Institution: EaStCHEM

Unit of Assessment: 8; Chemistry

Title of case study: Wound Care; Point of Care Diagnostic Platforms for fast detection of unlabelled infection biomarkers result in establishment of Mölnlycke Health Care AB in Scotland

1. Summary

Research; date; attribution:

Since 2005, EaStCHEM research expertise in electrochemistry and in sensing and detection, in partnership with University of Edinburgh researchers and expertise from the associated disciplines of medicine, engineering and physics and funded by the Scottish Intermediary Technology Institute (now Scottish Enterprise, SE) has formed a multidisciplinary team and developed the research outputs and novel platform technologies with enhanced detection characteristics (sensitivity, specificity, ability to handle clinical samples, rapid time–to-result) applicable to point-of-care diagnosis of wound infection state.

Significance: This technology was exclusively licensed from SE by Mölnlycke Health Care AB in 2012. Mölnlycke Health Care AB also established a new subsidiary, MHC Scotland Ltd in the BioQuarter in Edinburgh, to develop this technology, marking their entry into the multibillion dollar global point of care diagnostics market, as well as employing 5 UoE researchers.

Reach: Mölnlycke Health Care AB is a leading innovator in infection control in hospitals having ~7000 employees worldwide and with manufacturing plants in 9 countries.

Beneficiaries: The impact deriving from the underpinning research is to Mölnlycke Health Care AB as evidenced by formation of a significant new business venture and alteration of business practice, through the adoption and commercialisation of our new technology platform and the employment of 5 UoE staff from the research programme as human capital in MHC Scotland Ltd.

2. Underpinning research

Background

In 2003, EaStCHEM research expertise in electrochemistry and in sensing and detection (led by Mount) played a central role in a University of Edinburgh (UoE) multidisciplinary (with physics, medicine and electronic engineering) programme to produce a novel DNA nanoswitch platform technology. Competitively funded as one of only six national DTI Beacon projects in Harnessing Genomics, this work produced a new type of DNA nanoswitch, based on the Holliday Junction (HJ), that used a combination of binding and conformational switching to enable specific label-free detection of synthetic and cellular DNA and RNA (Anal. Chem. 2007, 79, 4724-28). In this work we led the physicochemical characterisation [1] and surface functionalised electrode development required to produce a platform technology with electrochemical control [2] and interrogation of HJs anchored to a silicon substrate in a label-free detection device.

A significant output was a UoE multidisciplinary team of researchers capable of developing specific healthcare sensing/detection platforms. Exploiting this, in 2005 the team won competitive funding from ITI Techmedia for four years to develop a Biosensor Platform for diagnosis and treatment of infectious diseases. (ITI, the Intermediary Technology Institute, was the publicly funded organisation established to lever Scotland's research excellence, funding early stage technology R&D programmes to develop market-driven intellectual property (IP) for the benefit of the Scottish economy. It is now part of Scottish Enterprise (SE), Scotland's economic, enterprise, innovation and investment agency). In this award, which involved working with specific industrial partners, the UoE research programme was the majority of the £10.2M total funding, and involved the development and combination of sensors, microsystems, and custom and high density bioarray / microarray platforms. The aim was to develop theranostic platforms, each of which combined the measurement and analysis of specific diagnostic data to reduce the cost and complexity and increase the speed and accuracy of disease diagnosis. Our work resulted in four patents on the development of electrochemical detection and the combination of electrochemical and optical detection for enhanced sensitivity (WO2008084114-A1; WO2008090229-A1; WO2009112537-A1; WO2009141180-A1).

