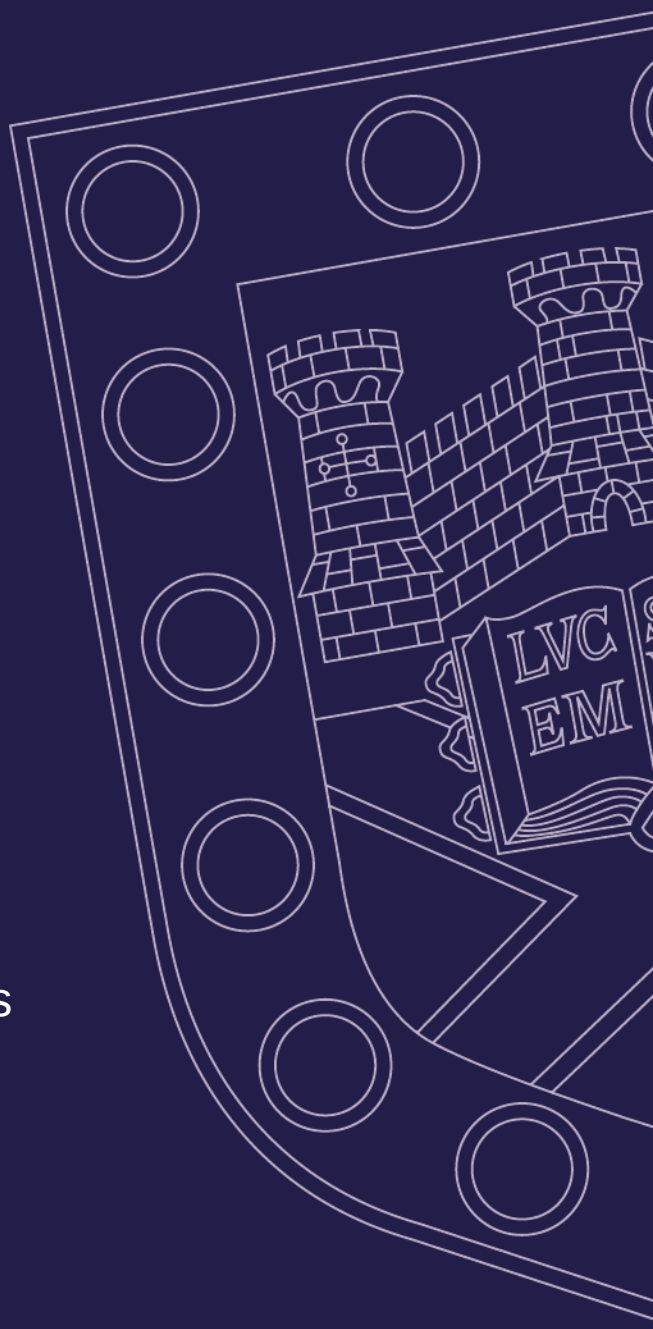
UNIVERSITY OF EXETER

Impact and Engaged Research Network: Skills for impact: Impact capture and evidence

Tuesday 15 December 2015, 12.30 – 13.30

Building:One, Matrix Lecture Theatre, Streatham Campus



Skills for impact: Impact capture and evidence

Dr Chris Thornton, Associate Professor of Fungal Immunology and Director of Impact & Industry, Biosciences, College of Life and Environmental Sciences

