Unit-level environment template (REF5b)



Institution: University of Liverpool

Unit of Assessment: UOA1 Clinical Medicine



# 1. Unit context and structure, research and impact strategy

#### 1A. OVERVIEW

The University of Liverpool (UoL) UOA1 submission comprises 205 people (190.15 FTE), all of whom are members of the Faculty of Health and Life Science (FHLS). Staff returned to UOA1 have complementary expertise in discovery-led biomedical, translational, and clinical research. Building on strategic changes implemented since REF 2014, we have established three research themes which enable effective collaboration with eight regional NHS hospital trusts and local HEI partners including the Liverpool School of Tropical Medicine (LSTM). These partnerships enable us to successfully align areas of research excellence with regional, national and international health priorities, providing new pathways to impact and substantial increases in joint funding and civic investment. This reorganisation has enabled impressive new clinical academic appointments and improved opportunities for clinical academic training in the UK and overseas. A key driver of our strategy has been a strong relationship with the people of our region and the need to address the high burden of ill health that they experience. Liverpool residents have the lowest life expectancy in England, four years below the national average, and the incidence of many major communicable and non-communicable diseases is among the highest in the UK. We have therefore created multi-disciplinary Clinical Research Centres to address key challenges in regional and global health. Our growing ability to effect positive change is reflected in an expanded portfolio of collaborative research programmes, each with well-defined pathways to impact.

Our research is focused around two major clinical themes, **Infection and Global Health** and **Life Course and Chronic Disease** (Figure 1) which operate alongside a refocused theme of **Cancer**. This theme has been invigorated in response to external review and consolidated activity around basic research, early detection and therapy in areas where Liverpool has an established international profile and can contribute to significantly address the local burden of disease. Activity in each of the research themes is supported by access to extensive local biobanking resources



**Figure 1.** Major clinical themes and cross-cutting capabilities that underpin our success.

(Section 3B.3) and well-established crosscutting excellence in Clinical Pharmacology and Therapeutics (Pirmohamed, Park, Hope, Turner, Owen, Khoo), internationally recognised expertise in Multi-Omics and Systems Biology (Kell, Goodacre, Eyers), Biostatistics and Clinical Trials (Williamson\*), and Health Data Science (Buchan\*) (\*UOA2; also Pirmohamed is Director of HDR UK North).

The impact and reach of our research

is enhanced by a large network of national and international collaborators including academic institutions, the NHS, Public Health England, >100 industrial partners, and organisations in over 100 countries.

#### 1A.1. Faculty Structure

FHLS is the largest of the three Faculties in the University with >2,300 staff, including 412 Principal Investigators and annual responsibility for ~6,000 undergraduates and ~900 postgraduate students. FHLS consists of four research institutes comprising 18 departments (Figure 2). Four cross-cutting directorates provide oversight and governance of strategic investment, regulatory compliance and the enhancement of research, education, and workplace culture.

The Clinical Directorate has been established to provide additional support to clinical academic staff at all career stages in terms of career development, progression and job planning, to facilitate better interactions between fundamental and applied clinical research, and to overcome fragmentation in the local health economy by improving connectivity and research access to patients (Sections 1A.2 &

Infrastructure and **Environment Directorate facilitates** access to sustainable, state-ofthe-art facilities in addition to coordinating strategic investment in new technologies (Section 3B.5) such as: pre-clinical imaging, microscopy, research computing, multi-omic technologies and animal husbandry, which have

2A.1.2).

**FACULTY OF HEALTH AND LIFE SCIENCES CLINICAL DIRECTORATE** Clinical Academic Office, Joint Research ntre, Biobanking and GCP Oversigh **EDUCATION DIRECTORATE** Centre for Educational Development, Student Experience and Engage ent Team, Teaching and Learning Team INFRASTRUCTURE AND ENVIRONMENT DIRECTORATE Technology Directorate, Technology RESEARCH AND IMPACT DIRECTORATE Research and Impact Delivery Team, Postgraduate Res Institute of Life Institute of Infection, Institute of Institute of Systems, Course and Medical Population Health Molecular and Veterinary and Ecology Sciences Sciences Integrative Biology Clinical Infection, Cardiovascular & Health Data Biochemistry & Microbiology & Immunology Metabolic Medicine Systems Biology Primary Care & Mental Health Eye & Vision Molecular & Clinical Infection Biology Cancer Medicine Sciences Vet. Anatomy Physiology & Molecular Physiology & Cell Signalling Musculoskeletal & Psychology Ageing Science Pathology Equine Clinical Public Health Policy Pharmacology & Children's Health Sciences & Systems Therapeutics Livestock & One Health Small Animal Clinical Sciences Ecology, Evolution & Behaviour Figure 2. Faculty of Health and Life Sciences (FHLS) structure.

Departments containing UOA1 staff are highlighted in pink.

facilitated UOA1 research productivity and impact.

The Research and Impact Directorate holds both internal and external (e.g. Wellcome ISSF, MRC Confidence in Concept, BBSRC Impact Acceleration award) funds, which are used to help leverage additional income, support delivery of impact (Sections 3A.2 & 1C.1) and ECR development. The Directorate ensures effective coordination of our postgraduate strategy (Section 2B), enables a positive 'Team Science' culture across research institutes (Section 1D), and provides support for Specialist Research Centres, bringing together staff and resources from across the Faculty to address focused questions within each clinical research theme (Table 1).

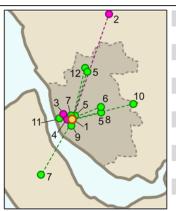
	Centre of Excellence in Infectious Diseases Research (CEIDR)	<b>A • +</b>	
Infection and	Centre of Excellence in Long-acting Therapeutics (CELT)	<b>A • +</b>	
Global Health	Centre for Global Vaccines Research (CGVR) ■	<b>A • •</b>	
Global Health	Health Protection Research Unit: Emerging and Zoonotic Infections ■.	$\triangle \bullet \Diamond$	
	Health Protection Research Unit: Gastrointestinal Infections	$\blacktriangle \bullet \diamondsuit$	
	Arthritis Research UK Experimental Arthritis Treatment Centre for ■	$\triangle \bullet \Diamond$	
	Children		
Life Course and	Liverpool Centre for Cardiovascular Science (LCCS)	$\triangle \bullet \Diamond$	
Life Course and	. , ,	$\triangle \bullet \diamond$	
Chronic Diseases		404	
	Musculoskeletal Ageing (CIMA)		
	MRC Hub for Regenerative Medicine	$\land \bullet \diamond$	
_	Experimental Cancer Medicine Centre (ECMC)	A • +	
Cancer	Liverpool Cancer Research Institute (LCRI)	A • +	
	Centre for Genomics Research	<b>A • +</b>	
	Centre for Metabolomics Research	A • +	
Di	Centre for Proteomics Research	A • +	
Pharmacology and	Health Data Research UK North ■	$\triangle \bullet \Diamond$	
Therapeutics &	Liverpool Clinical Trials Centre (LCTC)	$\land \bullet \diamond$	
Multi-Omics		$\triangle \bullet \bullet$	
		A • •	
	Wolfson Centre for Personalised Medicine	A • •	
Table 1. UOA1 Specialist Research Centres. Sources of funding and support: ■: University,			
	maniferance and a firm and a firm and a firm and bear in a firm and a firm and bear in a firm and a firm a firm a firm and a firm a fi	,	

▲: NHS/heath care providers, •: charity or research council, •: industry.



## 1A.2. Engagement with NHS, Regional, National and International Partners

Liverpool has the highest density of NHS Trusts in the UK outside of London; historically this impeded the development of a coordinated, mutually beneficial strategy to tackle regional health priorities. However, the formation of a regional academic health science consortium called Liverpool Health Partners (LHP), comprising eight local NHS Trusts and regional academic institutions (Figure 3) has turned the challenge of having so many specialist NHS Trusts into a key asset for the University and the Liverpool region. Working together with LHP, we have aligned the research strategies of the University and NHS Trusts to facilitate access to resources, enhance clinical research and translate research into clinical impact. An example of the success of this close working relationship with civic and health partners was in our response to COVID-19 where lain Buchan (UOA2) and Louise Kenny helped to lead the introduction and evaluation of lateral flow testing and disease mapping in the local population.



- 1. The University of Liverpool
- 2. Edge Hill University
- 3. Liverpool John Moore's University
- 4. Liverpool School of Tropical Medicine
- 5. Liverpool University Hospitals NHS Foundation Trust
- 6. Alder Hey Children's NHS Foundation Trust
- 7. The Clatterbridge Cancer Centre NHS Foundation Trust
- 8. Liverpool Heart and Chest Hospital NHS Foundation Trust
- 9. Liverpool Women's NHS Foundation Trust
- 10. Mersey Care NHS Foundation Trust
- 11. NHS Liverpool Clinical Commissioning Group
- 12. The Walton Centre NHS Foundation Trust

**Figure 3.** Liverpool Health Partners (LHP). A University-initiated consortium facilitating clinical research activity and delivery between the University, the NHS and regional academic partners.

Each of our research themes share space, resources and staff with multiple NHS Trusts, and research centres that form part of LHP (Table 1). Recent exemplars include the formation of the Centre for Excellence in Infectious Diseases Research (CEIDR), Liverpool Cancer Research Institute (LCRI), the Liverpool Head and Neck Centre and the Liverpool Centre for Cardiovascular Science (LCCS), all of which address health priorities associated with health inequality. National partnerships developed during the REF period include those established through our NIHR Health Protection Research Units (HPRUs) in Emerging Infections & Zoonoses (with Public Health England, LSTM and Oxford University) and in Gastrointestinal Infections (with Public Health England and University of Warwick). Multiple international partnerships are led by UOA1 staff with a major focus on lower middle-income countries to support world-leading programmes of research.

# 1.A.3. A Vibrant and Diverse Research Environment that Underpins Success

The vitality and sustainability of our research is demonstrated by our major scientific discoveries across a wide spectrum, significant investment in infrastructure, deep integration of research across basic and clinical disciplines, well-developed training and support initiatives, and an ability to translate research into real world impact across each of our research themes.

#### This is underpinned by:

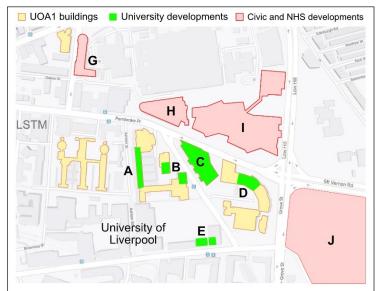
 A well-developed research base: In total, the FHLS comprises 412 research-active principal investigators, including 96 clinical academics. In July 2020, associated research groups totalled 508 postdocs and 861 PhD/MD students with ~45% of these staff and



- students associated with UOA1 research. A further ~300 core funded technical and research support staff are funded by the FHLS.
- Investment in our estate with NHS and other regional partners: UOA1 research occupies predominantly open-plan, multi-group laboratories located on the main University campus and has additional shared occupancy on eight sites with NHS partners and LSTM. During this REF period there has been significant NHS and regional investment, which has led to the revitalisation and co-location of major NHS and commercial clinical providers with core University estate, housing clinical research staff within UOA1 (Figure 4).

These investments, together with sequential phases of Faculty reorganisation, have facilitated a more effective integration of research across basic and clinical disciplines, providing improved opportunities for staff training and career development. Examples include:

> Succession planning: recruitment strategy aims to attract the brightest talent; these include a total of 61 new Category A staff (28 senior staff and 33 ECRs), the majority of ECRs through Tenure Track **Fellowships** (TTFs), innovative scheme launched in 2012. All TTF appointments made since 2014 strategically aligned with our research strategy, contributing new vibrancy and skills to each of the UOA1 themes and ensuring continued productivity and success of each discipline. 33 UOA1 REF1a staff are either



- A: £7M refurbishment to relocate Cancer, Precision Medicine and Pharmacology and Therapeutics researchers together.
- B: £4M refurbishment to accommodate a new MRI and create a Pre-Clinical Imaging facility. C: £25M new building to co-locate Infection, Life Course & Cancer researchers.
- D: £2M refurbishment to better integrate Multi-Omics facilities and recruits.
- E: £1M to expand the Data Centre that improves support for UOA1 research computing. F: £52M (£23.5M) to build the Materials Innovation Factory integrating UOA1 research with
- Chemistry and industry partners (not shown).
- G: £25M LSTM Life Sciences Accelerator to support industry engagement.
- H: £165M relocation of Clatterbridge Cancer Hospital adjacent to the University to improve research integration.
- I: >£650M new Royal Liverpool University Hospital.
- J: £600M Liverpool City Council investment in the Liverpool Knowledge Quarter.
- K: £260M (£16.5M) Institute in the Park, new UOA1 research labs at Alder Hey Children's Hospital (not shown).
- L: £10M CREATOR building in Malawi supporting postgraduate training of African scientists (UoL/LSTM collaboration).
- Figure 4. Campus and major local developments relevant to UOA1. University investment is indicated in red

independent fellowship holders or recruited via the TTF scheme.

