**Institution: Newcastle University**

**Unit of Assessment: UoA1- Clinical Medicine**

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

### 1.1 Overview

Our UoA1 submission includes 168 staff (159.8 FTE), of whom 66 are clinical academics and 25 are early career researchers (ECRs). Research in this UoA combines discovery science with experimental medicine and clinical translation, supported by parallel programmes of clinical and non-clinical career development and training. It is based on a strong university-NHS partnership focussed on improving diagnostic technologies, treatments and patient outcomes, recognised with the recent award of Academic Health Science Centre status. We describe our progress across 5 domains: 1) **Cancer**; 2) **Immunity and Inflammation**; 3) **Long-term Conditions and Ageing**; 4) **Rare Diseases** and 5) **Regenerative Medicine, Transplantation and Advanced Therapies**, which map directly to our Faculty and University research themes and Centres. Our academic clinical training approach has informed national policy (**Jones** is NIHR Academy Dean) and we cultivate next generation biomedical and clinical researchers through university academic track fellowships. There is strong cross-linkage between the UoA1 domains and important interdisciplinary links with other UoAs, examples include Neurodegeneration (UoA4); medicinal chemistry (UoA8) for Drug Discovery; computing around Digital Healthcare (UoA11); and applied health research in the context of trial design, biostatistics and economics of healthcare implementation (UoA2). We work with industry partners, particularly in clinical trials (Newcastle has been top three nationally for trial activity and patient recruitment in NIHR league tables over the past eight years) and drive economic benefit through spin-out creation.

### 1.2 Research Strategy

We pursue research in this UoA through strategic partnerships with Newcastle upon Tyne Hospitals NHS Foundation Trust (NuTH) and Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust (CNTW). Our three organisations form the core of our NIHR Academic Health Science Centre, *Newcastle Health Innovation Partners* (AHSC, 2020), alongside Newcastle City Council and the Academic Health Science Network (AHSN). Our AHSC aims to discover, develop and translate into practice, innovations in healthcare which tackle health inequalities and achieve better patient outcomes, thereby improving citizen health and generating economic growth. Central to our objectives are our NIHR Biomedical Research Centre (BRC) in Ageing and Long-Term Conditions and our specialist Clinical Research Facilities, which are jointly managed between NuTH and the Faculty, to enable our experimental medicine programmes and commercial interactions.

**Developments since REF2014**

We have fully delivered our 2014 strategic objectives by increasing our capacity to pursue high quality research with clinical impact.

We created a Translational Deanery to develop closer working between clinical and discovery science researchers, identify translational opportunities and achieve “pull-through” of research. We have secured new translation-enabling infrastructure including the NIHR Medtech and In Vitro

Diagnostic Co-operative, NIHR Innovation Observatory and National Innovation Centre for Ageing (NIC-A). Our expanded translational ecosystem now provides commercial expertise through a Translator in Residence (Wellcome Trust Translational Partnership, £0.8M), pump-priming funds (including £3.7M MRC Confidence in Concept) and a Translational Development support team who link researchers to key infrastructure and guide onward applications. Expertise in commissioning and adoption comes from strengthened links with the AHSN. Our priming support for early translational concepts has led to >£20M in onward projects (including 37 DPFS, NIHR EME & HTA programmes). We formed Diagnostics-NE (s3.4) to jointly promote university and NuTH infrastructure and expertise to academic and commercial partners. The success of our approach is evidenced by the day-to-day clinical impact of our research (see Impact Case Studies, ICS) and is recognised in the award of externally-funded research centres, infrastructure and networks (see Table). The Deanery continues to evolve and is at the heart of the new Translational and Clinical Research Institute.

Health informatics has been developed at the core of our BRC with links to the University Digital Institute (UoA11) and the National Innovation Centre for Data (NIC-D), hosted in Newcastle. This expertise is enabling digital healthcare projects using real-time patient data collection for monitoring and diagnosis, such as the IDEA-FAST (Sjögren's syndrome, **Ng**) and the MOBILISE-D (UoA4) programmes. Research can now link with electronic patient records across the region where the Great North Care Record covers a population of 3.6 million. This is enabling innovative programmes including multimorbidity clustering (e.g. ADMISSION, **A.Sayer**).

Leadership of our flagship fellowship programmes aligns with the Dean of Clinical Medicine (Clinical Academic Office, s2.2.3) having oversight of the entire clinical academic training pathway, and the Dean of Research & Innovation overseeing non-clinical training. We invested in Faculty and University fellowship schemes for non-clinical training. Investments in key appointments allowed cross-cutting mechanistic themes described in 2014 (e.g. Immunity and Therapeutics) to grow in size and become larger primary research areas.

**A new structure for the next decade**

To promote team science and create a research environment which is agile to future challenges, we recently restructured our Faculty of Medical Sciences. We moved from six largely independently operating and thematically focused institutes to three integrated institutes, reflecting the translational research pathway: the **Biosciences Institute (NUBI)**, the **Translational and Clinical Research Institute (NUTCRI)** and the **Population Health Sciences Institute (NUPHSI)**. Academics from these institutes work together in research themes spanning the entire translational pathway. We deliberately created innovative themes which pull together multi-disciplinary teams of researchers, allowing new fields of expertise to be recognised and nurtured.

Our largest and most comprehensive research areas are recognised within the University as Centres of Research Excellence (NUCoREs, REF5a 2.2), which reach across Faculties and link with external organisations and industry to promote global visibility and impact. In UoA1, we established NUCoREs in Ageing and Inequalities, Cancer, Healthier Lives, Rare Diseases and Regulatory Science. These NUCoREs create new collaborations with academics in the humanities (e.g. medical ethics, law, business), and strengthen existing ties with the science faculty (e.g. digital health technologies, biomedical engineering) and the NHS.