Dr Christopher Thornton

Associate Professor of Fungal Immunology

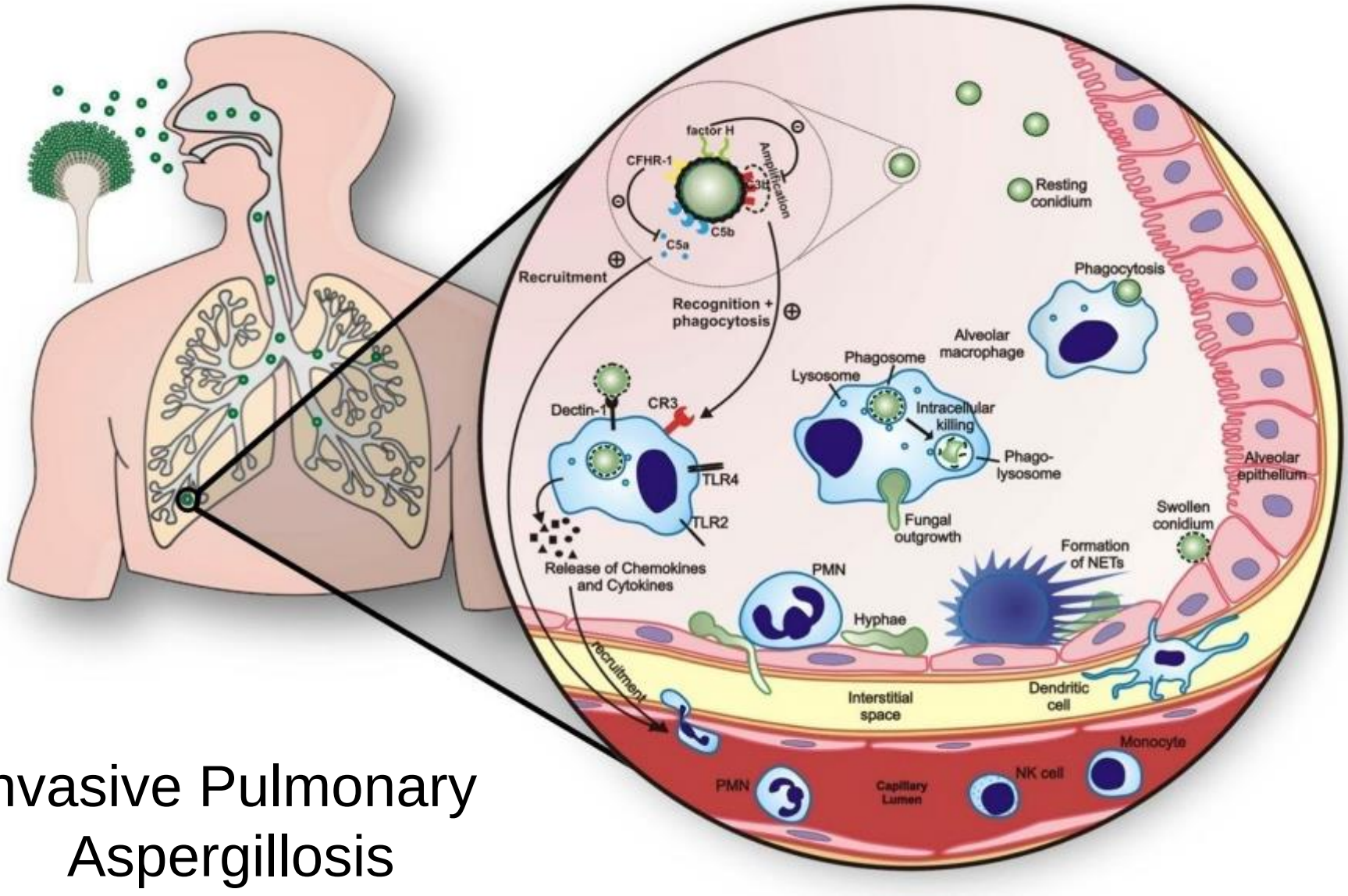
Director of Impact & Industry

Biosciences (CLES)

