Institution: University of Bath

Unit of Assessment: A5 Biological Sciences

Title of case study: Atlas Genetics Limited: a University of Bath spin-out company providing novel technology for rapid diagnosis of infectious diseases

1. Summary of the impact

Atlas Genetics Ltd is a University of Bath spin-out company established in 2005 by Dr John Clarkson, a former lecturer in the Department of Biology and Biochemistry (DBB). In collaboration with DBB researchers, Atlas Genetics developed novel technology for rapid (<30 minute) and robust detection of infectious diseases at the point-of-care. Atlas Genetics has raised over £22m funding specifically to develop the Atlas io™ detection system, which combines a patented electrochemical detection system with probes for specific micro-organisms within a small disposable cartridge. Different probe cartridges are used to detect a range of pathogens that have critical clinical importance and large-scale socio-economic significance, including *Candida*, methicillin resistant *Staphylococcus aureus* (MRSA), bacterial meningitis, and sexually transmitted diseases (STDs) *Trichomonas, Chlamydia* and *Gonorrhoea*. *Candida* research in DBB underpinned the specificity, sensitivity and application of the technology to clinical samples and was used in seeking capitalization for Atlas.

Atlas Genetics re-located from the University to a nearby business park and employs 35 full-time staff, some having moved from academia into the company largely thanks to the synergistic relationship with University of Bath researchers. The io™ platform has undergone successful clinical tests on *Chlamydia* and *Trichomonas* at Johns Hopkins University, USA. The io™ platform and *Chlamydia* test is scheduled for clinical trials in 2014, with roll out in Europe and the USA, pending regulatory approval, providing global reach within the $42bn *in vitro* diagnostics market.

2. Underpinning research

The prompt diagnosis and treatment of life-threatening diseases not only improves clinical outcomes but impacts on the cost of healthcare provision and can lead to changes in clinical practice. The Atlas system comprises test-specific disposable cartridges containing all reagents to extract and amplify DNA from a clinical sample, and detect target organisms. Existing DNA sensor technology is largely based on fluorescence detection, whereas the Atlas io™ (formerly Velox™) system is based on electrochemistry. The core electrochemistry was being developed in Dr John Clarkson's laboratory in the Department of Biology and Biochemistry (DBB) in 1996 by a post doctoral researcher, Dr B. Cobb, who became an early employee of the first company formed, Molecular Sensors Ltd, which listed in 1999 as Molecular Sensing plc.

The detection assay technology was taken further and adapted in collaboration with the University of Bath Department of Chemistry. The basis of the assay is that the T7 exonuclease exhibits 5'–3' exonuclease activity on double strand (ds) DNA, thereby cleaving the terminal nucleotide at the 5' end of the probe. The higher diffusion mobility and enhanced access of the enzymatically cleaved ferrocene label to the electrode surface results in an increase in ferrocene oxidation current at an electrode, allowing for sensor applications. It was soon realised that this approach could be used for recognition of any oligonucleotide sequence. Atlas Genetics has patented these unique and powerful assays for detection of DNA and RNA using target-specific probes labelled with an electro-detectable tag [see Section 5].

Subsequent developments by the DBB team involved further research using this assay for detection of sequences which identify infectious diseases that are both clinically and economically important, including bacterial meningitis and methicillin-resistant *Staphylococcus aureus* (MRSA), and the pathogenic yeast *Candida.* In parallel and in Atlas funded collaboration, in DBB Dr Wheals developed methods for simultaneous detection of multiple pathogens in a single reaction [1]. In the case of *Candida*, five species (*C. albicans, C. glabrata, C. parapsilosis* complex*, C. tropicalis* and *C. krusei*) account for over 90% of fungal infections in the UK (Linton et al., 2007, *J Clin Microbiol* 45: 1152-1158) and are associated with mortality rates of up to 70% (Krcmery et al., 2002, *J Hosp*

Infect 50: 243-260). In the USA, fungal pathogenic diseases are the *fourth* most common cause of death from infections.

Importantly, electrochemical probes developed by Atlas/DBB **reliably distinguish the five *Candida* species from each other, and from other fungal pathogens, in the presence of human DNA** [2]. **Probe sensitivity allows detection of one genome equivalent in one ml of sample** [3] **or around 10 yeast cells in one ml of human blood** [2], values which are suitable for application to clinical samples (Loeffler et al., 2000, *J Clin Microbiol* 38: 586-590). The development of this into point of care application was driven by the current situation, where most hospital microbiological laboratories are usually unable to detect and/or identify fungal pathogens. Consequently, samples are sent by post to the National Mycology Reference Laboratory in Bristol. This delays diagnosis by up to a week which has considerable implications for patient outcomes.

Dr John Clarkson, a member of staff in DBB from 1985-2000, and Dr Alan Wheals (DBB) developed the technology for Atlas Genetics, together with colleagues from the Department of Chemistry. Dr Clarkson's company was based in DBB laboratories from September 2005 to January 2008. He continues to interact with several members of DBB, including Dr Wheals on *Candida* species and Dr Ruth Massey on MRSA.