| Table. Overview of externally funded research centres, infrastructure, facilities & networks |
|---|
| Cancer |
| CRUK Newcastle Cancer Research Centre (2014-17) **renewed** (2018-22) |
| CRUK Newcastle Experimental Cancer Medicine Centre (2017-22) |
| CRUK Drug Discovery Programme (2015-20), **renewed** (2021-25) |
| Immunity and Inflammation |
| National Renal Complement Therapeutics Centre (Established 2016) |
| Cystic Fibrosis Trust Strategic Research Centre (2016-21) |
| Long-term conditions and Ageing |
| NIHR Biomedical Research Centre (BRC3) in Ageing and Long-Term Conditions (2012-17), **renewed** (2017-22) |
| BEIS/MRC National Innovation Centre for Ageing (2018 onwards) |
| NIHR Policy Research Unit (PRU) Older People and Frailty (2019-23) |
| NIHR Applied Research Collaboration (ARC North East and North Cumbria) (2019-24) |
| MRC Lifelong Health and Wellbeing Centre in Ageing and Vitality (2014-19) |
| MRC/ARUK Centre for Integrated Musculoskeletal Ageing (2012-17), **renewed** (2017-22) |
| Rare Diseases |
| Wellcome Trust Centre for Mitochondrial Research (2012-20), **renewed** (2020-24) |
| MRC Centre for Neuromuscular Diseases (2008-18) |
| MRC International Centre for Genomic Medicine in Neuromuscular Diseases (2019-24) |
| Regenerative Medicine, Transplantation and Advanced Therapies |
| NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation (2015-22) |
| Versus Arthritis Experimental Arthritis Treatment Centre (2012-18) |
| Versus Arthritis Rheumatoid Arthritis Centre of Excellence (2013-19, **renewed** 2020-25) |
| Northern Alliance Advanced Therapies Treatment Centre (2018-21) |
| Infrastructure Awards |
| MRC/EPSRC Molecular Pathology Node (2015-19) |
| MRC Newcastle University Single Cell Functional Genomics Unit (2015-18) |
| MRC Human Developmental Biology Resource (2013-18, **renewed** 2018-23) |
| NIHR Newcastle Diagnostic Evidence Co-operative (2013-17) |
| NIHR Newcastle Medtech & In Vitro Diagnostics Co-operative, (MIC, 2018-22) |
| NIHR Innovation Observatory (NIHRIO, 2017-22) |
| NIHR Clinical Ageing Research Unit / Clinical Research Facility (2008-22) |
| NIHR Health Protection Research Unit (2014-20) |
| NIHR Research Design Service – North East North Cumbria (2012-18, **renewed** 2018-23) |
| Training/DTPs |
| MRC Doctoral Training Partnership - Discovery Medicine North (DiMeN) (2016-21) |
| BBSRC Doctoral Training Partnership (2010, **renewed** 2015, 2020) |
| Wellcome Trust 4ward North Clinical PhD Academy (2016-22) |

### 1.3 Research Achievements

We present our research activity, impact and strategy grouped into five major research domains:

#### 1.3.1 Cancer

Research from Newcastle University (NU) has directly improved clinical care and outcomes for cancer patients. Our translational strengths include drug discovery, experimental medicine, early detection and prevention, cancer pharmacology, paediatric oncology and haematology, liver and colorectal cancer.

NU is a CRUK Centre and a Blood Cancer UK Research Centre of Excellence. We attract significant programmatic funding from MRC (**Endicott**, **Noble**), NIHR/CRUK (ECMC, **Plummer**), CRUK (**Clifford**, **Heidenreich**, **D.Mann**, **Moorman**, **Plummer**, **Wedge**), EU (**Harrison**, **Reeves**), Blood Cancer UK (**Allan**, **Harrison**, **Moorman**), GUTS UK (**Rees**) and industry (including an alliance with Astex Pharmaceuticals, >£5M, **Wedge**). We lead large-scale network awards in liver cancer (HUNTER £4.6M, **D.Mann**, **Reeves**, CRUK), childhood brain tumours (INSTINCT £1M, **Clifford**, The Brain Tumour Charity/Children with Cancer UK/GOSH Charity), and major national/international clinical trials grants from CRUK (**Burn**, **Clifford**, **Greystoke**). We established the NUCoRE Centre for Cancer (**Clifford**, Director) in 2019, bringing together all cancer-related investigators and research across the University, in conjunction with key external stakeholders. The Centre hosts 104 investigators including ECRs, of which 52 contribute to UoA1 themes.

**Activity:**

**Discovery and Developmental Bioscience** underpins our cancer strategy. Themes and key examples include: Cell Signalling, uncovering critical roles for RUNX1/ETO in leukaemic transformation (**Heidenreich**, CancerCell2018); Structural Biology, elucidation of a RanGDP-associated nuclear import pathway (**Endicott**, Cell2014); Tumour Immunology and Microenvironment, advancing theories of branching morphogenesis in the developing prostate (**Heer**, Cell2017), and investigating androgen receptors as therapeutic targets in prostate cancer (**Coffey**, **Elliot**, **Gaughan**, **McCracken**, **Munkley**, **C.Robson**, eLife2019, NucleicAcidsRes2020) and Chromosomes and the Cell Cycle, defining disease-relevant chromatin states in atypical teratoid-rhabdoid tumours (**Williamson**, CancerCell2019) and discovering mechanisms of chromosome 21 rearrangement in leukaemia (**Harrison**, Nature2014).

These discovery initiatives feed programmes in **Precision Medicine, Genomics and Informatics**, which focus on clinical delivery. Within Paediatric Oncology and Haematology, our leukaemia research teams (**Allan**, **Enshaei**, **Harrison**, **Irving**, **Moorman**, **Russell**, **van Delft**) host an internationally accessible leukaemia cytogenetics database. The 30,000 members allow in-depth study of the nature, clinical and prognostic relevance of genetic aberrations in childhood and adult leukaemias, leading to biomarkers and genomic profiles being incorporated into clinical trials and routine clinical practice (JClinOncology2014, JClinOncology2018). Discoveries by the childhood medulloblastoma group (**Clifford**, **Hicks**, **Williamson**) have re-defined risk-stratification and strongly influenced design of risk-adapted international clinical trials (CancerCell2015, LancetOncology2017), and underpin the WHO classification of medulloblastoma, internationally adopted into routine diagnostic practice (**Clifford** ICS "*Treatment stratification for childhood medulloblastoma patients*"). In liver cancer, collaborations between Cancer, Ageing and Immunity researchers (**D.Mann**, **J.Mann**, **Oakley**, **Tiniakos**, **C.Wilson**) led to discovery of critical disease

roles for neutrophil infiltration across human disease and model systems (NatCommun2015). This group lead the HUNTER international accelerator network, designed to deliver translational advances into clinical trials and practice. The programme has resulted in a CRUK/AstraZeneca-sponsored phase I/II study of a combination therapy of CXCR2 inhibitor AZD5069 and Durvalumab in patients with advanced HCC. Our pharmacology/therapeutic drug monitoring (TDM) programme (**Veal**, CRUK/NIHR funding) hosts the National Centre for TDM in childhood cancer, delivering real-time TDM to support personalised treatment of some of the most challenging childhood cancer patient groups across the UK, and now embedded in national treatment guidelines.