UNIVERSITY OF EXETER

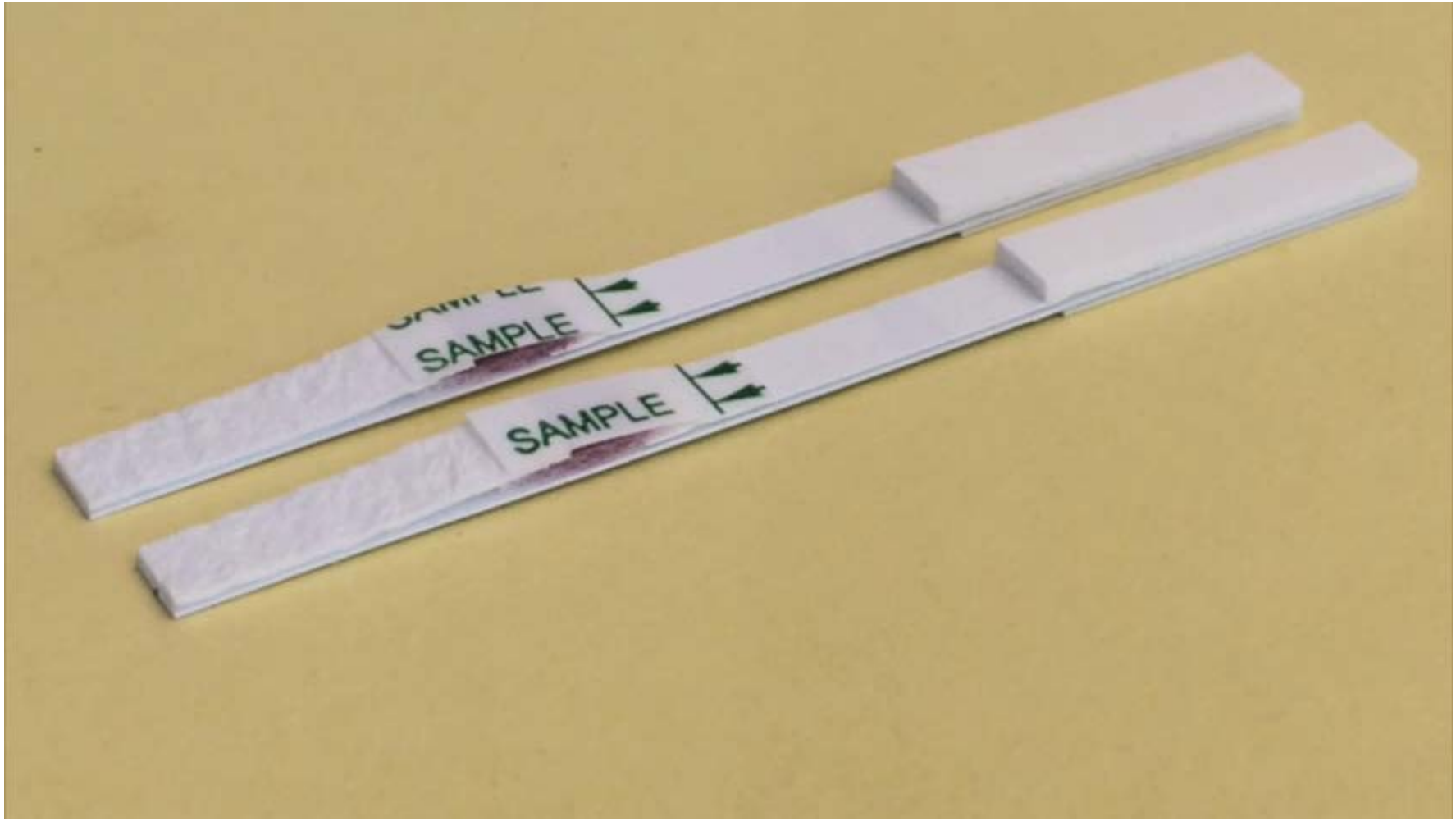
sca diagnostics

Case Study ‘Case Study’



Invasive Pulmonary Aspergillosis

Bedside Diagnosis of Invasive Pulmonary Aspergillosis



Lateral-Flow Assay

Pathways to Impact

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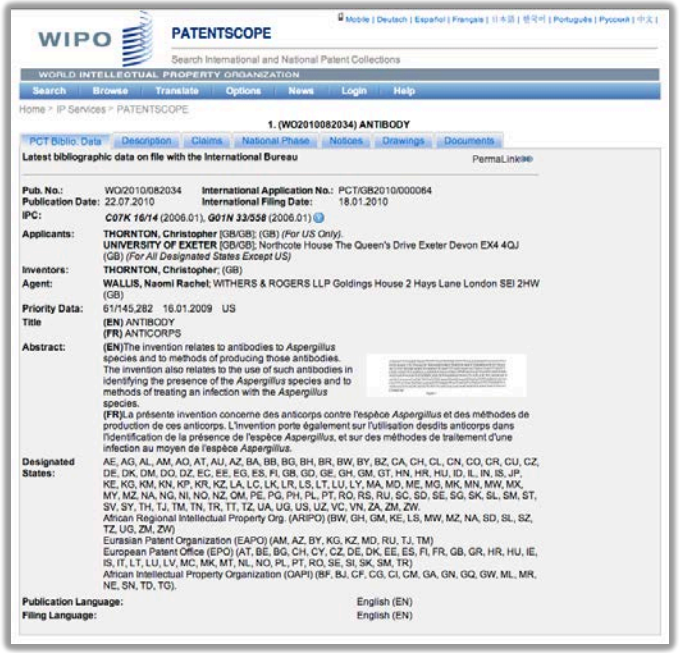
Institute to Industry

Isca diagnostics

www.iscadiagnostics.co.uk



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1. (WO2010082034) ANTIBODY

PCT Biblio. Data | Description | Claims | National Phase | Notices | Drawings | Documents

