can expect to see even better antibodies; this might be achieved by adding new activities to existing antibodies or by using smaller antibody fragments with better tissue penetration. Another possibility involves replacing the bulk of an antibody with a chemical core - this may ultimately lead to small orally available antibody mimics without the weaknesses of previous generations of peptide-based therapeutics, the principle behind Bicycle Therapeutics Ltd."

Derek Jones, CEO of Babraham Bioscience Technologies Ltd concluded, "The more that emerging biologics technologies cluster together to deliver groundbreaking research and innovation across academia and industry, the greater the potential impact on our economy and our future health and wellbeing."

Immunology research points to new therapies

Institute scientists Drs Klaus Okkenhaug and Anne Corcoran have revealed that genes from the Phosphatidylinositol 3-kinase (PI3Ks) family of enzymes are critical in enabling

B cells to produce antibodies. This discovery builds on fundamental research to define the mechanism and action of PI3Ks, which areinvolved in cell growth, proliferation, motility, survival and intracellular trafficking. Faults in these processes can cause cancer; and consequently PI3Ks are among the most hotly pursued drug targets in the pharmaceutical industry.

Meanwhile, Dr Martin Turner's group, studying how RNA binding proteins control transcription, have discovered a new mechanism underlying a type of leukaemia. The research, funded by BBSRC, Cancer Research UK and the MRC, revealed that mice missing certain RNA-binding proteins called 'silencers', which play a key role in RNA degradation, develop an aggressive form of cancer similar to Acute Lymphoblastic Leukaemia. This research shows for the first time that 'silencer' proteins acting directly on specific mRNAs may prevent cancer, which may pave the way for new therapeutic strategies.

Further reading

Deletion of the RNA-binding proteins ZFP36L1 and ZFP36L2 leads to perturbed thymic development and T lymphoblastic leukaemia doi: 10.1038/ni.1901

The PI3K isoforms p110α and p110δ are essential for pre-B cell receptor signaling and B cell development. doi: 10.1126/scisignal.2001104

Notes

1. Andy Sandman was appointed non-executive Chairman of Bicycle Therapeutics as of 06 January 2011

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