3. References to the research

[1] Muir A., Harrison E, **Wheals, A.** (2011) A multiplex set of species-specific primers for rapid identification of members of the genus *Saccharomyces*. *FEMS Yeast Res*, 11: 552-563. DOI: 10.1111/j.1567-1364.2011.00745.x

[2] **Muir AD**, Forrest G, **Clarkson J, Wheals AE** (2011) Detection of *Candida albicans* DNA from blood samples using a novel electrochemical assay. *J Med Microbiol* 60: 467-471. DOI: 10.1099/jmm.0.026229-0

[3] **Muir A**, Jenkins ATA, Forrest G, **Clarkson J, Wheals AE** (2009) Rapid electrochemical identification of pathogenic *Candida* species*. J Med Microbiol* 58: 1182-1189. DOI: 10.1099/jmm.0.009183-0

Funding to Department of Biology and Biochemistry:
1997 Hybaid funded post doctoral RO.
2006-2009 BBSRC CASE with Atlas; 2006-2009 BBSRC CASE with Unilever plc.
2005 University of Bath Sulis Seedcorn Fund £250,000.

4. Details of the impact

The novel technologies initiated in the DBB, together with subsequent research involving DBB staff, has (i) provided proof of principle for the application of Atlas Genetics technology to clinical diagnostics (ii) assisted in capitalization of Atlas (iii) led to expansion of Atlas Genetics activity to include bacterial and fungal pathogen targets, for which clinical evaluation has been reached (*Chlamydia, Trichomonas*) or is planned (*Candida*). The Atlas CEO commented:

"*The creation of Atlas Genetics was only possible thanks to research carried out in the Department of Biology and Biochemistry (DBB). University of Bath support came as: funding (departmental BBSRC studentship and University Sulis Fund); encouragement from the incumbent HoD (Prof. S. Reynolds) and provision of laboratory space. Early patents to Molecular Sensing arose during this period. Long term and ongoing collaborations with academic staff, in particular Dr A. Wheals, have contributed to the development of intellectual property and essential capitalization. Atlas funded a BBSRC Case studentship to DBB in 2006 and the resulting Candida research confirmed the speed of the technology and its ability to be adapted to detect general groups (pan-fungal probe) and distinct pathogen species.* ***Exquisite sensitivity, even from blood samples was a crucial demonstration. Multiplexing will enable simultaneous detection of diverse pathogens.*** *Associated DBB links with the National Mycology Reference Laboratory Bristol provided critical access to and advice from clinicians. Candida, as a major cause of sepsis, was used as one of several targets when seeking venture capital, before the eventual focus post-2011 on Chlamydia*

as STDs grew in importance. Candida remains a future potential Atlas target for hospital acquired infections and Atlas remains committed to providing diagnostics solutions for sepsis.

This novel technology will enter clinical trials in 2014 and we are confident that its speed and accuracy means that it will change practices by allowing point of care application to result in direct and rapid treatment of patients" [A].

Impacts from this work: company, investment, people and a new technology

- A spin-out or new business has been created [B]. Jobs have been created.
- Industry (including overseas industry) has invested in research and development.
- Highly skilled people have taken up specialist roles in companies
- The health sectors in USA and Europe are trialling a new technology

Background

Molecular Sensors Ltd was the initial University of Bath spin-out company, formed in 1996, listed as Molecular Sensing plc in 1999, then sold in 2004 to the US-based diagnostics business Osmetech plc. Atlas Genetics was launched with £500,000 initial funding, 50% of which came in part from the Sulis Seedcorn Fund, established by the University of Bath to provide support for new businesses. Atlas was founded as a spin-out from the University and Osmetech plc in 2005. In 2007 Atlas completed Series A financing of £2 million and the company relocated to a 2,500 sq. ft. site on a business park close to Bath (Trowbridge, Wiltshire). The number of full time staff increased to 12 and a commercial programme to develop the Atlas system was initiated. STDs and sepsis and in particular *Candida*, were proposed as key targets to potential investors.

Impact – development of the company arising from DBB underpinning research

In 2010 Atlas obtained a grant from the Regional Development Agency grant for the development of a Syphilis assay. Atlas was also awarded a Technology Strategy Board grant for £1.6m in partnership with Randox Laboratories and the Health Protection Agency (HPA). In early 2011 Atlas secured £1.5m Series B funding from Consort Medical plc and other investors in a synergistic partnership, to utilise the plastic device manufacturing expertise of one of Consort's group companies, Bespak Europe Ltd. Atlas then raised £16.9 million later in 2011 from a syndicate of new and existing investors led by Novartis Venture Funds to further develop the io™ system, including a molecular *Chlamydia* test. The new investors in this Series B financing are Novartis Venture Funds, Life Sciences Partners (LSP), BB Biotech Ventures and Johnson & Johnson Development Corporation.