- Training the next generation of researchers: Research activity during the REF period has been supported by ~800 MRes/MPhil students, 30 UOA1 MD and 526 UOA1 PhD students including students from the BBSRC-NLD, MRC-DiMeN, NERC-ACCE and Wellcome Molecular & Cellular Physiology doctoral training programmes (DTPs), the MRC Clinical Pharmacology PhD training programme (with involvement from Roche, UCB, Eli Lilly, and Novartis), the UoL/LSTM Wellcome Clinical PhD Programme in Health Priorities in Resource Limited Settings; the NIHR HPRUs, and 16 international institutions with whom we have joint/dual PGR training programmes.
- **High quality partnerships** (Section 4):
  - Clinically aligned research centres (LCRI, CEIDR, CELT, LCCS and CIMA; Sections 1B & 3B) within each of our thematic areas co-ordinate academic, industry and healthcare sector partners in focused activities aligned with the strategic goals of the research theme.



- Research associated with the MRC CDSS has involved productive collaboration with >10 industrial partners including leading four European IMI grants (Mip-DILI, Trans-Bioline, Trans-QST, Web-RADR) in addition to a recent Accelerating research & development for advanced therapies (ARDAT) IMI award.
- Membership and lead roles in major regional health and research partnerships: the N8; Health Data Research UK North (Director: Pirmohamed); Northern Health Science Alliance; Liverpool Health Partners.
- National partnerships with Public Health England, LSTM, and the Universities of Oxford and Warwick, via the Liverpool-led NIHR HPRUs in Emerging & Zoonotic Infections and in Gastrointestinal Infections, ensure that UOA1 staff are at the forefront of research to help protect the UK population from infection threats to human health (including COVID-19 through the ISARIC consortium), and help train the next generation of public health-facing infection researchers.
- Longstanding international partnerships with low-and-middle-income countries in Africa, Asia and South America, which underpin our Infection and Global Health theme (Sections 1B & 3B). Recently NIHR funded Global Health Research Groups have brought together researchers in UK, Malawi, India and Brazil (ZikaPLAN, Brain Infections); and UK, South Africa and Uganda (warfarin anticoagulation in patients with cardiovascular disease).
- **Improved clinical academic training:** We established an integrated clinical academic training pathway and appointed a Director of Clinical Academic Development (2A 1.2).
- A fair research environment: Our sector leading approaches have been recognised by the award of a Gold Athena SWAN Charter Award in 2017 and Office for Students and Research England Catalyst funding for innovative improvements to postgraduate mental health and wellbeing support.

These developments have been important for sustaining and enhancing our research capacity and delivering outputs addressing regional and global health challenges. Examples of our success include:

- Research investment: UOA1 activities cover a wide spectrum of biomedical research supported by a strong and diverse research funding portfolio with total grant expenditure of ~£245M over the REF period. UOA1 academics have contributed to 70 successful large (>£1M) grant applications during the REF period (UOA1 share: ~£84M) with major funding (UOA1 share: ~£39.6M) for the research centres (Table 1) underpinning our research strategy.
- Outputs: UOA1 academics have contributed to over 4,000 publications during the REF period (430 included in this return), reflecting activity across all areas of biomedical science and wider interdisciplinarity (Figure 5). ~21% of our publications are in the top 10% field-weighted citation percentiles worldwide. Collaborative publications with industry have increased from ~5% in 2014 to ~11% in 2020, consistent with our strategy for enhancing the translational potential of our work.
- **Societal benefit:** 10 REF impact cases with many others being developed and promoted through our local 'Impact Matters' initiative.



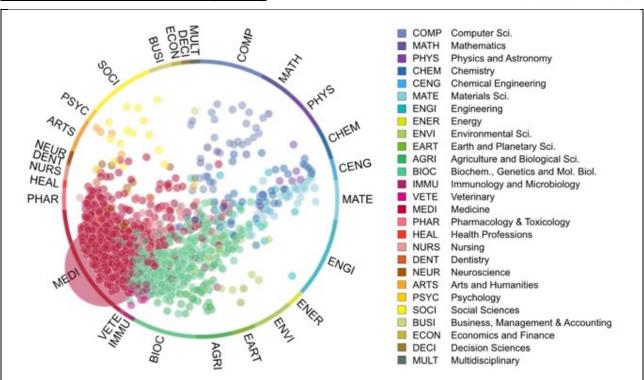


Figure 5. Topic analysis for all University of Liverpool UoA1 publications in the REF period. Each dot represents a distinct SciVal topic in which we have published; dot size indicates the number of publications in that topic (Source: SciVal).

# **1B. RESEARCH STRATEGY**

1B.1 Research Objectives and Plans during the 2014 assessment period

Over the assessment period, the research aims for UOA1 have sought to:

- 1. Develop strong and sustainable partnerships with regional NHS Trusts.
- 2. Address regional and global health priorities through translation of world-leading research for societal benefit.
- 3. Foster a fair and inclusive research environment that supports all staff and students at all stages of their career.
- 4. Develop a diverse and sustainable funding base.
- 5. Invest and build on our unique strengths in underpinning technologies.
- 6. Expand mutually beneficial partnerships with industry and academic institutes in the UK and internationally.

To achieve these goals, we have focused investment on a limited number of established and emerging areas of clinical excellence. We have appointed 68 new members of staff including seven UOA1 research centre and departmental leads; six senior appointments to lead expansion of underpinning technologies; and 33 research/Tenure Track Fellows who constitute our next generation of research leaders.



# Research themes, strategic objectives and priority areas

#### Infection and Global Health

~40 UOA1 researchers undertake research in Infection and Global Health, with 139 active research awards and 481 (£71.3M; investigator/funder contribution) total awards during the REF period. Through the Centre of Excellence in Infectious Diseases Research (CEIDR, in partnership with LSTM), the Centre for Global Vaccine Research (CGVR), and the Centre of Excellence in Long-acting Therapeutics (CELT), we have engaged with industrial partners to develop and deliver the next generation of diagnostics, therapeutics and vaccines with a major focus on sepsis, emerging infections and antimicrobial resistance (Section 3B.4). Through the recently renewed national NIHR HPRUs in Emerging & Zoonotic Infections and in Gastrointestinal Infections, we work with Public Health England to protect the UK population from established and emerging infection threats to health. We address globally important infections including brain, respiratory and gastrointestinal infections, and maternal and neonatal sepsis, through our overseas programmes in Malawi, Uganda, India and Brazil. We work closely with colleagues returned to UOA6, where possible adopting a "One Health" approach to address Infection and Global Health Challenges (e.g. through a £8M GCRF funded One Health Programme in the Horn of Africa). Our existing infrastructure and expertise enabled us (e.g. Semple, Solomon, Khoo, French, Darby) to act rapidly and make significant contributions to both local, national and international responses to the COVID-19 pandemic, exemplified by Liverpool's leadership of the clinical characterisation of COVID-19 through the ISARIC consortium and contributions to SAGE and NERVTAG (Semple).

Strategic priorities					
l la de minaia a	• improved understanding of host response and infection pathogenesis.				
Underpinning mechanisms	• improved understanding the spread of emerging and drug resistant infections.				
Translation	development of new diagnostic tests for infectious diseases.				
& clinical	<ul> <li>development of new vaccines and antimicrobial therapies.</li> </ul>				
application	provide evidence to predict and mitigate global infection spread.				
Focus areas					
diagnostics	Development and evaluation of novel diagnostics to common infection				
ulagriostics	syndromes eg. sepsis, meningitis, pneumonia and gastroenteritis.				
epidemiology	Tracking infection spread eg. COVID19, Ebola, Lassa, HIV, Influenza,				
сріастіююду	Pneumococcus. Measuring the burden of vaccine-preventable infections.				
host response & pathogenesis					
thoropoution	Development of small molecules, phages and immune adjuvants to treat				
therapeutics	drug resistant microbial infections. Precision dosing to mitigate resistance.				
Vaccinos	Development and evaluation of vaccines against established (eg Rotavirus,				
vaccines	Pneumococcus) and emerging (eg. Zika) infectious agents.				
Figure 6. Infection a	Figure 6. Infection and Global Health strategic priorities and major focus areas.				



#### Life Course and Chronic Disease

~70 UOA1 researchers actively contribute to this theme, which incorporates major research programmes ranging from neonatal and childbirth through to child health and aspects of age-related chronic disease. Current research is supported by 173 active awards with ~£48M in funding during the REF period. Research in this theme benefits from close partnerships with the largest specialist Women's Hospital in Europe, Alder Hey Children's Hospital, and the Walton Centre, which offers one of the most comprehensive neurosurgery and neuroradiology services in the UK.

Major research initiatives include: the Harris WoW Centre for Preterm Birth Research; the Wellcome funded Children Growing up in Liverpool (C-GULL) programme, which is the UK's first birth cohort in two decades; the European Medicines Agency Connect4Children (C4C) initiative (€140M); and the NIHR Alder Hey Clinical Research Facility for Experimental Medicine which is one of Europe's leading Paediatric Rheumatology Research Centres. Michael Beresford hosts and coordinates Liverpool's EULAR Centre of Excellence Arthritis Research and the UK Paediatric Rheumatology Clinical Studies Group. The theme of rheumatology extends through to ageing and chronic disease led by researchers in the MRC-Arthritis Research UK Centre for Integrated Research into Musculoskeletal Ageing (CIMA). Other expanding areas of research include eye and vision disorders, epilepsy and pain research (in partnership with Walton Centre), and the new Liverpool Centre for Cardiovascular Science (Director: Lip). The unifying aim of all of our age-related research is to understand risk factors for chronic disorders and the development of new preventative and personalised therapeutic interventions in order to improve lifetime health and reduce costs to the NHS and other healthcare systems.

Strategic priorities				
	<ul> <li>improved understanding of cardiovascular and metabolic disease.</li> </ul>			
Underpinning	<ul> <li>improved understanding of cross-species musculoskeletal disorders.</li> </ul>			
mechanisms	• improved understanding of early life determinants of health and wellbeing.			
	<ul> <li>improved understanding of eye and vision pathophysiology.</li> </ul>			
T	development of new tests and diagnostic tools.			
Translation & clinical	• development of new treatments, nutrition or exercise-based interventions			
application	to reduce the risk of age-related musculoskeletal disorders.			
аррисацоп	Exploit new therapeutic targets to treat eye diseases.			
Focus areas				
ageing	mechanisms underpinning early life health and chronic diseases of ageing.			
musculoskeletal eye and vision	materials and technologies for improvement of vision, musculoskeletal and cardiovascular function.			
cardiovascular & metabolic medicine	lifestyle, behaviour and clinical sciences relating to cardiovascular health and pathophysiology and metabolic medicine.			
Figure 7. Life Course and Chronic Diseases strategic priorities and major focus areas.				

#### **Cancer Medicine**

~60 UOA1 researchers work within the Cancer Medicine theme, contributing ~20% of our research income. During the REF period, external review of our cancer strategy supported a refocus of our research into areas of clear strength and prompted the establishment of the new Liverpool Cancer Research Institute (LCRI) and the Liverpool Head and Neck Centre. Together with the Liverpool Experimental Cancer Medicine Centre (pancreatic and haematological cancers), this has enabled us to better consolidate our research activity around specific areas of Cancer Research where Liverpool has an established international profile (*i.e.* lung cancer screening and early detection, head and neck cancer, pancreatic cancer, uveal melanoma, therapeutic safety and precision medicine), while also addressing the regional demands of cancer



burden. Two new expanding areas of cancer research include immunotherapy (head and neck cancer) driven by the recent appointment of Christian Ottensmeier, and the mitigation of adverse cardiovascular side-effects of chemotherapy, led by a partnership between the MRC CDSS (Pirmohamed), LCCS (Lip) and the Liverpool Heart and Chest Hospital NHS Foundation Trust.

Strategic priorities			
Underpinning	• improved understanding of cancer genetics, biochemistry and cell biology.		
mechanisms	• improved understanding of drug resistance and therapeutic responses.		
Translation	<ul> <li>development of new tests and diagnostic tools for early detection and then subsequent monitoring of cancer progression.</li> </ul>		
& clinical	• development of new treatments & improve responses to current therapies.		
application	• inform cancer prevention and treatment policy to reduce disease burden.		
Focus areas			
cell signalling	drug targets, kinase and ubiquitin biology, systems biology of cancer.		
early detection biomarkers, population studies, health inequalities. microenvironment drug interactions, extracellular matrix biology, tumour heterogeneity.			
			mutagenesis DNA damage/repair, sensitisation to chemotherapy and radiother
therapy responses	clinical trials, drug resistance, patient stratification.		
tumour types	blood cancers, head & neck, liver, lung, pancreatic, uveal melanoma		
Figure 8. Cancer Medicine strategic priorities and major focus areas.			