Latest bibliographic data on file with the International Bureau

PermaLink

Pub. No.:	WO2010/082034
Publication Date:	22.07.2010
International Application No.:	PCT/GB2010/000064
International Filing Date:	18.01.2010
IPC:	*C07K 16/14* (2006.01), *G01N 33/558* (2006.01)
Applicants:	**THORNTON, Christopher** [GB/GB]; (GB) *(For US Only)*. **UNIVERSITY OF EXETER** [GB/GB]; Northcote House The Queen's Drive Exeter Devon EX4 4QJ (GB) *(For All Designated States Except US)*
Inventors:	**THORNTON, Christopher**; (GB)
Agent:	**WALLIS, Naomi Rachel**; WITHERS & ROGERS LLP Goldings House 2 Hays Lane London SE1 2HW (GB)
Priority Data:	61/145,282 16.01.2009 US
Title	**(EN)** ANTIBODY **(FR)** ANTICORPS
Abstract:	**(EN)**The invention relates to antibodies to *Aspergillus* species and to methods of producing those antibodies. The invention also relates to the use of such antibodies in identifying the presence of the *Aspergillus* species and to methods of treating an infection with the *Aspergillus* species. **(FR)**La présente invention concerne des anticorps contre l'espèce *Aspergillus* et des méthodes de production de ces anticorps. L'invention porte également sur l'utilisation desdits anticorps dans l'identification de la présence de l'espèce *Aspergillus*, et sur des méthodes de traitement d'une infection au moyen de l'espèce *Aspergillus*.
Designated States:	AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW. African Regional Intellectual Property Org. (ARIPO) (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW) Eurasian Patent Organization (EAPO) (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM) European Patent Office (EPO) (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR) African Intellectual Property Organization (OAPI) (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
Publication Language:	English (EN)
Filing Language:	English (EN)

UoE licences
IP to spinout

Patent to Product

Marketing, Sales
& Distribution

Bench to Bedside

What does an Impact Case Study look like?

Impact case study (REF3b)

REF2014 Research Excellence Framework

Institution: University of Exeter

Unit of Assessment: 5

Title of case study:
Commercialisation of a Novel Diagnostic Test for Invasive Pulmonary Aspergillosis

1. Summary of the impact (indicative maximum 100 words)

Invasive pulmonary aspergillosis (IPA) is a frequently fatal disease of haematological malignancy patients, caused by fungi from the genus *Aspergillus*. Dr Christopher Thornton has developed and commercialised a novel point-of-care test for the diagnosis of IPA with an *Aspergillus*-specific monoclonal antibody (mAb) JF5 generated using hybridoma technology. Using this mAb, he has developed a lateral-flow device (LFD) for the rapid detection of *Aspergillus* antigen in human serum and bronchoalveolar lavage fluids (BALf) that signifies active infection. Commercial exploitation of the patented technology has been met through the establishment of a University of Exeter spin-out company, Isca Diagnostics Limited.

2. Underpinning research (indicative maximum 500 words)

Dr Thornton's (appointed to Exeter as Lecturer, 2003-07, Senior Lecturer 2007-present) research focuses on the development of next generation monoclonal antibodies for use in fungal biology, and he has a particular interest in IPA which is a leading cause of morbidity and mortality in haematological malignancy patients and hematopoietic stem cell transplant recipients [1], with an estimated 200,000 cases per year worldwide and a death rate in excess of 50%. Diagnosis of IPA represents a formidable diagnostic challenge and usually relies on a combination of clinical data, microbiology and histopathology, none of which provide a definitive differential diagnosis. There are no nucleic acid based tests and currently available enzyme immunoassays are unreliable. The Thornton lab has addressed this problem and developed a series of next-generation monoclonal antibody (mAb)-based assays that detect markers of active infection.

In 2008 Thornton described the generation of an *Aspergillus*-specific mAb (JF5) using hybridoma technology, and its use to develop an immuno-chromatographic lateral-flow device (LFD), similar to those used in many pregnancy tests, for the rapid (10 min) point-of-care diagnosis of IPA [2]. Funding from the US National Institute of Allergy & Infectious Diseases allowed Dr Thornton to validate the LFD in an animal model of IPA [3, 4]. Subsequent funding from Pfizer Ltd allowed Dr Thornton to collaborate with haemato-oncologists at St. Bartholomew's hospital (London), King's College hospital (London), the Royal Devon and Exeter hospital (Exeter), the Medical University of Graz (Austria) and with medical mycologists at Cardiff University hospital, to undertake clinical trials of the LFD in humans. Results of the LFD trials, demonstrated a 100% negative predictive value for IPA diagnosis using human BALf and 100% positive predictive value when used as an adjunct test with PCR of human serum [4-6]. The specificity, ease-of-use, low cost (~£10 per test), and compatibility of the *Aspergillus* LFD with routine hospital practices [1, 5, 6] means that the onset of IPA can be quickly and accurately monitored using a simple and cheap blood test for circulating *Aspergillus* antigen [2, 5, 6] or with BALf collected during bronchoscopy and lung biopsy [3,4]. Importantly the test does not suffer from the false-positivity seen with commercial Beta-glucan and galactomannan assays due to antibiotics, anti-cancer drugs or the presence of other fungi [1, 2, 4-6]. This is vitally important in establishing a differential diagnosis of IPA.