In **Drug Discovery and Pre-Clinical Development**, our CRUK Drug Discovery Unit was among the first academic teams to apply structure-based drug design to discover anti-cancer medicines, and Newcastle is one of only a few UK academic groups to contribute to the development of licensed drugs. The programme is led by **Hickson**, **Endicott**, **Noble** and **Wedge** with colleagues in Medicinal Chemistry (UoA8). The first-in-class PARP inhibitor Rucaparib (Rubraca), developed from concept through to clinic by the Newcastle team, was licensed for use in ovarian cancer in 2016 (**Curtin**, **Drew**, **Plummer**, ICS *"Rucaparib targeted therapy for a range of cancers characterised by homologous repair deficiency"*). The Unit has a strategic alliance with Astex Pharmaceuticals, following a collaboration that identified the selective FGFR inhibitor Erdafitinib (Balversa, UoA5 ICS, **Irving**, **Newell**, MolCancerTherap2011), licensed clinically as a treatment for bladder cancer in 2019. The team also discovered DNA-PKcs inhibitors (JClinInvest2020), and collaboration with AstraZeneca and Astex Pharmaceuticals to identify AZD7648 and ASTX295, with both drugs now in Phase I/IIa clinical trials.

Our **Clinical Trials** programme leads and supports **Early Phase** trials in adult patients where we focus on lung cancer (**Greystoke**, BrJCancer2017), and collaborate in international studies on skin cancers (**Plummer**, NEJM2017), complemented by the childhood cancer programme at the Great North Children's Hospital (**Campbell-Hewson**, LancetOncol2019). We are an Innovative Therapies for Children with Cancer in Europe first-in-child clinical site, and lead the INCLUDE network (Newcastle, Glasgow, Edinburgh, Belfast, Aberdeen) which delivers childhood early-phase trials in the North of the UK. Our **Late Phase** trials link to the Centre's strategic research areas: **O'Brien** co-led the large multicentre phase III trial of tyrosine kinase inhibitors in chronic myeloid leukaemia (NEJM2017). **Clifford** leads pan-European clinical trials and associated biological studies in medulloblastoma (e.g. LancetOncology2018, ICS *"Treatment stratification for childhood medulloblastoma patients"*), and **Moorman** leads on genetic risk stratification for the European 'ALLTogether' trial in childhood ALL. **Veal** has led pharmacology analyses within international Phase III trials (e.g. LancetOncology2017).

**Toxicity and Survivorship** programmes focus on reducing the burden of cancer and its treatments on patients and their families, linking into UoA2 (**Sharp**). Work within UoA1 includes: development of sodium thiosulphate as a chemo-protectant against cisplatin-induced hearing loss (**Veal**, NEJM2018); assessment of patient-reported survivorship outcomes in BRAF-mutated melanoma patients following targeted therapies (**Plummer**, LancetOncology2019); and development of international evidence-based surveillance guidelines for major late effects in survivors of childhood and young adult cancer (**Skinner**, LancetOncology2017).

In **Prevention and Screening**, **Rees** together with **Sharp** (UoA2) led investigation into cancer risk factors and how to optimise personalised screening and diagnostic processes. This includes the SEAFOOD polyp prevention trial, (**Rees**, Lancet2018) and multi-award winning studies of tools to

improve diagnosis, which have led to international development and adoption into clinical practice of the Endocuff Vision device (**Rees**, Gut2019, ICS *"Endocuff Vision: a simple tool to increase early detection of cancerous lesions in the colon"*). **Rutter** and **Sharp** lead the UK-wide national endoscopy database (Gut2020), which has been used to assess the impact of COVID-19 (Gut2020) Ongoing work includes building on CAPP2 (**Burn**, Lancet2020 ICS *"Aspirin to decrease the risk of colorectal cancer for patients with Lynch syndrome")*, to develop the use of aspirin to prevent colorectal cancer in Lynch syndrome (CaPP3 Phase III trial), and leading national networks in chemo-prevention and early detection (**Rees**, COLOSPEED) of colorectal cancer.

### 1.3.2 Immunity and Inflammation

Our research portfolio in **Immunity and Inflammation** has grown in breadth and depth since 2014 by developing shared infrastructure and critical mass and by external partnering for clinical impact. Together with the Institute of Child Health in London, we co-host the £1.9M **MRC-Wellcome Trust Human Developmental Biology Resource (HDBR)** (**Henderson** lead, hdbr.org) a unique open tissue resource. This has allowed leaders such as **Haniffa** to position Newcastle as a central player in international initiatives including the **Human Cell Atlas** (Science2020), with an open data resource supported by £750k industrial funding, used in >50 publications since its launch. We actively participate in the **UK COVID Immunology Consortium** (section 4.6), **Isaacs** contributed to COVID-19 rheumatological disease guidelines (AnnRheu2020) and led a work-package in RTCure, an EU IMI2 project aiming to prevent rheumatoid arthritis (RA) by targeting 'at risk' individuals with tolerogenic therapies (**Isaacs**, €6M). We coordinate another EU IMI2 project focused on identifying digital measures of fatigue and disordered sleep to improve both our understanding and therapy options in neurodegenerative and immune-mediated inflammatory disease (**Ng**, IDEA-FAST, €43M). Since inflammation is clearly implicated in carcinogenesis, there are strong links to **Cancer** (s1.3.1).

**Activity:**

**Immunopoiesis and Immunomics**. The study of immune cell development, heterogeneity and function provides a unifying focus for researchers from diverse backgrounds (**Bigley**, **Collin**, **Hambleton**, **Haniffa**). Notable contributions include dissecting the overlapping and distinct origins and function of dendritic cells, monocytes and tissue macrophages (Blood2015, Immunity2020). Methodologically, we have matured from predominantly flow cytometric and functional approaches to increasingly comprehensive (single cell) transcriptomic and proteomic profiling, (**Haniffa**, **Payne**) leading to the discovery of new cell types both within and outside the immune system (Science2017, Nature2018). We can now model and perturb *in vitro* models of human haematopoiesis based on human CD34+ or induced pluripotent stem cell culture and differentiation (**Bigley**, **Hambleton**, CellReports2018; Blood2020).

**Tolerance and Immune Dysregulation**. Our research on immune dysregulation related to autoimmune disease covers the full spectrum from basic science to first-in-human clinical trials. Exploration of inborn errors of immunity presenting as immune dysregulation has provided a strong mechanistic backdrop (**Hambleton**, Cell2014, JExpMed2019, new insights (NatureImmunol2019) and further opportunity for cross-disciplinary team science across the faculty (e.g. with **Duncan**, SciImmunol2019, and **Hambleton** Blood2020).