# <u>Cross-cutting excellence in Pharmacology and Therapeutics</u>

The University of Liverpool has a long-established international reputation in the area of Clinical Pharmacology, Drug Safety and Personalised Medicine, being awarded the Queen's Anniversary Prize for work towards improving the safety and effectiveness of medicines in 2017. This is a major focus of our research activity with ~40 researchers providing a range of molecular, computational, and clinical expertise, generating ~£51M in awards during the REF period. Expanding on the foundations developed through the MRC Centre for Drug Safety Science (CDSS), this cross-cutting theme provides valuable expertise and infrastructure to facilitate effective translational research in all three of our research themes, including the implementation of Personalised Medicine (Pirmohamed, Alfirevic), Drug Safety Science (Park, Pirmohamed), Infection Pharmacology (Khoo, Owen, Turner), Antimicrobial Pharmacology (Hope), Neuropharmacology (Marson, UoA4), the avoidance/mitigation of therapeutic adverse drug effects (Pirmohamed, Sharma, Lip, Lane) and novel nanotherapeutics (Owen). Our themes also benefit from a large complement of specialised infrastructure and internationally recognised expertise in Multi-Omics (Section 3B).

# 1B.2. Achievement Against Strategy During the REF Period

Our strategy has been focused on facilitating outstanding discovery-led science and driving translation and impact that will have long-term benefits for patients and the public. Strategic aims implemented during the current REF period have had a significant positive effect in the following areas:

#### i) Enhancing societal impact

Over the reporting period, UOA1 impact cases and research outputs have led to significant regional, national and international benefits to society. Exemplars are shown in Figure 9.



	Δ International genetics database leading to improved transplantation success (Jones
New testing,	△ Genetic screening to avoid adverse drug reactions (Pirmohamed)
screening	□○ NHS ocular screening to detect diabetic retinopathy (Harding)
and methods	<ul> <li>Lung cancer CT screening to stratify high risk individuals (Field)</li> </ul>
	△○ Liverpool prognosticator tool to stratify uveal melanoma metastatic risk (Coupland)
	<ul> <li>☼ Novel antimicrobials to overcome antimicrobial resistance (Hope)</li> </ul>
New	□ Development of the first effective therapy for Alkaptonuria (Gallagher)
treatments	☐ SGLT2 inhibitor drugs for diabetes treatment (Wilding)
treatments	Transforming children's lives through the Experimental Arthritis Treatment Centre for Children ( <b>Beresford</b> )
	□ Improving the management of brain infections in the UK (Solomon)
01	O HPV vaccinations for boys to address rise in HPV-associated cancers (Jones)
Changes to guidelines & policy	Introduction of global rotavirus vaccination programmes - saving ~500,000 lives per year (Cunliffe)
α μοπογ	⊕ Improved control of viral haemorrhaghic fever (Hiscox)
	△ Improved decision support for drug interactions (Khoo)

# Figure 9. Outputs and impact exemplars leading to societal benefit.

Strategic themes: ⊕ Infection, □ Life Course, ○ Cancer, △ Pharmacology and Therapeutics.

# ii) A fair and inclusive research environment

Over the assessment period, we have devoted considerable time to analysis of our practices and culture and implemented significant organisational and operational changes to ensure equality of opportunity for all our staff and students. Our sector-leading approaches have been recognised with the award of a Gold Athena SWAN Charter Award in 2017 (Section 2C.1) and we have advanced plans for extending this accreditation to all of our remaining departments currently holding Silver awards.

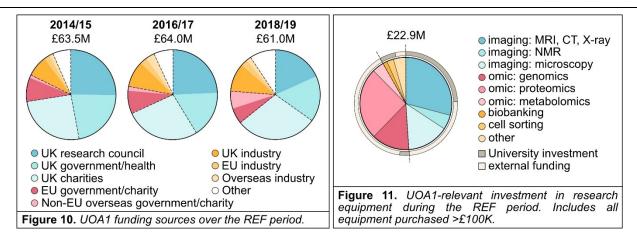
# iii) A diverse and sustainable funding base

Our research income over the reporting period has exceeded £230M. Funding has come from ~2,000 research awards (Section 3A.1) from 368 different funders including 113 companies (Figure 10). Research income has been sustained over time and support from pump-priming schemes and improved internal communication about funding opportunities has helped us to successfully diversify our funding portfolio by proportionally increasing contributions from industry and overseas governments and charities. New strategies for pump-priming and peer-reviewing research grant applications before submission (Sections 2A.4, 3A.2) have helped to improve UOA1 Research Council grant success rates. The most recent data available from these funders indicate that between 2013/14 and 2017/18 our national rankings for total awards improved from 26th to 13th and 16th to 4th for the MRC and BBSRC respectively.

# iv) Enhanced integration of capabilities and supporting infrastructure

Our research is underpinned by exceptional Shared Research Facilities (SRF) that operate under the auspices of LIV-SRF (Section 3B.5) and offer a comprehensive range of capabilities. During the REF period there has been significant strategic investment in imaging technologies and our support for multi-omic analysis has leveraged substantial EU and Research Council funding (Figure 11). We have also further expanded our existing expertise in 'omics and systems biology through the recruitment of Kell and Goodacre to lead GeneMill and our new Centre for Metabolomics Research.





v) Enhancement of interdisciplinarity and mutually beneficial partnerships with the NHS, Public Health England, industry and academic institutions

FHLS was reorganised in 2019/2020 to focus on areas of internationally recognised research strength within four new institutes and to increase critical mass in strategically important areas that align with University research themes (Advanced Materials; Personalised Health; Infectious Diseases; and Starting Well, Living Well, Ageing Well). This drives inter-Faculty collaboration and has created opportunities for the development of new interdisciplinary research areas to maximise impact via strategic appointments and investment.

Researcher training represents an active area for developing and driving interdisciplinarity. Over the REF period, CASE and industry-funded PhD students from a diverse portfolio were registered in FHLS that were associated with UOA1 laboratories (Section 2B.1). Relationships with companies such as Pfizer, AstraZeneca, Gilead Roche, UCB, Eli Lilly, Novartis, Unilever, and GSK that were associated with these studentships were facilitated by the pump-priming schemes provided by FHLS for this purpose (Section 3A.2). Data sciences have crosscutting relevance to UOA1 researchers; this is increasingly a compulsory component of postgraduate training as exemplified by all of our BBSRC-funded PhD students being enrolled on the SysMIC online and bespoke UoL systems biology training courses. This type of interdisciplinarity is also a fundamental feature of our MRC-funded North West Hub for Trials Methodology Research, and now the MRC/NIHR Trials Methodology Research Partnership.

Each of the UOA1 research themes has established clinically aligned research centres to focus research activity and build partnerships with NHS and industry (Section 3B.4). An exemplar is Infection and Global Health where CEIDR co-ordinates research activity between UoL, LSTM, NHS Trusts and industry partners. Antimicrobial resistance (AMR) is a priority area for CEIDR and, uniquely amongst the network of UK AMR Centres, Liverpool researchers focus on precision dosing of antimicrobials, supported by the long-standing cross-Faculty expertise in Pharmacology and Drug Safety Sciences. The Centre of Excellence in Long-acting Therapeutics (CELT) was established to build upon the long-standing and successful collaborative activity between UOA1 and UOA9 staff working in precision medicine, infection biology and nanomedicine development. CELT was awarded £24.5M for the LONGEVITY project that aims to develop long-acting formulations for malaria and TB prevention, and a single-injection cure for hepatitis C. The project is creating drug-nanoparticle conjugates that will transform treatments by introducing long-acting injectable formats for diseases that currently affect 300 million people worldwide.

<u>Case study</u>: LONGEVITY builds upon long-term inter-Faculty collaboration with colleagues in Chemistry to develop nanomedicines. Their work to conjugate anti-HIV drugs to nanoparticles has significantly increased the bioavailability of these drugs with the potential to reduce the manufacturing capacity required for effective global HIV treatment by 50%.



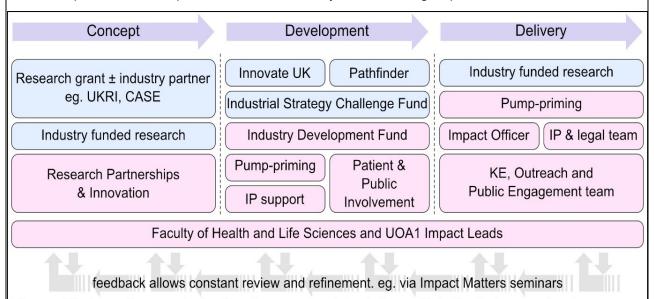
## 1B.3. Future Strategic Aims and Goals for Research

The impact of the re-organisation of FHLS started in 2019 and the associated improvements to our research environment, research culture and support structures will be realised over the forthcoming REF cycle. At the heart of the re-organisation was the goal to further improve the connections between discovery-led and clinical research, the NHS, public health partners and industry to tackle health inequalities and improve health outcomes across the Liverpool City Region and beyond. Importantly, the three clinical UOA1 research themes are retained as major focus areas of three (of the four) FHLS research institutes (Figures 1 and 2), and their strategic priorities and focus areas (Section 1B.1) remain relevant and supported for the next REF cycle.

# 1C. RESEARCH IMPACT

Key to our strategy is the requirement of staff to fully embed impact considerations into all stages of research, which is enabled by bespoke staff training and development. Impact is incentivised as part of the University's core obligation to maximise the public benefits of research; it is embedded within our recruitment criteria, specifically recognised within our promotion structure and accounted for in our workload models. Our focused training and networking events, including the Impact Matters seminar series, raise awareness and encourage involvement from all staff from the earliest career stages. We have launched a new module delivered to all masters and first year PhD students which includes formal sessions on Public Understanding of Science and Making a Business out of Science.

The Faculty Research and Impact Directorate promotes an active impact culture and environment, including coordinated support via a team of Institute-facing Impact Officers and Faculty-managed funds such as Impact Accelerator Awards. We have long recognised that significant investment is required to deliver high quality impact and we have invested heavily at each step in the impact 'pipeline', with the range and scope of support growing year on year (Figure 12). Our strategy to achieve impact extends well beyond those activities presented as formal impact cases and provides benefit to many stakeholder groups.



**Figure 12.** Impact support pipeline from concept to delivery. UoL funded support schemes are highlighted in pink.



## 1D. POSITIVE RESEARCH CULTURE

# 1D.1. University Commitments to an Open Research Environment

We are committed to disseminating the outputs of our research and scholarship as widely as possible. All researchers commit to the University of Liverpool's Open Access Publication Policy. The University acknowledges the benefits of open access publication in terms of greater visibility, potential for more rapid dissemination, and greater research impact. To support this, all author accepted manuscripts are required to be deposited in the University repository within three months of acceptance. Where Gold Open Access is required and cost is not covered by the funder, the University provides an Institutional Fund for Open Access that has helped to ensure that UOA1 papers are open-access compliant. Staff within UOA1 are encouraged to place pre-prints of their work in appropriate repositories and the Institutional Repository is provided to facilitate open access to articles, data and other outputs.

# 1D.2. Data Management, Storage and Security

UOA1 subscribes to the University's Research Data Management policy, which illustrates our commitment to maintaining the highest standards of rigour and integrity in research. The policy recognises that data collected during a research project is a key asset that will continue to yield benefits after the conclusion of the project. The University recognises its duty to protect the confidentiality of the personal research data in keeping with its responsibilities under the General Data Protection Regulation, and any research project that collects personal data must have formal ethical approval from the University. All UOA1 Principal Investigators are required to complete a data management plan (DMP) prior to the commencement of research projects. In the case of personal research data, the DMP is a required component of the application for research ethics review. Primary responsibility for the management of data produced during research activities lies with the Principal Investigator. When research is conducted with other institutions and independent researchers, all parties are required to agree to a plan for managing the data generated during the study.

# 1D.3. Research Integrity and Compliance

The University of Liverpool made a commitment in 2017 to follow the recommendations within the Concordat to Research Integrity. As part of that commitment, the University was one of the first 12 academic members of the United Kingdom Reproducibility Network, a peer-led consortium that aims to ensure the UK retains its place as a centre for world-leading research, by investigating the factors that contribute to robust research, providing training in research integrity and data management, and disseminating best practice. It includes representation from research councils, charities and major journals.

We have established robust systems of oversight that have been successful in detecting malpractice and this has led to commensurate disciplinary responses and engagement with journals and funders about irregularities that have been identified. We are continually reflecting on our experiences and introducing further improvements that are intended to increase our ability to detect malpractice and mitigate its impact. For example, we are piloting a requirement to deposit all primary data and associated contextual information prior to publication into a read-only University archive that can be independently cross-referenced if the integrity of any data is challenged. We will also be piloting electronic lab notebooks (commencing Jan 2021) across FHLS for better data management and evaluation and instigating periodic research integrity audits.

To ensure that staff are fully aware of their responsibilities, FHLS has a robust system of ethics support and a committee structure that supports good ethical practice across all areas of UOA1. The University provides online research integrity courses to provide a common foundation



for responsible research practices. Courses in research integrity, developed by the Epigeum consortium, are designed to give researchers an essential understanding of responsible research practices. Culturally, we foster a highly collaborative team approach to our science that minimises researchers working in isolation.