Evidence of the success of this UoE research programme was the award of a further £7.9M SE/ITI Techmedia R&D programme in Chronic Wound Care in 2009. This exploited EaStCHEM-led expertise in the development of electrochemical detection and the design of specific probe sensing modified electrode layers for specific label-free target detection. It also utilised electrochemical impedance spectroscopy (EIS, in which EaStCHEM through the Mount group has particular expertise) as a detection method. The majority of this funding was again to UoE, to develop a point of care diagnostic device using multiparameter EIS detection that could be readily applied to diagnose and monitor wound infection both in a clinical environment and in the community. The programme focused on diabetes-related chronic wounds e.g. diabetic foot ulcers, although the technology platform was also intended to be applicable to other major wound categories and other markets. Our research outputs developed methods for rapid detection [6] and satisfied the requirements for point of care (PoC) testing by producing rapid, sensitive and specific label free EIS detection from clinically relevant samples of: three biomarkers diagnostic of wound infection [3]; the antibiotic-resistant *mecA* gene sequence in DNA fragments produced by PCR; and an MRSA specific assay which did not require polymerase chain reaction (PCR) amplification of the target DNA [5]. Along with the development of a mini-potentiostat system, this enables MRSA diagnosis in less than an hour [5]. Systematic optimisation of e.g. probe chemistry, electrode film structure and DNA fragmentation protocols were key in optimising assay performance.

Research Team;
A.R. Mount: Group leader, EaStCHEM, Senior Lecturer 2003-, Reader 2005-, Professor 2012-. EaStCHEM PDRAs: Ciani, Corrigan, Evans, Ferapontova. C. Campbell (now Senior lecturer in EaStCHEM).
Crain, Walton, Ghazal and their respective groups: collaborators working in the UoE during the period that the underpinning research was performed. All outputs published by UoE.

3. References to the research

Underpinning research has been published in international, high-quality, peer reviewed, journals and reports, and receives citations from across the research area: these are the top journals in the field of biosensors research.

[1] The stability and characteristics of a DNA Holliday junction switch A. R. Mount, C. P. Mountford, S. A. G. Evans, T. J. Su, A. H. Buck, P. Dickinson, C. J. Campbell, L. M. Keane, J. G. Terry, J. S. Beattie, A. J. Walton, P. Ghazal, J. Crain, *Biophys. Chem.* **2006**, *124*, 214-221. DOI: 10.1016/j.bpc.2006.03.020 [4 cits, JIF: 2.1]

[2] Electrochemical control of a DNA Holliday Junction nanoswitch by Mg^{2+} ions E.E. Ferapontova C.P. Mountford, J. Crain, A.H. Buck, P. Dickinson, J.S. Beattie, P. Ghazal, J.G. Terry, A.J. Walton, A.R. Mount, *Biosensors & Bioelectronics* **2008**, *24*, 422–428. http://dx.doi.org/10.1016/j.bios.2008.04.021

[3] * Development of immunosensors for direct detection of three wound infection biomarkers at point of care using electrochemical impedance spectroscopy I. Ciani, H. Schulze, D. K. Corrigan, G. Henihan, G. Giraud, J. G. Terry, A. J. Walton, R. Pethig, P. Ghazal, J. Crain, C. J. Campbell, T. T. Bachmann and A. R. Mount, *Biosensors & Bioelectronics*, **2012**, *31*, 413. DOI: 10.1016/j.bios.2011.11.004 [8 cits, JIF:5.39]

[4] * Impedimetric detection of single-stranded PCR products derived from methicillin resistant *Staphylococcus aureus* (MRSA) isolates D. K. Corrigan, H. Schulze, G. Henihan, I. Ciani, G. Giraud, J. G. Terry, A. J. Walton, R. Pethig, P. Ghazal, J. Crain, C. J. Campbell, A. R. Mount and T. T. Bachmann, *Biosensors & Bioelectronics*, **2012**, *34*, 178. DOI: 10.1016/j.bios.2012.01.040 [3 cits, JIF: 5.39]

[5] * Development of a PCR-free electrochemical point of care test for clinical detection of methicillin resistant *Staphylococcus aureus* (MRSA) D. K. Corrigan, H. Schulze, G. Henihan, A. Hardie, I. Ciani, G. Giraud, J. G. Terry, A. J. Walton, R. Pethig, P. Ghazal, J. Crain, C. J. Campbell, K. E. Templeton, A. R. Mount and T. T. Bachmann, Analyst, **2013**, DOI: 10.1039/c3an01319g