**Rheumatological Disease** is a long-term focus (**Isaacs**, **Hilkens**, **Ng**, **Pratt**; **Reynard**, ECRs **Baker**, **Reynolds**) and we are a EULAR Centre of Excellence, a member of the MRC/Versus Arthritis CIMA, and the Versus Arthritis Inflammatory Arthritis Centre of Excellence (£4.5M).

Recent highlights include the demonstration of safety in the first ever trial (phase 1) of intra-articular tolerogenic dendritic cells (tolDC, **Isaacs**, AnnRheumDis2017) and a longitudinal study tracking biomarkers of drug-free remission in rheumatoid arthritis (RA) patients from whom treatment was withdrawn (JAutoimm2019). This work informed a larger study on personalised therapy withdrawal by understanding the biological factors that underpin disease flare (BIO-FLARE, MRC-funded, £2.8M) which has just completed recruitment. Our finding that altered DNA methylation associated with RA risk variants affects the expression of genes relevant to immune dysregulation (**Reynard**, JAllergyClinImmunol2020) suggests potential therapeutic targets. Current therapeutic projects include further development of autologous tolDC cell therapy to investigate mode and timing of delivery (AuToDeCRAII, £1.1M Versus Arthritis-funded, with **Advanced Therapies** (s1.3.5)) and the first ever clinical trial to target synovial fibroblast proliferation in RA, utilising a repurposed cancer drug in partnership with the SME Cyclacel (TRAFIC, £1M, MRC-funded). **Pearce** co-led a successful first-in-woman study to treat mild Graves' Disease with tolerising TSHR peptides (Thyroid2019, MRC DPFS-funded); and was recently awarded >£900K to explore plasma cell depleting therapy for the same indication using a novel two-stage adaptive design with **Wason** (UoA2) (MRC DPFS). **Ng** is part of an open data EU consortium to understand the natural history, stratification and therapy of Sjögren's syndrome (LancetRhematology2019).

**Inflammation**. Arising from our past translational research in individuals with atypical Haemolytic Uraemic Syndrome (aHUS) and C3 glomerulopathy, Newcastle is now commissioned as the National Renal Complement Therapeutics Centre to deliver advanced diagnostics and precision medicine to such patients (**J.Goodship**, **T.Goodship**, **Kavanagh**, **Sheerin** ICS*: "Approval of eculizumab and establishment of a national service to treat patients with Atypical Haemolytic Uraemic Syndrome"*), with recent research examining long-term treatment response (**Kavanagh**, KidneyInt2020). Research on mucosal inflammation is gaining critical mass in Newcastle with particular expertise in tissue immunopathology. This is reflected by leadership of bowel disease consensus guidelines (**Lamb**, Gut2019), and IBD-Response (MRC; **Lamb**, **Stewart**, both ECRs), a multicentre study of inflammatory bowel disease relating therapeutic outcomes to molecular tissue immunopathology and gut microbiota in an inception cohort. **Stewart** brings extensive expertise in the analysis of complex microbiome datasets across different clinical settings (e.g. sepsis and type 1 diabetes) in preterm infants to neonates to early childhood (Microbiome2017, Nature2018).

*In vitro* modelling of Cystic Fibrosis pathogenesis has yielded new appreciation of the role of perturbed sphingosine metabolism in bacterial susceptibility (**Brodlie**, CellHostMicrobe2017). Our translational respiratory research (**Simpson**) developed diagnostic tests for ventilator-acquired pneumonia, whose efficacy was shown in clinical trials (LancetRespMed2020) and clinical prediction of bronchiectasis (RespMed2017).

**Innate Immunity to Infection**. **Duncan** and **Hambleton** study innate antiviral immunity. They made the seminal discovery of type 1 interferon receptor deficiency in children intrinsically predisposed to severe viral illness (SciTranslMed2015), a pathway recently implicated in susceptibility to severe COVID-19. In tandem, they described pathological neuroinflammation in siblings with faulty negative feedback to the interferon signalling pathway (SciImmunol2019).

### 1.3.3 Long-term Conditions and Ageing

Newcastle was one of the first institutions to recognise opportunities, health and societal issues associated with an ageing population. We are international leaders in the interdisciplinary investigation of ageing, and our researchers are policy opinion leaders. **A.Sayer** and **Witham** contributed oral evidence, alongside written evidence from the wider NU Ageing research community, to the House of Lords Science and Technology Committee into Healthy Ageing. Ageing is identified as one of the five beacons of excellence in the University's 2018 research strategy, reaffirming our commitment in this field. We focus on translating understanding of the biology of ageing into advances in prevention, diagnosis and treatment of ageing syndromes, including **Sarcopenia, Frailty and Multimorbidity**. We also address the complexities of long-term conditions associated with ageing including **Liver Disease, Diabetes and Cardiovascular Disease** where our research has directly changed disease management.

Central to this research is the NIHR Newcastle Biomedical Research Centre (BRC) focused around ageing and long-term conditions (£16.6M 2012-17; £16.2M, 2017-22). We lead the largest EU project on obesity/diabetes-related non-alcoholic fatty liver disease (**Anstee**, NAFLD, IMI2, €46.5M), studying blood and imaging-based biomarkers for diagnosis and risk-stratification to support clinical trials. Newcastle also leads the National Innovation Centre for Ageing (NIC-A, £40M co-investment with UK Government), bringing together scientists, industry, health and care providers and the public to create solutions to the impact of ageing. These initiatives link to the UK Government Ageing Society Grand Challenge to deliver healthier ageing and reduced health and social inequalities.

**Activity:**

**Diabetes**. Our pioneering research into type 2 diabetes (T2D) has led to major changes in policy and direct clinical impact in the NHS (£500K Diabetes UK). **Hollingsworth**, **R.Taylor** demonstrated that dietary restriction and weight-loss reduces liver and pancreatic fat, reduces triacylglycerol levels and normalises functional β-cell capacity, leading to remission of T2D (**R.Taylor**, CellMetab2018, DiabetesCare2017, DiabetesCare2020). Our subsequent multicentre clinical trial (DiRECT with Glasgow) showed feasibility of achieving this weight-loss in primary care (**R.Taylor**, Lancet2018) and that remission is maintained (**Hollingsworth**, **R.Taylor** LancetDiabEndocrinol2019, ICS "*Remission of type 2 diabetes using a low calorie diet*"). We translated that finding into a digital health platform (**Trenell**) for education and behaviour change and formed the spin-out company Changing Health which delivers the digital behaviour change platform for NHS England. We have expanded our genetic research in T2D through participation in the Genetics of Insulin Sensitivity consortium (**M.Walker**, JClinInvest2015) and contributed improved understanding of genetic predisposition (**Viñuela**, ECR, NatCommun2020).