3. References to the research (indicative maximum of six references)

Evidence of the quality of the research: this work has been published in high quality peer reviewed journals, has attracted significant external grant funding, has resulted in the granting of patents and establishment of a spin-out company.

Research publications:

1. Thornton CR. Detection of Invasive Aspergillosis. (2010). *Advances in Applied Microbiology* **70:** 187-216.
2. Thornton CR. Development of an immunochromatographic lateral-flow device for rapid serodiagnosis of invasive aspergillosis. (2008). *Clinical and Vaccine Immunology* **15:** 1095-1105.
3. Wiederhold NP, Najvar LK, Bocanegra R, Kirkpatrick WR, Patterson TF, & Thornton CR. (2013). Inter-Laboratory and Inter-Study Reproducibility of a Novel Lateral-Flow Device and the Influence of Antifungal Therapy on the Detection of Invasive Pulmonary Aspergillosis. *Journal of Clinical Microbiology* **51:** 459-465.
4. Thornton C, Johnson G, & Agrawal S. Detection of invasive pulmonary aspergillosis in haematological malignancy patients by using lateral-flow technology. (2012). *Journal of Visualised Experiments* **61:** e3721, DOI: 10.391/3721. URL:
5. Hoenigl M, Koidl C, Duettmann W, Seeber K, Wagner J, Wofler A, Raggam RB, Thornton C, & Krause, R. Bronchoalveolar lavage lateral-flow device test for invasive pulmonary aspergillosis diagnosis in haematological malignancy and solid organ transplant patients. (2012). *Journal of Infection* **65:** 588-591.
6. White PL, Parr C, Thornton CR, & Barnes RA. (2013). An Evaluation of Real-Time PCR, Galactomannan ELISA and a Novel Lateral-Flow Device for the Diagnosis of Invasive Aspergillosis. *Journal of Clinical Microbiology* **51:** 1510-1516.

Research grants:

7. Wiederhold N (University of Texas) and Thornton CR (UoE), Invasive Aspergillosis Diagnosis by Antigen Capture with Lateral-Flow Technology, US National Institutes of Health/National Institute of Allergy and Infectious Diseases 01/06/10 to /05/12, $230,262.
8. Thornton CR. (UoE), Clinical Evaluation of a Lateral-Flow Device for Rapid Diagnosis of Invasive Aspergillosis, Pfizer Ltd., 01/10/10 to 30/09/11, £59,617.
9. Thornton CR (UoE). Development of a lateral-flow device for rapid serodiagnosis of invasive aspergillosis. Higher Education Innovation Fund 4, 2010, £15,000.
10. Thornton CR (UoE). Creation of Isca Diagnostics Ltd., a University of Exeter Spin-Out Company. Higher Education Innovation Fund 5, 25/05/12 to present, £4,750.
11. Thornton CR (Isca Diagnostics Ltd.). New Molecular-Functional Imaging Technologies and Therapeutic Strategies for Theranostic of Invasive Aspergillosis. European Commission FP7-HEALTH-2013-INNOVATION-1 SME-targeted Collaborative Project, 2013-2018, €1,397,800.

Impact case study (REF3b)

REF2014 Research Excellence Framework

What does an Impact Case Study look like?

4. Details of the impact (indicative maximum 750 words)

The commercial value of Dr Thornton's research in fungal immunodiagnostics has led to protection of his intellectual property through a patent application in 2008 (section 5; source 1), and commercial exploitation of the *Aspergillus* LFD through establishment of a University of Exeter spin-out company, Isca Diagnostics Limited (www.iscadiagnostics.co.uk, section 5; source 2-4), and a global distribution agreement with OLM Medical (www.olmmedical.com, section 5; source 5).[14] Dr Thornton, as CEO of Isca, was also awarded€1.4M as an SME participant in a 5 year FP7 HEALTH-INNOVATION-1 consortium grant in 2013. Dr Thornton's role is to generate JF5 antibody fragments (Fabs, scFvs, minibodies) and a humanised JF5 antibody for radio-immunotherapy and Positron-Emission-Tomography/MRI imaging of IPA in animal models and in human clinical trials (http://www.mathias-imaging.eu).

1. Intellectual Property Protection and Patenting of the LFD and mAb JF5
A patent "New Method of Detecting and Diagnosing Invasive Aspergillosis", with Dr Thornton as the named inventor, was filed by the University of Exeter in the US in Jan 2009 (US61/145,282), and PCT filing (PCT/GB2010/000064) in Jan 2010 (section 5; source 1). Regional and National Phase registration was initiated in July 2011, with protection being sought in the US, EU, Russia, China and India. In line with the Budapest treaty, the variable heavy and light chains (V_H and V_L) and Complementarity Determining Regions (CDRs) of mAb JF5 were sequenced and published, and the hybridoma cell line deposited in the European Collection of Cell Cultures (ECACC). The sequencing and deposition work was funded by a HEIF 4 grant to Dr Thornton.