[6] Detecting analyte e.g. protease used for diagnosing impaired wound healing, involves applying alternating voltage to analyte and determining identity and/or quantity of analyte from electrochemical impedance spectrometry data, A. R. Mount, M. Khondoker, I. Ciani, T. Bachmann, P. Ghazal; **2011**, WO 2011069997-A2; WO2011069997-A3; EP2510342-A2; US2012285829-A1; CN102753965-A; JP2013513790-W

Key Grants

2003-2007 £1.48M. "Genomic Nanoprocessors" One of only 6 “Beacon Projects” funded by the then DTI as part of their multi-million pound 'Harnessing Genomics' programme to ensure that the UK’s world-leading bioscience R&D base was capable of being commercialised by a thriving biotechnology sector.
Principal Investigators: Mount (EaStCHEM), Crain, Ghazal, and Walton, all UoE academics.

2005-2009 £10.2M ITI Techmedia Biosensing Platform; competitively tendered; Consortium = The original UoE “Beacon” award group of PIs, plus Till Bachmann (project manager) and Partners Axis-Shield, Haptogen Ltd. and Lab901 Ltd.

2009-2011 £7.9M. ITI Techmedia Chronic Wound Care (CWC) programme. competitively-tendered; Consortium = The original UoE “Beacon” award group of PIs, plus Till Bachmann and SME Partners D3 Technologies (Now Renishaw Diagnostics), Zisys and Mologic.

4. Details of the impact

The grants from ITI Techmedia specified that the arising IP portfolio was to be owned and developed by them for the benefit of the Scottish economy. This responsibility passed onto SE on their amalgamation. Mölnlycke Health Care AB (a world leading manufacturer of wound care products and a major service provider to the healthcare sector with annual sales which have grown rapidly from £536M in Q4 2007 to £932M in 2012 of which ~40% currently derives from its Wound Care Division) recognised the pressing requirement for rapid and sensitive technologies suitable for PoC testing. The opportunity for rapid detection of MRSA was verified by ZinC (a health innovation, growth and market strategy consultancy) in 2008 *“as part of the Scottish Enterprise ITI Scotland Chronic Wound Care Programme. Using our Health Opportunity Design® methodology, ZinC uncovered a $4.3bn global opportunity for chronic wound infection. Prompt, MRSA detection, at the point-of-care, was deemed the most prescient opportunity in a product development roadmap, devised by ZinC, that encompassed a series of increasingly complex technologies to target not just MRSA but other critical bacterial infections, and to meet the prioritized and precisely defined unmet needs of a global wound care practitioner base.*[S1] In April 2012, the global PoC diagnostics market was estimated to be in excess of $4.3B and was forecast to grow to $7B by 2018, with infectious diseases being the most dynamic sector [S2, S3]. Mölnlycke Healthcare AB has ~7000 employees and manufacturing plants in Belgium, the Czech Republic, Finland, France, Malaysia, Thailand, Poland, the UK and the US. A route to establishing a competitive presence in the global diagnostics market was therefore a priority for Mölnlycke.

Seeing the opportunity that the IP and associated UoE expertise presented, Mölnlycke Healthcare AB secured an exclusive license from SE in 2012 (details commercially confidential) and established a new subsidiary, MHC Scotland Ltd in the BioQuarter in Edinburgh [S4], to develop this technology for the diagnostics market. The Head of Chemical Sciences at SE has said “*The Edinburgh University research team were key in delivering a positive outcome from the programme due to their acknowledged world-class capabilities in the field of small-scale surface detection technologies in general and your [EaStCHEM] expertise in electrochemical detection in particular. This progress enabled the developed detection technology and associated IP to be attractive to a world class healthcare company (Mölnlycke Health Care) and was the reason this company chose to set up Mölnlycke Health Care Scotland (MHS) in the BioQuarter in Edinburgh”.*[F1] The CEO of Mölnlycke Health Care AB, has confirmed the value to the company in 2012 [S2] *“We are delighted to be expanding our capabilities and product offering in close collaboration with Scottish Enterprise and the University of Edinburgh. This initiative marks our entry into the diagnostic market. We are very proud to be extending our offering of efficient infection control and prevention solutions that*

make life easier and safer for health care professionals and patients."