The expansion of our School of Biomedical sciences to include Sports and Exercise Science has catalysed new research across the faculty, for example in Type 1 diabetes (**Shaw**, **Stevenson**, **M.Walker**, **West**) where we improved strategies for glycaemic control through exercise and diet, key factors influencing diabetic control, cardiovascular risk and early mortality (BMJOpenDiabetesResCare2015), and achieved sustained 20-fold reduction in severe hypoglycaemia in a multi-centre type 1 diabetes RCT (**Shaw**, DiabetesCare2019).

**Liver Disease**. We are leaders in non-viral liver disease with major programmes in metabolic (NAFLD) and rare liver diseases focusing on Autoimmune Liver Disease, including Primary Biliary Cholangitis (PBC) and Autoimmune Hepatitis (AIH). Clinical research (**Anstee**, **Day**, **Daly**, **Jones)**

is complemented by a mechanistic biology programme in Liver Fibrosis (**D.Mann**, **J.Mann**) which strengthens our work in hepatocellular carcinoma (HCC, **Reeves**).

NAFLD is strongly associated with obesity, T2D, hypertension and dyslipidaemia, a real exemplar for multimorbidity and a key driver of early death in the North East. The European NAFLD Registry established by **Day**, with **Anstee** and is now the largest international NAFLD cohort with an associated bioresource and patients under longitudinal follow-up (ContempClinicalTrials2020). Active in 14 countries, it has enrolled >7,500 biopsy-proven NAFLD patients. NU investigators have leveraged this to conduct the largest genome-wide association study for histologically-characterised NAFLD, the most comprehensive hepatic transcriptomics analysis across the full histological spectrum of NAFLD, identifying and validating novel modifiers and new disease biomarkers, and shown that age is a confounding factor for the non-invasive diagnosis of advanced NAFLD fibrosis (**Anstee** JHepatol2020, SciTranslMed2020, AmJGastroenterol2017)

NU leads the UK-PBC research consortium, the largest cohort of 9,000 fully phenotyped PBC patients, supported by MRC Stratified Medicine funding and industry. This allowed us to coordinate international trials of four new PBC treatment regimens (**Jones**, Lancet2017, NEJM2018; **Newton**, Hepatology2019), showing significant improvements in fatigue and pruritus symptoms and reduced mortality risk factors. Stratified therapy identified and validated by this approach has entered routine NHS practice. The uniquely deep phenotyped UK-AIH patient cohort has increased to >2,000 patients. Research in this cohort identified unmet clinical needs in AIH, a low rate of disease remission, over-reliance on steroid therapy, and a significant impact of steroids on health utility (**Jones**, Hepatology2018). This has led to the first trials in AIH in a generation.

**Sarcopenia, Frailty and Multimorbidity**. The MASS (Muscle Ageing and Sarcopenia Studies) research programme involves deep characterisation of skeletal muscle to understand pathophysiological processes underlying ageing, and to identify targets for diagnosis, treatment and prevention of sarcopenia. We demonstrated that sarcopenia is driven by altered mitochondrial metabolism leading to pathological loss of muscle mass and function in older people (**A.Sayer**, NatureComms19). This work is defining international research direction and clinical practice, with **A.Sayer** co-authoring the first Lancet Seminar on sarcopenia (Lancet2019) and revised European consensus Sarcopenia Guidelines (AgeAgeing2019), with subsequent estimates showing high prevalence in a population study (EurGeriatrMed2020, **Dodds**, **Robinson**, **A.Sayer**). This has led to the MASS Lifecourse study, a world first epidemiological and deep phenotyping study recruiting participants from mid-life through to later life (160 individuals). **Witham** leads on developing interventional studies and clinical trials tailored to older people (AgeAgeing2020), including improving inclusion (Trials2020). Our frailty research investigates worldwide ageing populations (**Witham**, WellcomeOpenRes2019), as well as potential treatments for precursors of frailty such as orthostatic hypotension (**Frith**, AgeAgeing2020, NIHR, £1.4M).

Understanding multimorbidity is a research priority and links epidemiology and health informatics with mechanistic and interventional studies across UoAs. We have grown our capacity in this field and lead two new consortia: the ADMISSION UK Multimorbidity Research Collaborative focusing on multiple long-term conditions in hospital (**A.Sayer**, MRC, £3.8M) and inter-relationships between polypharmacy and multiple long-term conditions (**Reynolds**, NIHR consortia building grant) which both strengthen the links between our Faculty and the Digital Institute (an Alan Turing Institute partner).

**Vascular Biology and Medicine.** Our vascular research investigates fundamental mechanisms involved in homeostasis and inflammation, aimed at developing new treatments for vascular diseases. Treatment of aged mice with navitoclax pointed to senolytics as a potential new therapeutic avenue for myocardial infarction (**Richardson**, AgeingCell2019). Clearance of senescent cells during cardiac ischemia-reperfusion injury was also shown to improve recovery (AgeingCell2020). We showed that leukocyte subsets expressing the fractalkine receptor CX3CR1 decrease in peripheral and coronary artery blood, correlating with severity of acute myocardial infarcts and outcome and increasing with age (**Spyridopoulos**, JClinInvest2015). Recently recruited PI **Stellos** (ERC Starter Grant €1.5M) is leading international work on amyloid-beta in atherosclerosis and mortality prediction in coronary artery disease (AnnInternMed2018, JAmCollegeCardiol2020), and the underpinning role for RNA editing in vascular disease (NatureMed2016) which has potential for RNA therapeutics in cardiovascular precision medicine (FrontPhysiol2018). Our cardiovascular work, encompassing our expertise in ageing (**Kunadian**), found that women and older people continue to have suboptimal outcomes from percutaneous coronary intervention (AmJCardiology2017), leading to the ongoing SENIOR-RITA trial (BHF £1.7M).

### 1.3.4 Rare Diseases

Newcastle has a distinguished history of research into rare diseases. Our international rare disease portfolio is led from the John Walton Muscular Dystrophy Research Centre (JWMDRC, **Bushby**, **Hedley**, **Lochmüller**, **Straub**) and the Wellcome Trust Centre for Mitochondrial Research (WTCMR, **Chrzanowska-Lightowlers**, **Greaves**, **Gorman**, **Herbert**, **Hudson**, **Horvath**, **McFarland**, **Payne**, **RW.Taylor**, **Turnbull**; renewal £6.1M). Since 2014, these colleagues have led EU and international initiatives designed to improve diagnostics, treatment, care and research for rare diseases; including EUCERD JA; RD-ACTION; RD-Connect; Rare-Best practices; Rare 2030; EJP RD; Connect44Children; Solve-RD, Share4Rare and Digital tools 4 Rare Diseases (EJP RD).