To inculcate good practice from the beginning, Year 1 PhD students attend compulsory training workshops that focus on principles of data management, reproducible research, ethics and open science. Research 'Away Days' have also provided us with the opportunity to run institute-wide sessions on scientific fraud, their causes and their impact.

# 1D.3.1. Clinical Samples

Access to patients and human samples is essential for the research of most groups within UOA1. The Human Material Oversight Committee ensures compliance with Human Tissue Act regulations and the University's Research Integrity Policies. The Faculty's three research ethics committees consider research involving human participants, human tissues, and personal data. All ethics committee members have had Epigeum training, in-house ethics training is regularly offered and there are regular drop-in sessions organised by the University ethics team. University sponsorship of projects also ensures ethics oversight and the requirements for Good Clinical Practice training.

#### 1D.3.2. Pre-Clinical Research and In Vivo Experiments

All UOA1 research is fully compliant with University, Home Office and relevant national and international regulations. The Facilities and Infrastructure Directorate co-ordinates support and expert review panels that approve proposals and oversee ongoing compliance with health and safety, genetic modification, animal welfare and ethical approval for their use. UOA1 researchers have access to a range of experienced peers and former panel members, case studies, training sessions and courses to help them to prepare their applications for ethical or regulatory approval.



# 2. People

#### 2A. STAFFING STRATEGY AND STAFF DEVELOPMENT

#### 2A.1. Staffing Strategy

Our strategy over the REF period has been to further develop and sustain research excellence in themes where we have significant critical mass of outstanding researchers and infrastructure (Table 2). ~30% of our return is comprised of staff recruited during the REF period.

	Primary Affiliation			total staff	
	Infection	Life Course	Cancer	Cross-cut.	0 20 40 60 80 100
TTF	3 (6)	5 (7)	3 (4)	4 (5)	
Lecturer	4 (5)	7 (12)	3 (8)	4 (9)	
Senior Lecturer	2 (7)	3 (15)	4 (14)	1 (4)	
Reader	1 (3)	1 (3)	1 (4)	0 (1)	
Professor	0 (18)	10 (35)	2 (30)	3 (13)	
Clinicians	5 (18)	13 (29)	6 (20)	2 (3)	■ clinician
Non-clinicians	5 (21)	13 (43)	7 (40)	10 (29)	non-clinician

**Table 2.** Recruitment and staffing overview. Staff recruitment to priority themes during REF, the total number of Cat 1A staff in each category at the census date are shown in brackets. TTF: Tenure track fellow; Cross-cutting - Pharmacology & Therapeutics, Multi-Omics

# 2A.1.1. Recruitment, Retention and Succession Planning

FHLS has recruited extensively during the REF period, resulting in 148 new academic appointments (61 returned in UOA1). Our strategy is delivered by securing and developing the next generation of research leaders (33 were appointed to their first independent position); this is balanced by substantive senior appointments in order to provide leadership and mentoring, and by recognising emergent research leaders through promotion. A key priority throughout REF has been to increase the critical mass of clinical academics at all levels. Clinical academics represented ~30% of UOA1 staff at the start of REF; almost half of all new recruits have been clinicians, including outstanding leaders in Cardiovascular (Lip), Maternal and Child Health (Kenny, Hedrich) and Cancer (Ottensmeier).

To ensure that we attract the widest possible pool of applicants we have an open and transparent recruitment policy; we advertise via a wide array of routes (e.g., University website, jobs.ac.uk, Nature, social media and professional networks such as WISE) and we have redesigned our internal and external facing websites to improve information on our working environment and policies.

<u>Case study:</u> The effectiveness of our recruitment policy is evidenced by the success of new UOA1 staff. 61 staff recruited since 2014 currently hold £27.6M of external awards and generated 845 publications eligible for our return.

All new lecturer-level academic appointments in our research institutes follow a 3+2 Year Tenure Track Fellowship (TTF) model. Applications for tenure for TTFs are reviewed at year three with confirmation of appointment being contingent upon successfully securing competitive external funding and making substantive research contributions. If required, up to two years of further salary funding is available to applicants to provide the opportunity to develop their tenure applications or to secure alternative employment. The TTF scheme has also been successfully used to attract externally funded research fellows that align with our strategic research priorities.



<u>Case study:</u> Jo Fothergill represents an example of our successful initiatives for developing future research leaders. She leveraged successful PhD and post-doctoral periods in Liverpool to secure a competitive Leverhulme Early Career Fellowship in 2012 and a place on the University TTF scheme. Mentoring, support and financial investment associated with the TTF contributed to the establishment of a productive research programme in Infection and Global Health and the award of a Medical Research Foundation Fellowship in Respiratory Diseases. Fothergill secured tenure in 2016 as a Lecturer and was promoted to Senior Lecturer in 2018. She has received numerous accolades, including Young Scientist of the Year award by the European Cystic Fibrosis Society.

### 2A.1.2. Clinical Academic Recruitment and Development

The Clinical Directorate ensures that clinical academic research, training and development of the ~250 clinical academic and research staff at the University is co-ordinated and connected with FHLS strategy, and regional & global health priorities. Delivery is facilitated by the Liverpool Integrated Clinical Academic Training (ICAT) team overseen by the recently appointed Director, Paul May. ICAT is based on a joint strategy developed by the University, LSTM, NIHR, Health Education England Northwest and NHS Teaching Trusts and focuses on academic foundation training, academic clinical fellows (ACFs), clinical PhDs, and academic clinical lecturers (ACLs, who must hold a PhD on appointment). Allied Health Professional academics are also part of the programme. Specific support and mentoring are provided for each stage and progress is reviewed annually via academic and subsequent formal Annual Review of Competency Progression (ARCP). The academic ARCP that we have developed is considered an exemplar by Health Education England and is now being trialled in other locations. Clinical lecturers receive specific support through protected academic time and association with a successful research group that is overseen by the ICAT programme. Having identified that retention of talented ACLs to senior clinical academic posts is a priority, we have established a new post-CCT clinical fellowship scheme where the University and NHS co-fund fixed term (three-year) senior clinical fellowships. These fellowships are competitively offered at Consultant level to ACLs who are nearing completion of clinical training, and aim to support the development of externally funded, intermediate-level clinical fellowships that are precursors to applying for tenure. These have been piloted in departments focusing on Infection and Global Health and clinical Pharmacology and Therapeutics, with the first two fellows successfully going on to secure externally funded clinical fellowships. This is now an established activity.

<u>Case study:</u> Our efforts to better understand the needs of ACFs has resulted in targeted support to enhance their opportunities for interactions with peers, mentors and advanced training, and led to 88% of ACFs progressing to PhD training, well above the national average of 50%. 100% of 20 NIHR ACFs have progressed to Wellcome or MRC PhD studentships.

#### 2A.1.3. Integration Between Clinical and Non-Clinical Researchers

The research institutes are configured around thematic groupings comprising clinical and non-clinical scientists. Collaboration between clinical and non-clinical researchers is encouraged through joint student supervision, pump-priming and large centre/programme applications and the University-led Liverpool Health Partners. ~250 University clinical staff and several hundred current honorary academic and clinical research support appointments have created a strong network of clinical research interactions. These honorary and joint appointments are spread throughout our



research institutes and they have access to offices and labs shared or co-located with their nonclinical colleagues that underpins our key aim (Section 1) of creating a better environment for fundamental and translational researchers working together. We have also invested in multiple new clinical and non-clinical appointments, at TTF and senior level, based within our overseas programmes.

# 2A.1.4. Support for New Staff and Early Career Researchers (ECRs)

All new staff receive tailored mentoring and financial support to transfer or initiate their research programmes in Liverpool. They are also protected largely from teaching and administrative duties to allow them to focus on establishing their independent research group. There is an active policy of supporting all ECRs through mentoring, prioritisation for internal research development awards and internal review of research grant applications. We run bespoke programmes of seminars and training workshops in areas such as grant writing and publication strategy specifically for ECRs. An example is the FLIGHT Initiative, which has supported fellowship applications from Infection and Global Health ECRs since 2014. This has delivered sustained growth in independent fellowship awards in this area, culminating in a success rate of 36% by number and 30% by value (UKRI report 2018/19), positioning us top of the Russell Group.

Our Wellcome Institutional Strategic Support Fund has provided £500K p.a. to ECRs to support our biomedical research strategy. We addressed the need for research training of clinical lecturers to allow them to prepare for external funding applications by the award of Clinical Short-Term Fellowships (6-12 months). For non-clinical researchers, we provided a strong platform for their transition to independence via funding the 3-5 year Tenure Track Fellowships that lead on to established posts and pump-priming funding (£10-25K) to generate data for external grant applications. In response to feedback from our ECRs about difficulties accessing wider training opportunities, in 2016 we redeployed one of our historical endowments to release £150,000 to establish the Johnston Researcher Development Fund to support research staff career development. To date, 24 UOA1 PDRAs have benefitted from this scheme. We have also provided PDRA Bridging Funding between external grants and we have sponsored a Faculty-wide ECR Leadership Group and Faculty workshops on how to apply for external fellowship funding. To date, our ISSF has supported 156 ECRs (54 UOA1 ECRs during the REF period).

<u>Case study:</u> Our approaches have seen our ECRs thrive. They have collectively secured >£8M over the REF period. 100% of UOA1 ECRs reaching the end of their TTFs have progressed to a tenured position; seven of these have since been promoted: five to Senior Lecturer, one to a Readership and one to a Personal Chair (Concordat Principles 1, 2, 3).

# 2A.2. Recognition and Value: Appraisal and Promotion

All research and academic staff are formally appraised annually via a Professional Development Review (PDR) undertaken with a senior management representative from their institute; clinical academics also undergo an annual joint NHS/University appraisal. A Faculty Workload Allocation Model is currently being trialled building on comprehensive workload models already in place in different parts of the Faculty that will provide up-to-date data on activity to allow transparent and fair discussions based on core expectations. Promotion is based on a University-wide set of robust processes with clear criteria for each grade and type of position. Promotions for academic staff consider research, teaching and administrative contributions and assessment of professional practice. Promotions to all levels are solely contingent on ability and achievement and are not a quota system or influenced by the availability of central funding. Since 2014, 103 UOA1 academic staff have been promoted, with 25 advancing to Professor, 13 to Reader and 28 to Senior Lecturer.



## 2A.3. Implementation of the Concordat to Support the Career Development of Researchers

In recognition of the University's commitment to the Researcher Development Concordat, it has continuously held the European Commission's HR Excellence in Research Award since September 2011, reviewed biannually. In July 2020, the University also became a signatory to the Revised Researcher Development Concordat. The University participates in both the Careers in Research Online Survey and Principal Investigator and Research Leaders Survey; analysis of the results informs the action plan associated with the HR Excellence Badge (Concordat Principle 7). Our staffing policy (section 2A.1) is based around recruiting and retaining excellent researchers (Concordat Principle 1). Our success in supporting staff depends upon clear and effective line management. Heads of Institute and Heads of Department undertake leadership development training through the University's Leadership Framework Programme (validated by the Institute of Leadership and Management). The role of the Head of Department (HOD) is to mentor academic staff, conduct staff appraisals (section 2A.2), ensure equality in workload allocation, address EDI challenges, and to facilitate internationally competitive research and effective teaching (Concordat Principles 2, 3, 4, 6).

Additional mentoring, open to all staff, is available via the University of Liverpool Mentoring Network which has over 700 staff registered from all roles/grades across the University. Notably, we developed the sector-leading PROSPER scheme that provides structured career and development support for PDRAs. Targeted support for junior and fixed-term contract staff is also available via the Career Coaching Scheme that gives participants access to mentors with subject-specific experience (Concordat Principles 3, 4, 5).

The University is also a signatory to the Science Council's Technician Commitment that ensures greater visibility, recognition, career development and sustainability for technicians across all disciplines. In line with our institutional action plan, the University has secured £25K for professional registration and training/development costs to support UoL technicians to participate in training courses to enhance their skills and that lead to formal professional accreditation with the Science Council (Concordat Principles 3, 4, 5). This has been matched with a further £15K from FHLS. We are about to introduce a Research Scientist and Technologist Pathway that will be better able to recognise the contributions and support the development of academic-related staff that manage our specialised research infrastructure and provide the data science capabilities that underpin UOA1 activity, as well as providing a recognised pathway for career advancement. We have also developed a technical skills matrix that defines roles and drives training and development, upskilling our technical workforce and future-proofing by identifying potential imminent skills gaps.

#### 2A.4. Support for Achieving Impact

We appreciate that staff require time to develop effective impact, and the PDR process is designed to ensure that workload is managed to accommodate these activities. Consultancy activity is embedded within all of our research institutes with 144 staff engaging in consultancies worth £4.75M since 2014 (UOA1: £2.3M, 70 staff). Our staff also benefit from policies supporting flexible employment arrangements to support research engagement activities. To improve the success of our grant applications we have developed a programme of frequent focused workshops to highlight opportunities, promote collaborative networks and discuss ideas at early stages of development. These are supplemented by a peer-review process that is compulsory for research council and major charity funder applications and for example has seen an almost doubling in the success rates of MRC grant applications since 2014. Specific support is provided for developing impact. Impact Officers are embedded within FHLS to provide advice and support. During the REF period UOA1 staff have secured ~£1M from a wide range of internal funding schemes designed to pump-prime and develop their research applications, outputs and impact (Sections 1C & 3A.2).