Atlas then relocated in 2011 to new 9,500 sq. ft. premises and following an expansion programme has increased the number of full-time staff to 35 (and 3 part time). Most have higher educational degrees in science, engineering or business. Alistair Muir, a PhD student in DBB is now an employee of Atlas Genetics (from 2012). Other Atlas investors include the South West Ventures Fund, Finance South West Growth Fund, Braveheart Ventures, Sulis Investment Management Fund, GEIF Ventures, Consort Medical plc, and private investors. Atlas is currently venture capital funded and to date has raised more than £23m. Dr Clarkson has been invited to numerous investment conferences [C]. Fifteen patents have been granted and nine applications are pending to date [D].

Impact – the Route to Clinical Implementation

Since 2008, the Atlas io™ system has been in further development and clinical testing, which has established its value in diagnosis of a range of infectious diseases in humans, including

Chlamydia, Gonorrhoea, MRSA, and bacterial meningitis. Highlights include:

- Clinical evaluation and trials for *Chlamydia* and *Trichomonas* infections

Chlamydia infection is one of the most common STDs, causing an estimated >95 million new cases globally of genital *Chlamydia* infection every year, with prevalence rates in young people at 5-10%. Rapid diagnosis is key to preventing disease spread. An independent evaluation was performed by Johns Hopkins University, Department of Medicine (Baltimore, USA). Results showed the clinical sensitivity and specificity of the io™ rapid *Chlamydia trachomatis* assay compared with slower, laboratory based Gen-Probe Aptima Combo 2™ and the Roche Cobas Amplicor™ as comparator tests. These clinical tests yielded impressive results that supported the adoption of the test in clinical environments and led to a collaborative agreement between Atlas and Johns Hopkins. The published collaboration showed sensitivity and specificity of >98% [E]; it was developed further for *Trichomonas*, showing sensitivity and specificity >95% [F]. *Trichomonas vaginalis* is the most prevalent, curable STD in the world, causing around 248 million new cases annually [G]. Trichomoniasis can lead to vaginitis, cervicitis, and urethritis, infection during pregnancy can lead to complications and can increase the risk of contracting HIV and other STDs.

- Clinical trials coordinated by Public Health England for the Atlas *Chlamydia* detection

product are due to commence late in 2013 with the final clinical evaluation in March 2014 [A]. The platform is scheduled to launch within Europe with CE certification in 2014, followed by roll-out in the USA pending regulatory approval.

- Development of tests with *Candida* [B] will follow the success with *Chlamydia*.

Impact – Scope for Growth

The *in vitro* diagnostics (IVD) market is $42 billion and growing at 6% annum. The most rapidly growing areas are molecular diagnostics (valued at $3b and growing at 15% pa) and the point of contact (PoC) market (valued at $2.5b and growing at 12% pa). Atlas's focus on PoC STD testing, embraces both these fast growing areas of diagnostics and offers substantial routes for expanded future impact in terms of both economic and clinical benefits.

5. Sources to corroborate the impact

[A] Testimonial from Atlas Genetics CEO.
[B] Atlas Genetics: http://www.atlasgenetics.com/
Capitalisation – http://www.atlasgenetics.com/press/18_jul_2011.html
"Atlas Genetics Ltd completes £16.9M series B financing led by Novartis Venture Funds"
Corroborating contacts – Atlas Genetics CEO; Managing Director, Novartis Venture Funds.
[C] Invitations as speaker at investment conferences: Healthios Investor Conf., Los Angeles, 2012; BioCapital Europe Investor Conf., Amsterdam, 2012; Molecular Tri-Conf., San Francisco, 2012;VentureFest, Bristol, 2011; SMI Point-of-Care Diagnostics Conf., London, 2011
[D] Patents 2003-2013: Nucleic acid probes, 8 granted, 1 pending. Electrochemically active compounds, 5 granted, 1 pending. Protease assays, 2 granted and 7 pending on; microbial assays; novel compounds; analytical methods. Patent (or application) codes available on request.
[E] Pearce D M, Shenton et al. (2011) Evaluation of a novel electrochemical detection method for *Chlamydia trachomatis*: Application for point-of-care diagnostics. *IEEE Trans Biomed Engin* 58: 755-758.
[F] Pearce DM, Styles DN, Hardick JP & Gaydos CA (2013). A new rapid molecular point-of-care assay for *Trichomonas vaginalis*: preliminary performance data. Sex Transm Infect; Published Online First: April 20, 2013. doi:10.1136/sextrans-2012-051000. *Pearce and Shenton are* ***Atlas employees****. This resulted from an* ***invited collaboration with Johns Hopkins University*** *MD, USA, funded by US NIH*.
[G] World Health Organisation (2011). Global prevalence & incidence of selected sexually transmitted infections *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, syphilis and *Trichomonas vaginalis*: methods and results used to generate 2005 estimates. WHO, Geneva.