A key accolade is Newcastle's role in the launch of the European Reference Networks (ERNs, 2017-2020). ERNs were designed to span care and research domains, which is essential to translate rare disease discoveries into effective adopted therapies. NU and NuTH established and coordinated 3 of 24 ERNs (until Brexit) in Immunodeficiency, Auto-inflammatory & Autoimmune Diseases; Liver Diseases; and Neuromuscular Diseases. Newcastle also participated in ERNs for rare bone, pulmonary and renal diseases. The Newcastle Research Biobank for Rare and Neuromuscular Diseases works with EuroBioBank and has more than 15,000 samples. We lead 8 rare disease patient registries: UK-PBC, UK-AIH, UK Myotonic Dystrophy Patient Registry, UK FSHD Patient Registry, UK SMA Patient Registry, UK Primary Sjögren's Syndrome Registry; Global FKRP Registry, and the International GNE Myopathy Registry. These registries have supported >50 programmes of research, from discovery science to Phase III trials.

In 2020, we launched the NUCoRE for Rare Diseases (**Jones**, Director), hosting >80 NU colleagues. This NUCoRE aims to bring together expertise across the various rare disease areas to strengthen and enhance Newcastle's reputation as a seat of multidisciplinary knowledge and expertise in rare diseases. Over half of our experts have NHS contracts, enabling us to deliver meaningful patient-focused research and translate our science from bench to bedside and back again.

**Activity:**

**Diagnostic Rare Disease Research.** Gene identification for rare disorders is facilitated by the University's Genomics Core Facility and Bioinformatic Support Unit, which jointly support studies aimed at characterising the molecular pathology underlying rare diseases. Gene and novel variant discovery has been successful in rare kidney diseases, helping to better understand Joubert syndrome (**Miles**, **J.Sayer**, PNAS2018, PNAS2020). Two Wellcome Trust-funded genomics projects in rare disease focus on immunodeficiency syndromes (**Hambleton**, Blood2020) and primary male infertility (**Veltman**, HumReprod2020). The WTCMR and the JWMDRC are both actively involved in international sequencing projects (**RW.Taylor**, JAMA2014, **Lochmuller**, EurJHumanGenet2020) that complement their National Highly Specialised Commissioned Diagnostic Services in mitochondrial diseases and limb girdle muscular dystrophies. Both teams were part of the MRC Centre for Neuromuscular Disease (2008-2018) and, together with UCL and Cambridge University, participate in the MRC-funded International Centre for Genomic Medicine in Neuromuscular Diseases (**Straub**, Co-Director). Genetic research is complemented by biomarker investigations, for example in rare histiocytic disorders **Bomken**, **Collin**, **Haniffa** (Blood2017).

**Disease Cohorts and Global Data Sharing.** Our strength in rare diseases is built on well-characterised disease cohorts, supported by the development of patient registries (**Straub**, JAMANeurol2019), rare disease biobanks and national and international networks (IMI2 c4c, TREAT-NMD, Horizon2020 Solve-RD). We have cohorts in rare liver disease, mitochondrial diseases, primary male infertility, neuromuscular diseases, rare endocrinological, eye, renal and skin diseases. EU-funded projects NeurOmics and EURenOmics generated -omics data and improved diagnosis and cohort building in rare neurological and rare renal diseases. RD-Connect (led by Newcastle, €12M) developed an infrastructure to facilitate the international sharing, systematic integration and analysis of these data.

**From Experimental Medicine to Phase III Trails.** These disease cohorts and our expertise in translating potential therapies into proof of concept and first-in-human clinical trials attract commercial partnerships. During 2019-2020 alone, we were involved in 91 trials in rare diseases, e.g. antisense oligonucleotide trials in Duchenne muscular dystrophy and spinal muscular atrophy (**Straub**, NEJM2017). Our translational research group for rare bone diseases coordinates an H2020 project in metaphyseal chondrodysplasia, type Schmid (MCDS), which results from mutations in collagen X (**Briggs**, **Wright**). This project aims to advance repurposing of carbamazepine for MCDS through a multicentre, multinational clinical trial. EU funding also supports the stem-cell based gene therapy programme for recombination-deficient SCID and the transfer of multivirus-specific T cells following transplantation (**Gennery**, JClinImmunol2018, 2021). Two MRC DPFS awards funded recently-completed clinical trials of the effect of adjuvant Rituximab in young patients with Graves' hyperthyroidism (**Cheetham**), and combined immunotherapy and trophic adrenocortical stimulation in new onset autoimmune Addison's disease (**Pearce**, JClinEndocrinolMetab2020). A third DPFS award funds an ongoing trial of the efficacy of acipimox in patients with mitochondrial myopathy (**Gorman**). The National Renal Complement Therapeutics Centre leads a multicentre study of the safety and impact of eculizumab withdrawal in patients with aHUS (**Sheerin**, SETS-aHUS). Additional ongoing clinical research projects around aHUS are supported by the Wellcome Trust, looking at the role of the RNA exosome component EXOSC3 (**Hambleton**, **Kavanagh**, **Marchbank**), and by MRC,

investigating the Properdin Paradox using C3 D1115N (**Marchbank**, **Kavanagh**, **Harris**). Clinical trials in primary biliary cholangitis, a rare liver disease, are supported by the NIHR (**Jones**, s1.3.3).

**Translation into Patient Benefits.** The WTCMR has been supported by NHS England for their translation of mitochondrial donation into clinical practice (**Gorman**, **Herbert**, **Turnbull** ICS *"A new technique to prevent transmission of mitochondrial disease",* Lancet2018). This pioneering technique, developed by the interdisciplinary team, prevents the transmission of mitochondrial disease to the next generation (**Turnbull**, Nature2016). The JWMDRC has been involved in clinical trials leading to marketing approval for Translarna® in Duchenne muscular dystrophy (**Bushby**, **Guglieri**, **Straub**, ICS *"Ataluren: the first approved oral treatment for Duchenne muscular dystrophy",* **Bushby**, MuscleNerve2014) and Nusinersen® for spinal muscular atrophy (**Straub**, NEJM2017). In addition, the Centre has been involved in trials leading to the approval of AAV-based gene replacement therapy (Zolgensma®) for SMA type 1 by the EMA and FDA approval of antisense oligonucleotides Golodirsen® (Neurology2020) and Casimersen® for patients with DMD.