#### **2B. RESEARCH STUDENTS**

FHLS registered 1,277 PhD (526 supervised by UOA1 groups), 52 MD (30 UOA1) and ~800 MRes students during the REF period. High-quality supervision of postgraduate (PGR) students is an expectation of all staff in UOA1 and discussed during the annual PDR process. In addition to academic staff, our supervisory teams include accredited honorary staff (e.g. NHS staff or industry collaborators) to ensure that students have the most appropriate guidance for their research.

UOA1 researchers pioneered the 1+3 model of research training with the establishment of the first Wellcome four-year PhD programme in the UK. The Wellcome Physiology PhD Programme led to the establishment of a large Biomedical MRes programme (~80 students per year) where a series of mini projects are structured to give students exposure to different research techniques and/or different well-funded research laboratories. Entry into MRes is now spread across all institutes as the standard approach for recruitment and training of research students. The 1+3 model also underpins many of our other externally funded PhD programmes and ensures that research students are better informed and engaged when subsequently developing their project for PhD study.

#### 2B.1. PhD Programmes

Substantial University investment (£2.1M 2013-2014 rising to £2.9M 2019-2020) has enabled all UOA1 research institutes to expand their PGR training. This internal funding has been used to lever matched funding from NHS Trust partners, RCUK, charity, industry and other sources. UOA1 academics have had access to externally funded PhD Programmes that have recruited 423 students during the REF period.

These include a UoL/LSTM clinical PhD programme funded by Wellcome (26 students), an MRC Clinical Pharmacology PhD Programme (15 students joint with Manchester and industry) and non-clinical PhD programmes funded by Wellcome (30 students registered during REF), MRC (59 students), BBSRC (88 students), North West Cancer Research (16 students). We have proactively developed research links with overseas partner institutions to develop collaborative PhD studentships. These initiatives have seen 45 PhD students enrol with us with up to 50% funding contributed by UoL. We have also established an International PhD Bursary Scheme where we pay all tuition fees and offer these scholarships competitively to international students each year.

Case study: The quality of the research training that we provide is exemplified by the Wellcome PhD Programme in Physiology where >80% of our graduates remain in science-related professions >10-years post-graduation, and 22 out of 98 graduates to date have achieved the equivalent of Principal Investigator status in academia or industry.

# 2B.2. Strong and Integrated Research Student Culture

# 2B.2.1. Research Integration of MDs and Clinical PhDs

ICAT works closely with the Liverpool Doctoral College, PGR teams and research institutes to ensure that they recognise the challenges of successfully balancing clinical and research training. Regular surveys of student experience and progression now provide a stronger evidence base for forward planning by ICAT to facilitate progression to clinical lectureship positions. These have also resulted in the introduction of enhanced networking, peer and senior mentoring support for students. It is paramount that our trainees and ACFs are working on high quality research projects in excellent research environments. ICAT carefully scrutinises each proposed clinical



academic post with speciality training programme directors and experienced academic supervisors to ensure the suitability/feasibility of projects and the quality of clinical and academic supervision.

# 2B.2.2. Postgraduate Support and Oversight

We have a highly structured system that supports students through their PhD and ensures 100% compliance with progress monitoring; alerting us to any concerns so that we can be proactive in addressing any issues. All PhD students record a meeting with supervisors at least once per month on our electronic system (once per two months if part-time). Students complete an Annual Report detailing research and training progress over the previous year and plans for the coming year, which forms the basis for the annual meeting with independent assessors to review progress (Independent Progress Assessment Panel, IPAP). They also complete an online report that includes training, publications and any issues or concerns. In the rare instances where progress is not satisfactory, the Institute Director of Postgraduate Research (IDPR), who coordinates the IPAP, facilitates an additional review process and mediates between supervisors and students with support from their HOD. There is the scope to change the supervisory team in the event of a breakdown in the supervisory/student relationship.

#### 2B.2.3. Student Wellbeing

We have established an annual Postgraduate Forum, which acts as a discussion forum around a different theme each year and a PGR Committee which meets three times each year. PGR students run a web survey annually and bring results to the Committee for discussion. Impact from this has included changing stipend payments to all PGRs in the University from every three months to monthly; and the inclusion of seminars about non-academic careers. Feedback from the Postgraduate Forum led to the establishment of a Pastoral Group for PhD students, a group of individuals drawn from all staff groups (professional services and academic) who are available to offer guidance and signpost students to appropriate support networks and structures within the University. In 2018 we were awarded a HEFCE/OfS PGR Mental Health and Wellbeing Catalyst project (£150k) which funded a full-time project manager and together with our other initiatives provided a multi-faceted support structure for PGR students including:

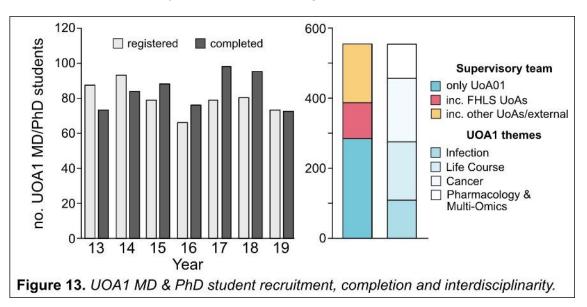
- Recruitment and implementation of 'Peer Wellbeing Ambassadors', to provide peer-to-peer support. PGR students have been recruited against a defined role description and attended a bespoke training programme, including Mental Health First Aid training in cross-cultural communication skills, bystander intervention, initial disclosure and managing boundaries. We now have 19 ambassadors across the Faculty and the scheme has been rolled out across the University.
- New students are assigned a Yr2/3 PhD 'buddy' student to help them settle in during their early months.
- Improvements to the induction of new PhD and MRes students starting in the 18/19
  academic year, consisting of induction day talks, highlighting the focus on PGR mental
  health and wellbeing. Those starting at other times of the year can also offer personal
  induction support from ambassadors.
- Online mental health and wellbeing training modules for supervisors which has now been made mandatory and is referenced in the Code of Practice for PGR supervision.
- Working in partnership, with the Science Council, Technician Commitment, and societies
  including the Royal Society of Biology, Royal Society of Chemistry and the Institute of
  Physics, we undertook a sector-wide survey, exploring the pastoral support technicians
  provide to students. This resulted in a sector wide webinar event and UoL issuing guidance
  to technical staff to support them in their pastoral roles.



 Development of a 'Campus Wellbeing Map' for all staff and students, to clearly identify support services for PGR students launched at the University 'Wellbeing Week', in May 2019.

# 2B.3. Successful Completion and Graduation

Since 2014, 591 PhDs/MDs have been registered with UOA1 academics as primary supervisor (Figure 13) and 156 as secondary/tertiary supervisor. 85% of 99 full-time (FT) and all 4 part-time (PT) students with primary UOA1 supervisors submitted their thesis on time (average 3.6 years for FT). Total completion rates in FHLS are 88.6% for FT and 89.6% for PT PhDs/MDs; these rates compare favourably with the UKRI average of ~60%.



# 2B.4. Preparation for Future Careers

We aim to develop motivated, resourceful, and skilled researchers capable of driving world-class research independently and as part of a team. Training and development needs are assessed at the outset of their project and then reviewed annually; this comprises a detailed skills audit based on the VITAE Researcher Development Framework. Whilst the first job for >70% of our PhD students is a postdoctoral position in academia or industry, we recognise that most graduates will move into other science-related careers as time progresses. To ensure that our students are better informed about likely career paths and opportunities, we hold careers workshops where internal and external role models from relevant sectors describe their experiences. Our long-term PhD programmes have extensive alumni networks, for example the Wellcome Physiology PhD programme has ~100 graduates. Reciprocal arrangements with regional RCUK and Wellcome DTPs further increases access for all of our students to alumni networks and careers advice.

# 2C. EQUALITY AND DIVERSITY

# 2C.1. Engagement and Delivery

### 2C.1.1. Athena SWAN

The University gained an Athena SWAN Silver Award in 2016. UOA1 staff are based in two departments with Gold Athena SWAN Awards and 12 with Silver Awards. 33% of UOA1 Cat. A staff are female with 24 female Professors acting as role models/mentors. We have actively encouraged female colleagues to take visible and key roles within UOA1 research institutes and



the wider University. Effective strategies have included all leadership roles being subject to open competition, with detailed job descriptions and person specifications by internal advert, flexible job plans and the desirability to see female colleagues applying for senior roles is emphasised. We have active programmes to support the recruitment and development of the next generation of female research leaders. This includes focused support such as the Springboard Programme to support the personal and professional development of female ECRs and the Aurora Women in Leadership Programme to facilitate the transition of fixed-term and core-funded female researchers to more senior roles (Concordat Principles 3, 4, 5, 6). As a result of these initiatives, we have increased the proportion of female Professorial staff from 14% in 2014 to 25% in 2020, with further progress expected over the next REF cycle. The University also supports a number of networks and groups which promote and celebrate women in STEM subjects that UOA1 are able to participate in. These include the Female ECR Network and the Liverpool Women in Science and Engineering Society.

# 2C.1.2. Equality and Diversity

We are members of an inclusive institution and our staff benefit from policies and activities that lead from commitments made by the University as a member of the Athena SWAN Charter, the Disability Confident Scheme, the Race Equality Charter and as a Stonewall Diversity Champion. Awareness is facilitated via institute and departmental newsletters and local events. Compulsory training (renewable on a 3- to 5-year ongoing cycle) ensures that all staff are aware of their rights and responsibilities; these include Diversity and Equality Training and Unconscious Bias Training (Concordat Principle 6). Enhanced training such as Equality Impact Assessment Training is available for staff involved in ensuring delivery of policy. The University also supports and promotes a wide range of organisations including the Disability Network, BAME Network and LGBT Staff (2.5%, 15.0% and 2.9% respectively of UOA1 staff have self-identified as personally relevant protected characteristics) as well as a PGR student network.

#### 2C.1.3 Equality and Diversity in the REF submission

The University's REF Code of Practice has been incorporated into every stage of the Unit's submission. Outputs were scored by a large and diverse group of academics. Each output was scored by at least two academics and initial scores were moderated by a group of experienced REF leads, all of whom had attended Faculty EDI and Bias Awareness training. Selection of outputs was manual following an algorithm to ensure optimal selections were made for all members of staff.

#### 2C.2. Employment Flexibility and Support

All University staff can access a range of family friendly options, notably parental, compassionate, domestic and personal leave. The University's flexible working policy allows individuals to vary or adjust their pattern of work based on their personal circumstances, including opportunities to work from home. This underpinned our resilience during the COVID lockdown where all non-COVID research activity and support transitioned to working from home. For postdoctoral and fixed-term contract staff, our research institutes cover the costs of maternity/paternity leave when other forms of funding are not available. ~25% of staff have returned from maternity/paternity leave to an agreed amended contract with reduced hours enabling satisfactory work-life balance. To further improve the ease and success of academic staff returning to work following maternity/paternity leave, £5K of flexible funds is available on application to support their research. Family Friendly Advisors (10 in FHLS) and support networks including the Carer's Network, Parent's Network and ECR Network provide information, guidance

# <u>Unit-level environment template (REF5b)</u>



and mentoring for staff. Employment flexibility also facilitates professional and research interactions, with FHLS staff able to join external organisations on joint appointments or full-time contracts to support collaborative or engagement activities, whilst retaining the opportunity to rejoin the University as before.



# 3. Income, infrastructure and facilities

# 3A. INCOME

### 3A.1. Research funding

Our research portfolio is built around multi-disciplinary translational medicine pipelines and clinically aligned fundamental research within each of our research priority areas. These areas together contribute to a diverse and sustainable funding portfolio with total awards during the REF period of  $\sim$ £245M (Table 3) and a total research income (spend) of £230m. This was aided by strong funding from the NIHR (£35M), MRC (£31M), BBSRC (£13M), Wellcome (£15M), CRUK (£10M) and EU science funding schemes (£19M).