2. Establishment of University of Exeter Spin-Out Company Isca Diagnostics Ltd.
On 29th March 2012, Dr Thornton, with financial and legal support from the University of Exeter and funding of £85k from private investors (section 5; source 3), established a spin-out company Isca Diagnostics Ltd. (section 5; source 4), for commercial exploitation of mAb JF5 and the *Aspergillus*-specific LFD. Subsequent funding in 2013 through an EC FP7 consortium grant has enabled Isca

to expand its portfolio of diagnostic and therapeutic agents for IPA over the next five years (2013-2018). It has also enabled Isca to employ a full-time R&D scientist and for Dr Thornton to spend 0.33FTE as an Isca employee (2013-2018).

3. Distribution and Sales of the *Aspergillus* LFD as a CE marked medical IVD.
MHRA CE marking of the LFD for use as a general medical IVD in the European Union was obtained in 2013 and external US evaluation of the LFD, conducted by the NIH/NIAID-funded *Aspergillus* Technology Consortium (www.astecdiagnostics.org), will commence in Nov 2013, providing the data for a 510k FDA approval. An agreement with OLM Medical has been signed for distribution and sales of the LFD worldwide (section 5; source 5). Prior to September 2013, purchase orders of the CE marked device had been received from Australian and Canadian hospitals (section 5; source 6), and internal validation audits of the LFD, prior to order placement, are currently being undertaken in hospitals in the UK, US, France, Germany, Austria, Israel, Turkey, Peru, Iran, and South Africa.

In addition to its commercial activities, Isca is a sponsor of the *Global Action Fund for Fungal Infection* (www.gaffi.org/our-partners/), a Geneva-based foundation whose vision is to reduce illness and death associated with fungal diseases worldwide. As a GAFFI partner, Isca supplies the *Aspergillus* LFD as a research tool for use by resource-limited countries.

Dr Thornton also entered into an IPR agreement with Pfizer Ltd. in November 2013, allowing Pfizer to promote the LFD alongside its antifungal voriconazole, VFend® (section 5; source 7).

The success of the LFD device, prompted by Dr Thornton's research and the subsequent incorporation of Isca Diagnostics Ltd has stimulated a large amount of interest in the media. A list of web references to these are included as section 5; source 8.

5. Sources to corroborate the impact (indicative maximum of 10 references)

Patent

1. New Method of Detecting and Diagnosing Invasive Aspergillosis", with Dr Thornton as the named inventor, was filed by the University of Exeter in the US in Jan 2009 (US61/145,282), and PCT filing (PCT/GB2010/000064) in Jan 2010.
   Details of the *Aspergillus* LFD and mAb JF5 patent can be found at:
   (http://www.wipo.int/pctdb/en/wo.jsp?WO=2010082034&IA=GB2010000064&DISPLAY=DESC)

Supporting documents relating to the establishment of Isca Diagnostics Ltd. and distribution and sales of the *Aspergillus* LFD.

2. Isca Diagnostics IP License Agreement.
3. Isca Diagnostics Shareholders Agreement and Written Resolutions.
4. Isca Diagnostics Incorporation Certificate.
5. OLM Medical Distribution Agreement.
6. LFD purchase orders from Australian and Canadian hospitals.
7. Isca Licence Agreement with Pfizer Ltd.

8. **Reports in public domain (web links)**
Media release by the Society for General Microbiology:
(http://www.alphagalileo.org/PrintView.aspx?ItemId=56558&CultureCode=en)
Other website coverage:
(http://aspergillusblog.blogspot.com/2009/04/quick-new-test-for-aspergillus.html)
(http://www.sciencecentric.com/news/article.php?q=09040225-a-new-test-deadly-fungal-infection-patients-with-damaged-immune-systems)
(http://www.physorg.com/news157869734.html)
(http://computescotland.com/2209.php)
(http://www.sciencedaily.com/releases/2009/04/090401200437.htm)

3* or 4*?

Absolutely no idea!

What about everyone else?