### 1.3.5 Regenerative Medicine, Transplantation and Advanced Therapies

We have nurtured significant growth in our capability, capacity and impact in Regenerative Medicine, Transplantation and Advanced Therapies, driven by major infrastructure awards and programme-level funding. These include the MRC Expand programme (**Shaw**, **Tiniakos**), Northern Alliance Advanced Therapies Treatment Centre (**Shaw**), NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation (**Fisher**, **Shaw**), ERC Consolidator Award (**Lako**) and NIHR SIGNET (**Dark**, **Fisher**, **Sheerin**, **Shaw**). We participated in a large EU IMI1-funded initiative, leading the derivation and characterisation of 1,500 human induced pluripotent stem cell lines now used worldwide for disease modelling drug discovery programmes and cell replacement proof of concept therapies StemBANCC, (**Armstrong**, **Lako**, €52M). Our growth is reflected in the creation of a cross-faculty research theme in Regenerative Medicine, Stem Cells and Transplantation which works with our NHS Trusts to facilitate translation and impact.

**Activity:**

**Regenerative Medicine.** We pioneered and introduced transformative limbal stem cell therapy for painful sight loss (**Figueiredo**, **Lako**, ICS *"Human-derived limbal cell transplant to treat chemical burns of the eye"*). Pluripotent stem cell derivation and modelling has provided a platform to generate functionally corrected cells for basic research and transplantation and delivered insights into the pathomechanism of inherited retinal disease (**Lako**, NatCommun2017, NatCommun2018). These activities established Newcastle pluripotent stem cell group as international leaders and led to creation of the first European iPSC bank (EbiSC), which distributes these cell lines for no profit to multiple stem cell labs and laid the foundation of NU spin-out Newcells Biotech (**Armstrong**).

We were the first to create light-sensitive retinal organoids from human pluripotent stem cells (**Lako**, StemCells2018). The HDBR, (MRC-Wellcome Trust-funded, s1.3.2) provided the ability to perform the first integrative transcriptional analysis of developing human retina (**Lako**, Development2019). This has led to three ongoing awards from BBSRC and MRC (£2M) to generate detailed single cell atlases of the developing eye as part of the **Human Cell Atlas Initiative**. These analyses made major contributions in identifying the ocular surface as an additional entry portal for SARS-CoV-2 (**Lako**, OculSurf2020e).

Studying adult stem cells, (**Loughlin**, **Reynard**, **Young**) have applied epigenomic and transcriptomic techniques to advance understanding of cartilage development (Development2017, FASEBJ2020) and destruction in osteoarthritis (NatGenet2017), leading to further programme grant funding from Versus Arthritis (**Loughlin**) and the Dunhill Medical Trust (**Young**). **Briggs** and **Piróg** use stem cells to mechanistically understand mutations causing rare bone diseases (JBoneMinerRes2020), including those encompassed within the EU H2020 project MCDS-Therapy (**Briggs**, s1.3.4).

We develop tissue relevant model systems and were the first to demonstrate 3D bio-printing of a human corneal stroma (**Connon**, ExpEyeRes2018), which led to NU spin-out 3D Bio-Tissues Ltd, which addresses the critical need for donor corneal tissue worldwide. Research with lipopeptides contributed to a new form of tissue engineering, termed Tissue Templating. This facilitates the ability of cells to change shape and size over time (**Connon**, AdvFunctMat2020), and led to NU spin-out CellulaREvolution Ltd, aimed at solving critical problems in cell manufacture. Research in niche limbal stem cell biology resulted in a new treatment for corneal burns, Biomechanical Modulation Therapy (**Connon**, NatComms2019), currently in clinical trials in India supported by the Ulverscroft Foundation.

**Organ Transplantation.** We have built on previous infrastructure investment (£30M) between NU and NuTH in opening the Institute of Transplantation (IoT), at the Freeman Hospital the only UK site to host all forms of solid organ transplantation (heart, lungs, liver, kidney, pancreas and islet cells) in a single dedicated facility. In 2015, our University-NHS team was awarded the NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation (with Cambridge £3.8M, extended £1.3M, 2020). **Fisher** leads the multi-disciplinary team with **Ali**, **Dark**, **Kirby**, **Shaw**, **Sheerin**, **CH.Wilson** combining research and patient care. This established Newcastle as a leading international research centre in organ preservation and transplantation.

Our research is leading *ex-situ* normothermic perfusion of donor organs as a means of objectively assessing function and improving organ quality for transplantation (**Fisher**, JHeartLungTransplant2014, EurJCardioSurg2017). We have established a Transplantation and Regenerative Medicine Laboratory Facility, operated by NU but hosted in the NHS Newcastle Blood Centre, as a dedicated organ perfusion laboratory for pre-clinical human and large animal models of organ perfusion.

In lung transplantation, we led the DEVELOP-UK study (**Fisher**, NIHR HTA) of donor *ex-vivo* lung perfusion (EVLP) which showed that EVLP applied to higher risk donor organs facilitates more lung transplants, reducing transplant waiting time (HTA2016), but with significantly higher cost (BMCHealtServRes2019). **Fisher**, and **Ali** identified a biomarker that predicts how well organs will function after transplant (JHeartLungTrans2017), developed by industry collaborator MyCartis into a rapid point of care assay. NuTH now has a clinical EVLP service in place based on this work. A recently funded EME study (C-CLAD-UK, **Fisher**) will use novel design features (Wason, Grayling UoA2) in a clinical trial to investigate the use of extracorporeal photophoresis in treating chronic lung allograft dysfunction. This follows Fisher's involvement in guidelines (JHeartLungTransp2019). In kidney transplantation, **Ali**, **Fisher**, **Mellor**, **Sheerin** and **CH.Wilson** worked with Athersys on the first effective use of cell-based therapeutics to treat human kidneys on an *ex-situ* normothermic circuit (**CH.Wilson**, AmJTransplant2020), reporting that improved function dampened inflammation. In islet cell transplantation, **Shaw** leads the UK Islet Transplant Consortium and multicentre studies demonstrating beta-cell dedifferentiation

(AmJTransplant2018), impact on glucose variability (DiabetesCare2015) and immune response (AMJTransplant2015). We were the only UK centre to participate in the first anti-inflammatory therapy RCT following pancreatic islet transplantation (**Shaw**, DiabCare2020). We developed a new platform to use oxygen persufflation to improve preservation and eliminate hypoxia in transport of pancreata (Shaw, Transplantation2019). This has been commercialised in a NU spin-out, ScubaTx.