Funding Source	Awards		
UK Research Councils	£51.1 M	• 1,977 funding awards	
UK Charities	£54.5 M	Infection ~29% Pharmacology ~21%	
UK Government/ Health	£52.2 M	Life Course ~20% Other ~11%	
EU Government/charity	£19 M	Cancer ~19%	
Overseas government/charity	£19.4 M	• 70 £1M+ research awards	
UK industry	£16.1 M	60.8M (£39.6M UoA01 share) funding for Research	
EU industry	£5 M	Centres/Networks	
Overseas industry	£8.2 M	105 Clinical Trial associated awards (£12.5M)	
Other	£19.8	51 clinical Training/Research Fellowships	
Grand Total	£245.3 M	48 Independent/Intermediate research fellowships	
Table 3. UOA1 research awards and external funding highlights during the REF period			

Our research outputs have benefitted from >500 excellent externally funded PhD/MD students who have contributed to 862 publications during the REF period as first author, and 208 of the publications in our REF return. Postgraduate training awards totalling £5.3M give all UOA1 groups access to a large and diverse pool of well-funded students. University investment (£2.1M 2013-2014 rising to £2.9M 2019-2020) has been used to leverage significant additional funding from NHS Trusts, industrial, government and charity partners including: Wellcome UoL/LSTM Clinical PhD Programme (£10.2M, 26 students, held since 2007); Wellcome PhD Programme in Physiology (£4.5M, 30 students, held since 1994); BBSRC (£1.1M, 35 students); MRC (£908K, 35 students); North West Cancer Research (£1.3M, 15 students); and EU-H2020 Innovative Training Network in kidney regenerative medicine (£1M, 8.6 students out of EU total of £4M, 12 students).

#### 3A.2. Strategies for generating income

We have invested in staff recruitment, including 61 new members of academic staff, to build critical mass, expertise and sustainability in priority areas, and support the infrastructure that underpins our research and to enhance technical provision. An external review of our clinical research strategy in 2017 recognised our success in strategically supporting our Centres of Excellence to help them to generate income that leads to significant outputs and impact (Table 1). This successful centre-based strategy has led us to establish new clinical research centres in 2018 that address significant regional health priorities. This was supported by the recruitment of world-leading clinical academics including Professor Gregory Lip (Director, Liverpool Centre for Cardiovascular Science). These centres will provide the clinical research leadership and focus required to secure programme and centre grant funding and industry engagement that is necessary to establish sustainable translational medicine pipelines. We are also investing in underpinning technologies and have significantly strengthened our multi 'omics and systems



biology capabilities through the appointment of Kell and Goodacre to lead the new Centre for Metabolomics Research and provide strategic direction for the GeneMill Synthetic Biology Centre.

To help our clinical academics to develop collaborative research projects with basic and interdisciplinary scientists we established the Translational Research Access Programme (TRAP) that awards up to £100K to each of six projects per year. We were also awarded a £600K Wellcome Translational Research Partnership award in 2019 to help the pull through of our basic research into translational studies. We recognise the challenges in establishing clinical and clinically aligned basic science careers and Tenure Track Fellowships (TTFs) and the Integrated Clinical Academic Training Pathway provide solid foundations where ECRs receive extensive mentoring and support to prepare grant applications. Ten UOA1 TTFs have been appointed during the REF period with 100% of those in post for at least 18 months successfully securing external funding. To date, the University has received £6.25M of Wellcome Institutional Strategic Support Funding (ISSF) that has been used to develop career progression and bridging schemes such as Clinical and non-Clinical Fellow Support.

<u>Case study:</u> In 2015 Daniel Neill received £20,000 ISSF non-Clinical Fellow Support that contributed to stabilising his position within the Institute of Infection and Global Health and enabled him to submit a successful application for a £0.8M Sir Henry Dale Fellowship and a £1.4M MRC grant as Co-Investigator to study the regulation of pneumococcal carriage and disease.

To ensure that we are agile in the way we respond to funding calls, the University (Research, Partnerships and Development) and Faculty (Research and Impact Directorate) have dedicated professional services staff who support the breadth of the research lifecycle, including scoping and communicating opportunities, facilitating sandpit events, supporting research and fellowship applications, and organising peer review. To improve the success of our applications we have developed a programme of focused workshops to highlight opportunities, promote collaborative networks and discuss ideas at early stages of development. These are supplemented by an extensive peer-review process which starts with informal discussion with mentors and progresses through peer-review stages to final application. University mentors and peer-review panels are comprised of senior staff with specific experience with relevant funding bodies and schemes. An example of the benefit of this enhanced support can be seen with our success in securing funding for NIHR HPRUs, successful applications for BBSRC ALERT research infrastructure funding in every year of the REF period, as well as MRC success rates that have improved from 16% in both 2013/14 and 2014/15 to 18%, 33% and 26% in 2015/16, 2016/17 and 2017/18 respectively.

More generally, a wide range of targeted funding opportunities are available within the University giving academics the chance to test early ideas, explore partnerships and establish networks. Designated funds allow academics to develop proof-of-concepts and begin successful research projects. Pump-priming funds such as MRC Proximity to Discovery and Confidence in Concept funding (£615K, 26 awards), together with University Knowledge Exchange Awards (£154K, 20 awards) and the Enterprise Investment Fund (£211K, 7 awards) have helped UOA1 researchers to generate essential data to establish translational networks and secure commercial partners to help advance ambitious clinically related projects. Developing these relationships is supported by Research Partnerships and Innovation (Section 4A.1) and through thematic translational organisations such as CEIDR that in partnership with LSTM provides £250K per year to pump-prime relationships with industry and academic organisations to advance drugs, vaccines and diagnostics towards market. We also recognise that the generation of high-quality outputs feeds directly into funding success and that this often relies on the recruitment of exceptional PGR



students. Here, we have invested (>£900K) co-funding PhD students on our 4-year DTP Programmes (Section 2B.1).

<u>Case studies:</u> Since 2014, 32 UOA1 academics have shared ~£1M of funding to support knowledge exchange/translational activities. Investment that led to significant outcomes includes £40K CIC funding to Michael Griffiths in 2014 to develop a novel blood test for bacterial meningitis resulting in two patents and £1.7M of MRC/industry investment from Fast Track Diagnostics. Another example is £30K CIC funding to Aras Kadioglou in 2015 to test the efficacy of a novel pneumococcal vaccine that resulted in £1.8M of Meningitis Now/MRC follow-on funding.

# 3A.3. Equality and diversity

Staff within UOA1 work within University institutes that hold Silver and Gold Athena SWAN Charter Awards. We have therefore developed robust systems for analysing our practices and culture and introduced significant organisational change to ensure equality of opportunity for all our staff and students. Schemes such as the University and Faculty's Returner's Funds and the Wellcome ISSF have supported 54 UOA1 individuals who have had career breaks or are at the early stages of a research career. Of relevance to infrastructure and facilities, the LIV-SRF Voucher Scheme gives subsidised access to core facilities. During the REF period, 224 such vouchers have been awarded, totalling ~£1M and leveraging a further ~£1M in pilot project funding. 123 of these vouchers were awarded to UOA1 staff. The scheme is particularly important for junior academics with limited available funding and 101 vouchers were awarded to 68 ECRs (51 to 32 UOA1 ECRs) to generate data for grant applications.

# 3B. INFRASTRUCTURE AND FACILITIES

#### 3B.1. Campus redevelopment

The University and NHS partners have been extensively redeveloping the biomedical estate so that clinically aligned groups are better co-located in purpose-built laboratories. This has resulted in a significant concentration of research groups into contiguous locations that has improved opportunities for collaboration, access to research resources and integrated support. Major examples are depicted in Figure 4.

### 3B.2. Engagement with Clinical Partners and Specialist Clinical Research Facilities

FHLS strategic planning has revolved around consolidating areas of research and clinical strength. Liverpool Health Partners (LHP) have been an important vehicle for improving collaboration, building clinical research capacity, resolving systemic barriers and coordinating strategic investment that improve clinical research and education delivery for the benefit of local patients. This is delivered via the Joint Research Service LHP-SPARK.

Supporting impact: LHP-SPARK is a 'one-stop shop' for the full process from clinical grant applications through to study set. It supports researchers on clinical research activities including developing a grant application, research and NHS costing, sponsorship, study registration, set up, contracts and general research governance. An example of the benefits of this joined up approach was seen in how LHP oversaw the streamlining of the transfer of patient data between NHS Trusts and our clinical research coordinators that has removed the delays that impacted clinical trial establishment, recruitment and data analysis.



## 3B.2.1 Clinical Research Facilities (CRFs)

NIHR funded CRFs at our partner NHS Trusts, Alder Hey and Liverpool University Hospitals, provide dedicated space, research nurses, support staff and data managers. They primarily support phase I-IV clinical trials and experimental medicine approaches to understand inflammation, infection, oncology and neurosciences. Clatterbridge Cancer Centre pioneered proton beam therapy for eye cancer and in 2014 created the UK's first radiobiology research laboratory dedicated to proton beam therapy with reserved UOA1 researcher access to the Douglas Cyclotron to develop strategies for improving cancer treatment.

#### 3B.2.2 Clinical Trials Units

The University has continued to further develop and consolidate its clinical research capability and infrastructure as part of the UK Clinical Research Collaboration (UKCRC)-Registered Clinical Trials Unit (CTU) Network. Following recommendations of an external review, in 2019 we launched the Liverpool Clinical Trials Centre (LCTC) - a single, fully integrated CTU created through a full-scale merger of the National Cancer Research Institute (NCRI)-accredited Liverpool Cancer Trials Unit (LCTU) and the Clinical Trials Research Centre (CTRC).

The LCTC supports a large portfolio of clinical trials specializing in high-quality national and international early- and late-phase trials with linked translational studies. It has a strong track record of developing and delivering practice-changing studies and receives NIHR CTU Support Funding in recognition of its NIHR-funded portfolio which is one of the largest in the UK. The LCTC collaborates with local and national investigators to design, conduct, lead and analyse clinical studies to improve patient care. It also supports the development of other local networks including the Liverpool Experimental Cancer Medicine Centre (funded by NIHR and Cancer Research UK), the North West Surgical Trials Centre (funded by the Royal College of Surgeons and Cancer Research UK) and the MRC-funded North West Hub for Trials Methodology Research (NWHTMR). The success of the NWHTMR, part of the MRC Hub Network for ten years, led to Liverpool now leading the new MRC/NIHR Trials Methodology Research Partnership involving six UK and Irish research networks together with 25 universities.

<u>Supporting impact:</u> The multicentre European Study Group for Pancreatic Cancer (ESPAC) led from Liverpool has conducted some of the biggest worldwide clinical trials on the disease. The latest to be reported (ESPAC-4) almost doubled the five-year survival rate to 29% versus standard treatment after surgery and has established gemcitabine and capecitabine as the new post-surgery treatment of choice for pancreatic ductal adenocarcinoma (Palmer).

#### 3B.2.3 GCP for clinical trials

The University has invested £10M in a suite of co-located GCP laboratories that link with Liverpool academic strengths in human disease and biology, and discovery medicine together with the Clinical Trials Units to deliver a fully integrated service for developing and testing new therapeutic agents and treatment strategies. The Bioanalytical Facility houses a bespoke proteomics facility that measures drug and metabolite concentrations for PK-PD analysis to assess drug efficacy and toxicity. They support Phase 0-1 first-in-man clinical trials through to large multicentre randomised trials and work closely with our drug safety and precision medicine research clusters (section 3B.4.2). The GCPLab comprises a suite of cytology, biochemistry, molecular biology and histology equipment and validated protocols for analysis and storage of samples derived from Phase I-IV clinical trials of anti-cancer agents.



Supporting impact: GCPLab has supported the identification of biomarkers such as TSP1 and ENT1 that are improving the early identification and stratified treatment of pancreatic cancer (Costello; Greenhalf). The Centre for Antimicrobial Pharmacodynamics has developed preclinical and early phase PK-PD models for new antibiotics to determine suitable population/individualised dosing regimens. They have also contributed to the better use of existing antibiotics, such as use within the NHS of Fosfomycin as a critical last-resort agent for treatment of multidrug-resistant bacterial infections (Hope).

# 3B.3. Biobanking resources

The University has 16 NHS REC approved Research Tissue Banks and ~400 biological collections of human samples totalling ~1 million stored samples. The Liverpool University Biobank was established in 2017 to initiate the consolidation of all new biobanking under one management. It currently offers access to archives of ~18,500 paraffin, ~23,000 fresh/frozen and ~7,000 plasma/serum samples suitable for immunohistochemistry, generating tissue microarrays, genetic analysis and biomarker profiling. Consent is centrally coordinated across four contributing local NHS Trusts to facilitate researcher access. Specialist biobanks e.g. lung cancer (~13,000 samples), leukaemia (~30,000 samples), pancreatic cancer (~10,000 samples), head and neck cancer (~12,000 samples), ocular oncology (~4,000 samples), musculoskeletal (~12,500 samples) and full access to NHS partner biobanks such as the Walton Research Tissue Bank (~2,500 brain-derived samples) give our researchers access to high-quality curated samples, including those derived from clinical trials, with extensive multimodal testing to facilitate patient stratification and longitudinal disease monitoring.

<u>Supporting impact:</u> Access to large, historic local collections of head and neck (H&N) cancer enabled UOA1 Cancer Medicine clinical researchers to demonstrate that recent increases in H&N cancer incidence are associated with human papilloma virus (HPV) infection. This has resulted in government policy changing to offer HPV vaccination to teenage boys (impact case UoL42HPVcancer).