- Feedback from REF2014 panel virtually non-existent
- Only way to gain insight is to look at exemplar REF returns

Institution code (UKPRN)	Institution name	Institution sort order	Main panel	Unit of assessment number	Unit of assessment name	Profile	FTE Category A staff submitted	Percentage of the submission meeting the standard for: 4*	3*	2*	1*	unclassified
10007167	University of York *	1920	A		5 Biological Sciences	Impact	44.37	92.0	8.0	0.0	0.0	0.0
10007803	University of St Andrews	6870	A		5 Biological Sciences	Impact	50.45	90.0	10.0	0.0	0.0	0.0
10003324	Institute of Cancer Research *	230	A		5 Biological Sciences	Impact	34.00	80.0	20.0	0.0	0.0	0.0
10007790	University of Edinburgh	6730	A		5 Biological Sciences	Impact	109.70	80.0	20.0	0.0	0.0	0.0
10007852	University of Dundee *	6720	A		5 Biological Sciences	Impact	73.20	75.0	25.0	0.0	0.0	0.0
10007795	University of Leeds	750	A		5 Biological Sciences	Impact	60.90	71.4	28.6	0.0	0.0	0.0
10007792	University of Exeter *	480	A		5 Biological Sciences	Impact	54.58	50.0	50.0	0.0	0.0	0.0

What makes an Impact Case Study?

General points for consideration:

1. Should have a single, clearly defined focus/outcome

2. Can be ‘industry-facing’, ‘policy-facing’ or ‘education-facing’

3. Research underpinning study may stretch over many years (forms narrative to part 2 ‘Underpinning research’), but REF2020 reporting period is a snapshot of current (2014-2019) impact activity

4. Ideally, evidence should be quantifiable

5. Evidence can’t be anecdotal and avoid testimonies

6. Evidence must be archived and must be corroborated

What makes a 4* 'industry-facing' case study?

Types of impact:

- University R&D has driven guidelines (e.g. NICE) for patient disease diagnosis or management
- University spin-out company, but with activities beyond mere company establishment
- A trading entity offering research products
- Provides technical services to industry
- May have a sizeable workforce (e.g. is an SME with say 30 employees)
- Is generating sizeable income from University licensed IP itself, or
- Is sub-licensing University IP or technical know-how to third parties and in doing so has a demonstrable revenue stream
- Third parties using sub-licensed IP have developed new products (e.g. drugs) and the products are (1) already marketed as trade marked products or (2) are in Phase I, II or III clinical trials
- **A combination of these activities!**

Types of evidence:

- IP licenses/sub-licenses - confidential information provided by licensee(s) or sub-licencee(s) (sales volumes, revenues from use of IP, royalty payments)
- First in-human clinical trials (ClinicalTrials.gov)
- For spin-out - Licensing/sub-licensing agreements, Investors & Shareholders agreement, Articles of Association, Business plan etc.

What makes a 4* 'policy-facing' case study?

Types of impact:

- University Research published in peer-reviewed journals has stimulated or directly influenced policy change
- University research has been used as evidence by regional governments, inter-governmental bodies etc. to drive change and to formulate documents/ guidelines/legislation in public domain
- Technologies or methodologies developed at University have been adopted by government agencies as model systems
- Arguably, regional and national influence is 3*, European Union-level, inter-governmental (e.g. Inter-governmental Panel on Climate Change) or World Health Organisation is 4*
- For 4* impact, activity should be at government-level (e.g. OECD or DEFRA at UK government level), not NGO level (3*)

Types of evidence:

- Research features in assessments reports by inter-governmental panels (e.g. Inter-Governmental Panel on Climate Change), is used as evidence in Council of the European Union legislative packages or is cited in UK Parliamentary committee reports
- Reports of public hearings citing research and used by authorities to enact resolutions and statutory changes to local, regional, national and international law

What makes a 4* ‘education-facing’ case study?

Types of impact:

- University research leading to novel approaches to data capture
- Development and customisation of teaching materials
- Educational DVDs and web-based educational resources
- Licensing of bespoke software tools to industrial partners

Types of evidence:

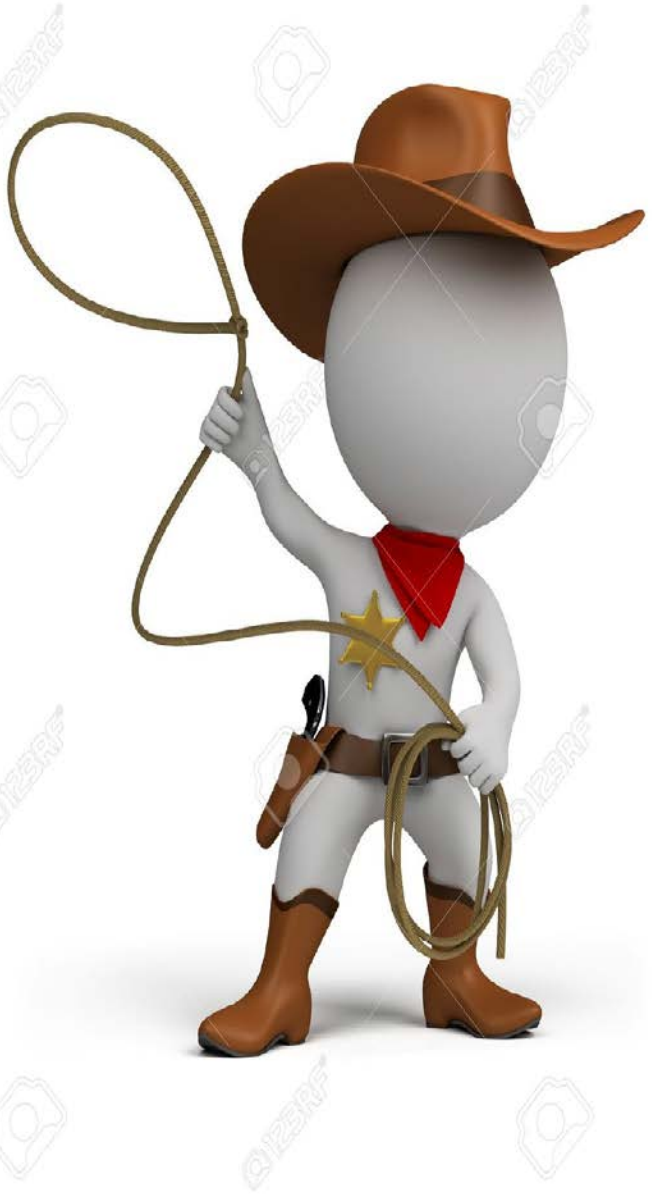
- Metrics demonstrating quantifiable uptake and use of software or other educational resources (e.g. use by 1,225 UK secondary schools and reaching >658,000 pupils)
- Awards for public engagement (e.g. RCUK ‘Innovator of the Year’)
- BBC documentaries
- Extensive media coverage (also applicable to industry and policy-facing ICS)

Skills for impact: Impact capture and evidence

Professor Liz Trinder, Professor of Socio-legal Studies, Law School, College of Social Sciences and International Studies

Impact capture

PROFESSOR LIZ TRINDER, LAW



You need a **tailored** Impact Capture Strategy

What type of impact?

Who/what are the impactees?

What type of evidence?

- Impact on policy
- Public debate
- Others …

What types of evidence to capture (see RKT *Guide to Research Impact Evidence Capture*)

- General info: testimonials, requests, funding
- Events: incl. feedback
- Media and social media coverage
- Policy/practice: 'outcomes'
- Commercialisation: sales, downloads, hits etc

- Evidence of impact, not just activity
- Read 2014 Case Studies: Is there a hierarchy of evidence in your UoA?

Mechanics of capture

- Reactive and proactive capture
- Offline and online capture
- Egosurfing
- Monitoring social media
- Other?

Psychology of evidence capture

Significance of testimonials [some UoAs]

Don’t be squeamish!

University can ask on your behalf

How do I record the captured data?

- What will work for you practically?
  - Super easy
  - Multi-media (incl. offline)
  - Reliable
- What will enable story-telling/chronology?
- Where can you get help?

Recording tools

- Software: symplectic, evernote ….

- Dropbox folder “My impact” docs, pdfs etc
- Email folder “My impact”
- Bookmark folder “My impact”
- Filing cabinet/box “My impact”
- Impact log – using Word and auto Table of Contents kept on Dropbox ….

12th Dec 2014 MoJ Family Justice Bulletin summarises research

12 Dec 2014. Paragraph on our research and their 'experimental' stats.

- Issue 5 Family Justice Bulletin.pdf

March 12th 2015 Justice Committee LASPO report– our study "thoughtful, high-quality, unique"

http://www.publications.parliament.uk/pa/cm201415/cmselect/cmjust/311/311.pdf

Para *95.* We are concerned that it took the Ministry of Justice over a year to publish the report on litigants in person carried out by Professor Liz Trinder and her team. The report seems to us a thoughtful and high-quality piece of work containing unique information capable of informing not only Government responses to the difficulties faced and presented by litigants in person but also those of other stakeholders, including the Judicial Working Group on Litigants in Person. The lack of availability of this report during our inquiry has adversely affected our ability to have an informed debate on this issue. Early consideration of the report could have mitigated the £3.4million knock-on costs for the courts from the rise in litigants in person identified by the National Audit Office. *We deeply regret the fact it took this Committee's intervention for the Trinder report to enter the public domain. We accept the Lord Chancellor's assurance that there was no ministerial involvement in the delay but still require an explanation for it.*

Thank you for attending.

Our next event:

Impact and Engaged Research Network
Funder in focus: RCUK

Monday 25 January, 14.30 – 16.00

Washington Singer, Room 219, Streatham Campus
video link to Daphne du Maurier, Seminar L, Penryn Campus