The central importance of the "innovative technology platform" developed by the underpinning research is confirmed by Mölnlycke Healthcare AB [S2, S3] and by SE; their Director of Commercialisation has stated [S2] "*…we have been able to identify and secure the opportunity for Mölnlycke Health Care to develop its innovative commercial product based on our platform technology at the Edinburgh BioQuarter in Scotland."* The Managing Director MHC Scotland Ltd [F2] has said *"The innovative detection technology…uses Electrochemical Impedance Spectroscopy (EIS) to identify and quantify biomarkers that show the presence of pathogens, such as Methicillin-resistant Staphylococcus aureus (MRSA). Current MRSA screening often involves centralised laboratory facilities that can take up to 48 hours to process results, during which time MRSA can spread. By using EIS we will be able to offer point of care testing (PoCT)."* [S3] The impact deriving from the underpinning research is therefore directly to Mölnlycke Health Care AB as evidenced by formation of a significant new business venture and alteration of business practice, through the adoption and commercialisation of our new technology platform.

Further evidence of the link between research and impact through company formation and commercialisation is the strong Human Capital transfer from UoE to MHC Scotland Ltd. Since 2012, Till Bachmann, the project manager for the ITI Programmes in UoE has been employed both in UoE and part-time on a consultancy basis as the Scientific Programme Director for MHC Scotland Ltd. Of the 8 personnel in MHC Scotland Ltd, 4 (Bachmann, PDRAs Ciani and Schulze, Henihan) were UoE personnel working on the ITI programmes whilst a fifth (Kaatz) is an EaStCHEM postdoctoral worker from Mount's group with expertise in bioelectrochemistry and impedance. Formation of MHC Scotland Ltd represents the first inward investment to the BioQuarter and an important part of Scottish Enterprise's delivery plan for economic benefit from the life sciences, as evidenced by the Head of Chemical Sciences at SE; *"As you know, Chemical Sciences are at the heart of Scotland's economy, and chemistry is indeed the 'science at the centre'. It also plays a key underpinning role with other key sectors e.g. life sciences, energy, chemicals and electronics. The research carried out at the University of Edinburgh which Mölnlycke Healthcare is commercialising is a prime example of the synthesis of research and technology excellence that Scottish Enterprise is supporting and promoting globally."* [F1].

5. Sources to corroborate the impact

[S1] http://www.zinc-healthcare.com/blogpost/achieving-success-in-health-innovation-through-a-focus-on-care-pathways which corroborates the economic significance of the Scottish Enterprise/ ITI Chronic Wound care programme which is underpinned by UoE research led by EaSTCHEM.

[S2] Press release [dated 11 December 2012] (cached website pdf supplied) which contains quoted market data from Original source ISBN: GDME0147 Point-of-Care Diagnostics - Global Pipeline Analysis, Competitive Landscape and Market Forecasts to 2018. It also includes statements from CEO of Mölnlycke Health Care AB and Director of Commercialisation, SE.

[S3] http://www.molnlycke360.com/joining-the-fight-against-superbugs/ contains the quote include in section 4 from Managing Director, MHC Scotland Ltd.

[S4] Edinburgh BioQuarter Q4 newsletter Dec 2012; http://www.edinburghbioquarter.com/news/item/m-lnlycke-locates-new-subsidiary-at-edinburgh-bioquarter/, which corroborates the establishment of MHC Scotland Ltd in the Edinburgh BioQuarter.

[F1] Head of Chemical Sciences at Scottish Enterprise corroborating the importance of the MHC Scotland Ltd/UoE development programme to the Scottish life sciences industry.

[F2] Managing Director, MHC Scotland Ltd will corroborate all Mölnlycke Healthcare AB and MHC Scotland Ltd related statements.