#### 3B.4. Specialist Research Clusters and Research Resources

#### 3B.4.1 Infection and Global Health Research Clusters

The Centre of Excellence in Infectious Diseases Research (CEIDR) engages with LSTM and industry partners to deliver the next generation of diagnostics, therapeutics and vaccines. The Centre for Global Vaccine Research (CGVR) (Co-Directors: French & Kadiloglou) was established in 2016 to build on a strong track record of international clinical vaccine research in Liverpool and enhance Infection and Global Health academic critical mass and the co-ordination of specialist research resources required for vaccine research. The CGVR is developing novel vaccines and investigating ways to improve on current vaccine performance. Local vaccine providers (Seqirus, Med-Immune) and access to specialist infrastructure including containment level 3 laboratories, pre-clinical animal facilities and downstream imaging and omic analytical pipelines (section 3B.2.1-3) have been integrated into the CGVR to deliver vaccines that can be trialled with international partners in Africa and Asia. The University leads two recently renewed NIHR funded (£8M) HPRUs focused on Emerging and Zoonotic Infections (Director: Solomon) and Gastrointestinal Infections (Director: Cunliffe). These national units capitalise on our world leading expertise in infection research to protect UK public health and their specialised infrastructure and management underpinned our rapid re-positioning to address COVID-19 research questions.

<u>Supporting impact:</u> For over 20 years UoL has led a collaborative research programme describing rotavirus disease burden and evaluating the efficacy, effectiveness and impact



of rotavirus vaccines in Malawi (Cunliffe). This has informed WHO global vaccine policy and has resulted in the implementation of infant immunisation schedules in 95 countries since 2009. Recent analysis revealed that worldwide child deaths from rotavirus have more than halved since 2009 to ~200,000 per year with major impacts in low and middle-income countries (impact caseUoL41RotavirusSSA).

# 3B.4.2 Drug Safety and Precision Medicine Research Clusters

The Centre for Drug Safety Sciences (CDSS) (Director: Pirmohamed) has established a critical mass of precision medicine academics, infrastructure and facilities to investigate adverse drug reactions. The Bioanalytical Facility (section 3B.2.3) together with wider omics support (section 3B.5.3) facilitates biomarker and drug/metabolite bioanalysis. Informatics expertise (section 3B.2.2 and 3B.5.3) integrates different omics datasets and modelling to predict drug effects, inform prognosis and suggest routes for stratifying patient treatment. The Wolfson Centre for Personalised Medicine (Director: Pirmohamed) integrates clinical sample collection, pharmacogenomics analysis and data science support. Approximately 60,000 patient and control DNA samples are currently archived for research into treatments for epilepsy, asthma and cardiac disease and side effects associated with drug-induced liver injury, antibiotics and antiretroviral therapies. The centres are supported with £11M of MRC funding and have leveraged £14M in further support from RCUK, EU and industry and played leading roles in major IMI awards: Mip-DILI, Trans-Bioline, Trans QST, Web-RADR and ARDAT.

<u>Supporting impact:</u> The FUTURE Initiative project was established in 2015 with £1M of University pump-priming funding to develop a panel of healthy volunteers and patients genotyped for polymorphisms in drug metabolising and transporter genes and consented to be contacted about recruitment into genotype-guided early phase clinical studies. More than 3,000 volunteers have been recruited to date with ongoing expansion to include 1,000 patients with renal and hepatic disorders that also represent an area of unmet need for recruitment to industry trials.

# 3B.4.3 Centre for Integrated research into Musculoskeletal Ageing (CIMA)

Supported with funding from the MRC and Arthritis UK (now Versus Arthritis), CIMA (Director: Jackson) was established in 2012 and renewed in 2017 to bring together <u>Life Course and Chronic Disease</u> clinicians and academics in Liverpool, Sheffield and Newcastle researching the effects of ageing on the musculoskeletal system. Clinical and pre-clinical imaging infrastructure (section 3B.5.2) together with the Biomechanics Research Suite offers bi-planar x-ray, video imaging and gait analysis that allows a full range of analysis from the molecular and genetic determinants through to in vivo characterisation of the consequences of disease and ageing-related musculoskeletal dysfunction.

#### 3B.4.4 Materials Innovation Factory (MIF)

The MIF provides flexible space for Liverpool academics and industry partners to co-locate for research residencies with access to a nationally leading range of analytical and materials science robotics infrastructure. This interdisciplinary translational environment has been particularly important for UOA1 academics Owen and Liptrott working on anti-HIV, anti-cancer and anti-malarial nanomedicines together with UOA8 Chemistry colleagues. During the REF period, this activity has resulted in two antiretroviral nanomedicines in Phase 1 clinical trials and >70 drug delivery patents. This strong track record has led to the successful establishment of the multidisciplinary Centre of Excellence in Long-acting Therapeutics (CELT) with £24.5M of Unitaid investment that aims to develop novel nanomedicines that address global health challenges.



## 3B.5. Provision of underpinning core research facilities

Twenty-three shared research facilities (SRFs), ~90 expert support staff and >£45M of specialised equipment deliver access to a wide range of high-quality technology and infrastructure for all of our research groups. Large facilities and strategic investment in all of our technology areas is overseen by LIV-SRF. LIV-SRF ensures efficient utilisation and long-term sustainability of core technologies whilst maintaining technological competitiveness that underpins academic excellence. LIV-SRF also inform wider Faculty investment in research equipment to ensure that it is feasible, sustainable, optimally located, accessible and targeted to areas of unmet need, allowing us to maintain our access to cutting-edge technology. For example, in 2018 LIV-SRF directed University investment of £1.5M into the Liverpool Magnetic Resonance Imaging Centre to purchase an MRI scanner to ensure long-term availability of this important clinical research platform. The success of our coordinated approach to the development and management of research facilities and equipment is also evidenced during the current REF period by eight successful BBSRC ALERT bids to purchase genomics, proteomics and imaging equipment, and a successful MRC Clinical Research Infrastructure bid to purchase NMR and Helios Mass Cytometry equipment (£5M with £1M University contribution).

<u>Supporting impact:</u> The LIV-SRF Voucher Scheme subsidises access for new academic appointments, ECRs, research fellows and unfunded pilot research projects. £1M invested into the voucher scheme over the REF period has generated a 23-fold return on investment through seeding further research grant income.

Several core technologies and large facilities have been particularly important for underpinning research and impact within UOA1 as follows:

# 3B.5.1 Biomedical Services Unit (BSU)

The £45M BSU was commissioned in 2011 and occupies approximately 9,300 m², including laboratory, surgery and procedure rooms and biological containment facilities for PC III organisms. The unit can house 24,000 mice and 7,500 rats in HEPA filtered individually ventilated cages with constant 24/7 monitoring of environment, automated watering and configurable feeding systems. All animal work at the University is overseen by the BSU including the longitudinal imaging and animal husbandry facilities within The Centre for Pre-Clinical Imaging (section 3B.5.2).

<u>Supporting impact:</u> The state-of-the-art Containment Level 3 facilities underpin our Infection and Global Health research. For example, the infection biology and treatment of >50 infectious agents (including COVID-19, Japanese Encephalitis Virus, Tuberculosis bacteria and Trypanosome parasites) have been investigated within the BSU since 2014.

# 3B.5.2 Imaging and cytometry

Our extensive array of infrastructure and associated protocols allow cross-platform correlative imaging from in vivo whole animal and patient imaging down to the nanoscale. Expert technical, image analysis and method development support are available in all imaging facilities for all clients. Liverpool Magnetic Resonance Imaging Centre (Siemens 3T MRI scanner) and the Centre for Preclinical Imaging (CPI) (Bruker 9.4T MRI scanner) provide clinically aligned researchers with full-time access to state-of-the-art magnetic resonance imaging and one of the most comprehensive and sensitive range of small animal imaging modalities available nationally.



<u>Supporting impact:</u> The University hosted the cross-council UK Regenerative Medicine Platform Safety and Efficacy Hub until 2018. Researchers within Liverpool developed novel multimodal imaging strategies to permit more accurate monitoring of kidney and liver architecture and function to allow evaluation of stem cell-based therapies. The CPI is also the lead hub in the £4M EU-wide kidney regenerative therapies PhD training network.

The Cell Sorting Facility offers up to 15 parameter fluorescence-activated cell sorting (FACS) and the first Helios Mass Cytometer to be installed in the UK. The Centre for Cell Imaging provides a focal point for advice, training and imaging provision with seven confocal microscopes including Light-sheet, AFM, and Photothermal microscopes. In addition, a distributed array of FACS and microscopes are located with specialist research groupings throughout the Faculty. An example is the co-location of four high-performance confocal microscopes including superresolution and fast FLIM/FRET/TIRF systems with the Biomedical Electron Microscopy Unit where they drive the generation of 4\* outputs relying on correlative light and EM imaging and 3D-EM analysis.

<u>Supporting impact</u>: The quality of our imaging facilities attracts world-leading external research groups. For example, correlative light and 3D-EM imaging generated the most comprehensive ultrastructural analysis to date of the human genome during cell division (Earnshaw (Edinburgh), Prior).

#### 3B.5.3 Multi-Omic technology

The Centre for Genomics Research houses ~£4M of next-generation sequencing, single cell sequencing and informatics infrastructure that has played a key role in our infection research to map the spread and evolution of Zika, Ebola and COVID-19. GeneMill Synthetic Biology Lab established with £4M of BBSRC investment offers rapid high-throughput construction and testing of synthetic DNA constructs used for genome editing, protein design and expression. The Centre of Proteome Research operates 12 mass spectrometry platforms that support a wide range of protein identification and quantitative applications. Specialised proteomics facilities are also embedded in research clusters focused on drug safety, stratified medicine and antimicrobial development (sections 3B.2.2 & 3B.4.2). The Liverpool Metabolomics Facility offers mass spectrometry and NMR-based metabolite analysis together with expert academic insight reinforced in 2018 by new Chair appointments (Goodacre and Kell) and £1.8M (MRC, EPSRC) funding during the REF period to purchase a new 700MHz spectrometer and upgrade the 800MHz NMR. The Computational Biology Facility has been the focus of significant strategic investment since 2014 (eight new staff, £0.5M redevelopment) to address the increasingly sophisticated data science needs of our clinically aligned researchers.

#### 3B.6. Shared use of research infrastructure

All of our equipment and facilities are openly accessible to external users on a cost recovery and/or collaborative basis. Formal reciprocal agreements coordinated by LIV-SRF have been agreed with regional HEIs and NHS partners to provide favourable access terms. Staff in UOA1 engage with partners across the N8 Universities in asset sharing. We encourage cross-HEI usage of our extensive facilities, for example: the Centre for Genomics Research has collaborated with over 250 different institutions; imaging platforms including the Centre for Cell Imaging and Biomedical EM Unit have published with academics from >100 external academic institutions; and the Materials Innovation Factory is a leading member of a European network of nanotechnology laboratories.



## 3B.7. Library and Research Computing Infrastructure

The University continues to invest in its libraries such that we subscribe to all of the national NESLi2 "big deal" site licences for journals. Liverpool Elements software together with Library Research Support Officers help co-ordinate long-term research data management and open access research output. Data networking is critical for UOA1 research activity and the University have a rolling programme of investment (~£1.6M since 2014) that provides ≥10 gbit/s network access; the University also work closely with Net North West which manages our wide area network connections and our high-speed resilient links to JANET. Our recently appointed, inaugural Head of Research Computing for FHLS is building a Faculty-wide Research Computing strategy, investment plan and service delivery roadmap to enhance provision in the coming years and support our strategic objective of growing our data science capabilities. Advanced research computing facilities, supporting data science underpinning our clinical research, have received significant investment during the REF period (£1.7M total). This includes 2 high-performance computer clusters with 4,200 and ~3,000 freely accessible cores and ~700 TB of storage to support analytical workflows. There is space and power to house project-specific hardware and we can easily burst onto AWS or Azure cloud resources to improve resilience. We also have a strategic partnership with the STFC-funded Hartree Centre at Daresbury enabling staff to access petascale high-performance computing facilities and computer science expertise. A team of support staff help researchers take full advantage of these facilities including helping to install and tune computational packages.

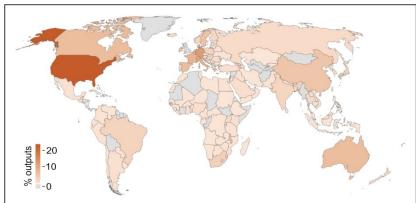


# 4. Collaboration and contribution to the research base, economy and society

#### 4A. COLLABORATIONS, NETWORKS AND PARTNERSHIPS

UOA1 staff work extensively with partners at national level and across the world, including research institutes, universities, industry, governments and foundations (Figure 14). Our partnerships are focused on developing new opportunities for research, including a commitment to staff and researcher mobility. The Faculty has established a number of key strategic alliances to further its research and training strategies at both national and international levels and have

enjoyed considerable success in securing and participating in major multi-centre awards. This is exemplified in postgraduate training, where we have 14 international DTPs and our large BBSRC and MRC funded DTPs involve successful long-term partnerships with LSTM, Newcastle, Durham, Sheffield and Leeds universities (section 2B.1). Similarly, our specialist research centres and facilities



**Figure 14.** *UOA1 international research collaborations.* % total publications co-authored by collaborators are indicated.

are all underpinned by a diverse array of well-established national and international research collaborations (described in section 3B and below).

# 4A.1. Enabling and facilitating collaboration

Strategies to facilitate collaboration at UoL are developed and delivered within the Research Partnerships and Innovation (RPI) directorate, via the Research and Partnerships Development (RPD) and the Industrial Strategy and Consultancy (ISC) teams. RPD focus their support on major research themes at UoL to build critical mass, to bring together diverse academic communities, to proactively develop new collaborations and to provide a means to unlock new research opportunities. They support PIs to hold events, workshops, run pump-priming schemes and sandpits and provide structured interdisciplinary networking sessions to generate new research ideas and collaborations. ISC focus their support on developing academic-industry collaborations. Internal pump-priming schemes overseen by RPI to support collaboration include the Overseas Development Agency Seed Fund that provides up to £10K for research in low-tomiddle income countries (~£720K for FHLS academics since 2016); the Enterprise Investment Fund (£800K University-wide funding since 2010); the Industrial Strategy Fund that promotes partnerships that benefit productivity in the UK and wider world (£1.3M University-wide funding since 2017); Knowledge Exchange and Impact Vouchers (~£550K for FHLS academics since 2009). Many of these funds specifically prioritise ECRs in recognition of our awareness and commitment to support ECRs. In 2020, we established PROSPER, a major £4.4M strategic project (together with the Universities of Manchester and Lancaster) to develop effective mechanisms of support for PDRAs within academia, enhancing their career opportunities.

#### 4B. ENGAGEMENT AND IMPACT

#### 4B.1. National and international collaborative networks

# 4B.1.1. Academic, NHS and clinical networks

**LHP** (Section 1A.2) is a major driver of regional clinical academic strategy and coordination. Liverpool leads the **HDR North** consortium (Director: Pirmohamed) that enhances



and leverages access to large-scale health data and analysis to understand the causes of disease and inform treatment strategies. It played an important role in our COVID-19 response contributing to ISARIC-CCP, RECOVERY, COG-UK and SAGE. Our centres in Infection (CEIDR, CELT, CGVR, NIHR HPRUs in Emerging Infection and Zoonoses), Life Course (CIMA, LCCS, MRC Hub for Regenerative Medicine), Cancer (LCRI, LCTC, ECMC) and Pharmacology (CDSS, Wolfson Centre for Personalised Medicine) are focal points for collaborative engagement with national and international clinical networks and industry. Through the Malawi-Liverpool-Wellcome Trust Clinical Research Programme in collaboration with LSTM and the Malawi Ministry of Health, we address major infectious diseases affecting the population of Malawi and other LMICs.

# 4B.1.2. Interdisciplinarity and industry engagement

During the REF period, we have developed and enhanced our links with UK and international industrial partners, both as collaborators and as advisors. This is evidenced by £29.3M of UOA1 industry-associated grant funding (including £5.5M of Innovative Medicines Initiative funding). In addition to Faculty support teams and internal funding that promotes industry engagement (section 4A.1), the University has invested >£80M since 2014 (together with industry and government partners) to establish flexible multidisciplinary space across campus where industry researchers can be based to benefit from the outstanding infrastructure and expertise that we have available to drive translational outputs and collaborations. This strategy is exemplified by the Materials Innovation Factory (MIF; section 3B.4.4, established in 2017) that supports UOA1 nanotechnology and nanomedicines outputs (Owen and Liptrott). Our research centres and facilities (section 3B) also act as hubs for interdisciplinarity and engagement with industry. For example, Liverpool has the largest concentration of public sector R&D expertise in infectious diseases in the UK and this attracts significant industry-associated funding and collaboration (section 3A.1). CELT (section 1B) builds on our strong nanomedicines track records and interdisciplinary collaborations between UOA1 and UOA8 academics to develop new drugs that target infectious diseases affecting >300 million people per year globally, whilst CEIDR includes industry partners to develop strategies to mitigate anti-microbial resistance.

<u>Case study:</u> The NW England MRC Fellowship Scheme in Clinical Pharmacology and Therapeutics is a partnership between the Universities of Liverpool and Manchester together with Novartis, Eli Lilly, Roche and UCB Pharma to develop clinical scientists able to bridge across academia, industry and health services. To date, it has recruited 13 clinical fellows who have worked on a diverse range of projects related to Drug Safety, Stratified Medicine and Systems Pharmacology.

# **4C. WIDER CONTRIBUTIONS TO SOCIETY**

#### 4C.1. Wider engagement with diverse communities and the public

We have vibrant and extensive public engagement programmes co-ordinated through our research centres, institutes, and the Faculty, with a number of posts exclusively focused on public engagement with research. Many of our major research centres and staff members also have active presences on major social media platforms to publicise our activities. Work within public engagement is supported by the Faculty Public Engagement Grant Scheme which is open to all staff and postgraduate research students. Grants of up to £2,000 are available, and each year the Faculty awards between £10-14K. The Faculty also runs a variety of Public Engagement training events for staff and students including designing hands-on activities, video-making and communication workshops run by external science communication professionals. To support and



reward staff who organise both public engagement and involvement initiatives, the Faculty holds a yearly showcase event with prizes awarded for both categories.

Public Engagement activities include:

- 'Meet the Scientists' events at the World Museum, Liverpool that engage over 6,000 visitors annually.
- Festivals: Cheltenham, Manchester and Edinburgh Science Festivals; Big Bang Fair; Royal Society Summer Science Exhibition; Pint of Science Liverpool (an international festival that sees scientists take to pubs to talk to the public about their research, ~500 members of the public attend annually).
- Interactive stands at many Merseyside hospitals to celebrate the NHS's birthday and mark World Cancer Day.
- A Continuing Education Cancer Course developed and piloted in 2019.
- Open house events, lab visits for schools, organisations and members of the public (weekly events across FHLS). School visits and guest classes by members of staff and students.
- Post-COVID virtual events including Scouse Science (monthly starting June 2020, ~35k views) and Liverpool Responds, (bi-weekly starting June 2020, ~39k views).

# 4D. CONTRIBUTION TO DISCIPLINE

#### 4D.1. Sustainability and interdisciplinarity

The sustainability of our discipline depends upon our ability to communicate its value/relevance, and to contribute solutions to problems that affect the lives of individuals around the world. Solutions to global challenges require increasingly multidisciplinary approaches and through our network of collaborators we are leading on projects to deliver tangible impact. We place a major focus on disseminating research impact to stakeholder groups, industry and the public. Impact lies firmly at the heart of the University's strategy and resources allocated to impact have grown year on year throughout the REF period. A number of support mechanisms, in the form of impact leads, local impact officers and pump priming funds have been put in place over the last few years, culminating in the Making an Impact Framework; a series of activities allowing researchers at every career stage to build a tailor-made programme to maximise research outputs based on their own research impact needs, ambitions and interests. The impact of our research extends well beyond those activities presented as formal impact cases and provides benefit to both stakeholders and the wider public.

#### 4D.2. Responsiveness to national and global priorities

UOA1 academics are all aligned within research themes that reflect national and international grand challenges. At a national level Liverpool is one of 24 strategic members of the Northern Health Science Alliance and one of eight strategic members of the N8 Research Partnership (2015-2020). N8 is a collective of the most research-intensive Universities in the North of England joint funded (£16M) by participating universities and HEFCE to maximise the impact of our research, promote collaboration and deliver innovative research capabilities. The reorganisation of FHLS has resulted in significant investment in programmes to address regional health inequalities. Furthermore, our significant critical mass and success in global health and anti-microbial research (sections 3A.1, 3B.2.3 & 3B.4.1) has a demonstrable record of being acutely responsive to emergent global health priorities (e.g., Zika, Ebola, COVID-19, antimicrobial resistance). This has included relocation of researchers to directly engage at the sites of outbreaks, such as our work with the European Mobile Laboratory in Guinea and Sierra Leone in 2014/2015 to aid with Ebola diagnosis and tracking of virus evolution.



#### 4D.2.1 COVID-19

Our response to COVID-19 demonstrated our agility in repurposing our extensive infrastructure and staff resources to enable nationally leading contributions and research impact as the pandemic developed. The University, LSTM and the NHS established a city-wide Liverpool STOP-COVID initiative that has allowed cohesive, rapid and scaled responses across the research pipeline. Liverpool STOP-COVID is contributing to 13 NIHR Urgent Public Health studies and UOA1 academics have project lead roles (see case studies). We played a leading role in the introduction and monitoring of lateral flow testing and ongoing health surveillance, with prominent roles in public health communication (Solomon, Semple). We contributed to key government advisory committees (Semple: NERVTAG, SAGE), NIHR Co-Leadership of the National Speciality Group for Infectious Diseases and membership of the UPH Committee (Hope), and MHRA Pharmacovigilance Committee Chair (Pirmohamed). The ranking of the North-West Coast Clinical Research Network in infectious diseases improved significantly, moving from the lowest tertile to 6th position nationally and by June 2019 following the first national lockdown UoL ranked 3rd behind Oxford and UCL for number of UKRI COVID grants. £1.2M of funds were repurposed from UoL, LSTM, NIHR and regional health charities to fund 22 projects that seeded ~£16M of grant income and impact via AGILE, ISARIC, PRONTO, COVID-CNS, and CCP-Cancer. These seed funds were also invested internationally to support the development and establishment of COVID diagnostics in Malawi.

<u>Case studies:</u> ISARIC (Co-Lead: Semple) has played a national role in coordinating COVID clinical data and sample collection and analysis. AGILE (Khoo) is a world-first for phase I evaluation in a platform trial that allows simultaneous testing of multiple potential treatments in a pandemic. COVID-LIV (French) is studying COVID spread within the community and households. These projects are supported by an extensive UoL genomics infrastructure that has sequenced a large proportion of the coronavirus genomes profiled in the UK.

# 4E. INDICATORS OF WIDER INFLUENCE

For Cat. 1A academics surveyed in 2019/2020:

- 51% have served on national (research council or similar) or international grants committees, 60% on learned societies, 40% on scientific advisory boards and 37% on professional bodies.
- 53% have served on journal editorial boards.
- 55% have participated in international conference organisation.
- 64% have engaged with industry through research or advisory capacities and 20% hold patents.
- 65% have engaged with non-academic users of research and 43% have incorporated PPI into their research.

Specific examples are described below that illustrate the range of activities undertaken by our academics.

#### 4E.1. Learned societies, prestigious research bodies and health organisations

Fellows: Royal Society (Dockray), Academy of Medical Sciences (Burgoyne, Dockray, Park, Pirmohamed, Wray), Institute of Physics (Hasnain), Royal Society of Chemistry (Goodacre, Hasnain, Yates, Eyers), NIHR Senior Investigators (Carrol, Lip, Pirmohamed, Solomon, Sutton), RAEng/Leverhulme Trust Senior Fellow (Williams). Academic Vice-President of Royal College of



Physicians (Toh), President of the Bone Research Society (Gallagher). Non-executive director of NHS England (Pirmohamed).

#### 4E.2. Major research prizes

NIHR/Royal College of Ophthalmologists Researcher of the Year 2018 (Kaye), European Pancreatic Club Gold Medal (Halloran), International Liver Cancer Association Nelson Fausto Award (Johnson).

#### 4E.3. Contributions to major advisory bodies

- ◆ The Office of Strategic Coordination of Health Research (NIHR & MRC) (Jackson)
- ♣ Department of Health, Scientific Advisory Group for Emergencies (SAGE) (Semple)
- ♣ New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) (Semple)
- Advisory Group of Global Experts (Cunliffe)
- ♠ MHRA working group on Yellow Fever vaccine safety (Turtle)
- ♦ WHO Department of Vaccines and Biologicals (French)
- ♠ NIHR CRN National Speciality Lead for Infection (Hope)
- European Society of Cardiology and European Heart Rhythm Association (**Lip** has chaired the generation of 6 sets of consensus guideline since 2014)
- MRC Expert Group on ME/Chronic Fatigue Syndrome (Jackson)
- 100k Genomes Project (GeCIP Head & Neck cancer lead) (Jones)
- National Cancer Research Institute, Haematological Clinical Studies Group (Pettitt (Chair))
- UK CLL Forum (Pettitt)
- ▲ Commission on Human Medicines (Park, Pirmohamed)
- ▲ MHRA Pharmacovigilance Expert Advisory Group (Pirmohamed (Chair))

Figure 15. Contributions to major external bodies.

Strategic themes: **♦** Infection, ■ Life Course, **♦** Cancer, **▲** Pharmacology, **♦** All.

<u>Supporting impact</u>: Greg Lip is a member of the executive steering committee of the European Society of Cardiology (ESC) EuroObservational Research Programme on Atrial Fibrillation (EORP-AF), defining the epidemiology and management of AF in Europe.