**Advanced Therapies.** We have significantly increased our industrial partnerships since 2014. We have a pipeline of cell and gene therapy trials with 15 different companies including Autolus, Pfizer, Avexis, Achilles and Chiesi, increasing from one trial in 2012-13 to 8 commencing in 2021 (e.g. Pfizer DMD Gene Therapy, **Straub**). The Northern Alliance Advanced Therapies Treatment Centre (Innovate UK), co-led by Newcastle (**Shaw**), has cemented Newcastle as a leader in advanced therapy translation, trials delivery and NHS adoption. Linking with **Cancer** (s1.3.1), we are one of only 7 centres nationally to offer CD19 CAR-T cells to adult multiple myeloma patients in a phase 1/2 study, and a first global phase 1 neoantigen receptor T-cell study in melanoma (THETIS, **Plummer**). Our expertise in advanced therapies is utilised in design and implementation, from first-in-human studies to registration trials in **Rare Diseases** (s1.3.4) and in developing our tolerogenic immune therapy in **Immunity and Inflammation** (s1.3.2).

**1.4 Future Strategy**

Our ambition is to be a global leader in translational research across our 5 research domains. We will exploit the recent faculty restructure as well as the local collaborations brought together in our AHSC to enhance multi-disciplinary working between clinical, non-clinical and applied health researchers and expand our translational pipeline. Our strategy has 3 pillars: (1) Enhancing Translation, (2) Data Science and Health Informatics, and (3) Capacity Building and Skills Training.

**1) Enhancing Translation**

We will expand our translational ecosystem, working through our AHSC, to develop an Innovation Pathway and Accelerator Test Bed for new medical technologies. This will enable us to identify transformative innovations, evaluate these in the NHS context, promote adoption at scale and monitor patient benefits. To deliver this vision we purchased the 29-acre Campus for Ageing and Vitality site (CAV, £8M) in 2019, where we plan new infrastructure at the interface between clinical research, NHS care and industry. The site currently accommodates our BRC, the AHSN, specialist NHS clinics, research imaging and clinical trial facilities (s3.2). We plan new “living-labs” for real-world trials and technology evaluation in the older person, synergistic with the capabilities of our National Innovation Centres in Ageing and Data (NIC-D), and with our Science Faculty for biomedical engineering innovations (devices and materials for advanced therapeutics and transplantation).

**2) Data Science and Health Informatics**

We will continue to expand our health informatics expertise, working closely with our colleagues in the University Digital Institute (UoA11), NIC-D and AHSC partners developing programmes which exploit the Great North Care Record. We will create a secure and agile research environment to enable large-scale biological and medical data analysis in areas ranging from single cell omics to multimorbidity.

**3) Capacity Building and Skills Training**

We will continue to invest in talent through fellowships and building excellence through our well-established support of ECRs. A major focus of the new AHSC training programme will be the development of a sector-leading model for clinical academic career support for nurses, midwives and allied health professionals (NMAHPs).

In **Cancer** we will establish a comprehensive Translational Cancer Centre, forming new multi-disciplinary teams focused on delivering practice-changing research, building on our strengths in drug discovery and clinical trials.

In **Immunity and Inflammation** we will broaden our research on host-microbe interaction through integrative analysis of the microbiome within clinical profiling of patient cohorts and disease modelling to identify new therapeutic targets. We will create new links between our bacterial cell biology (UoA5) and immunology researchers and our cancer drug discovery unit to develop new programmes addressing the international challenges of anti-microbial resistance. This approach will adopt our successful model for therapeutic developments in cancer, based on integration of fundamental bioscience, clinical understanding and commercial partnerships.

In **Long-term Conditions and Ageing** we will invest in appointments for Ageing and Informatics to underpin our current leadership in digital health projects. We will invest in skills in academic geriatric medicine and geriatric oncology to drive new programmes in ageing and multimorbidity: critical components of our AHSC vision.

In **Rare Diseases** we will expand our discovery research to prime new experimental and clinical studies and develop Newcastle-led therapies. We aim to fill the ERN void which formed at Brexit by creating and leading new national and international networks in rare disease research, policy and engagement.

In **Regenerative Medicine** we will work with partners in academia, the NHS and industry to establish a Northern Advanced Therapies Accelerator as part of the Innovation Pathway CAV developments.

Common to these domain-specific objectives is the drive to develop new therapeutic approaches. We will exploit the commonalities of these objectives to build cross-domain research programmes including in therapeutic manipulation of tolerance in immuno-oncology, inflammation medicine and advanced therapeutics.

**1.5 Impact Strategy**

In UoA1 we focus on patient impact, collaborating closely with NHS trusts and industry to deliver real healthcare and economic benefits. Our impact and research strategies are therefore closely connected. To ensure our strategy succeeds, our organisational structures are designed and supported to move findings robustly from basic science down the translational pathway.

We have five UoA1 impact champions (**Armstrong**, **Hicks, Loughlin**, **Wedge**, **West**). Working with the Faculty's Impact Officers, they identify potential impact from research. We encourage all colleagues to participate in impact-relevant University programmes including the Policy Academy, Global Challenges Research Academy and Enterprise Academy. We train colleagues in patient-

public engagement to inform research questions (e.g. VOICE, s4.7) and internally fund partnership building and impact activities.

**Impacts on Health and Wellbeing.** We have had significant impact on health and wellbeing through clinical collaborations, commercialisation of our research and adoption into the NHS. For example, ICS "*Remission of type 2 diabetes using a low calorie diet*" (**Taylor**), where our research led to the NHS England pilot of specialised diet interventions at 10 sites and for NHS Scotland to roll out specialised diet interventions across the country. A second example is "*Endocuff Vision: a simple tool to increase early detection of colorectal cancer and pre-cancer*" (**Rees**), describing improvements in adenoma detection during colonoscopy. Developed with industry, the resulting tool received NICE approval and NHS funding in 2019 and is now widely used in practice. UoA1 staff also led a UoA5 ICS on a "best-in-class" treatment for metastatic bladder cancers (s4.5).

**Impacts on Commerce and the Economy.** We have created a culture of commercial collaboration leading to economic impact. For example, interdisciplinary research of **Curtin**, **Drew**, **Plummer** and colleagues in Chemistry led to FDA, EMA and NICE approval of Rucaparib to treat germline and somatic ovarian and prostate cancers. In addition to the patient benefit, there has been substantial financial gain for the partner company, Clovis Oncology, who reported $376.5M net product revenue for Rucaparib (2016-2020). We also create economic impact via spin-out creation, including two examples where UoA1 staff contributed to UoA5 ICSs – see Alcyomics (s4.4) and Fibrofind (s4.5).

**Impacts on Public Policy, Law and Services.** Our specialist expertise contributes to wider aspects of science policy and we encourage all academics to engage with policy makers. For example, our research into mitochondrial disease informed the House of Commons, leading to a change to UK law in 2015. This allowed the Newcastle Fertility Centre to establish an NHS Highly Specialised Clinical Service: ICS "*A new technique to prevent transmission of mitochondrial disease*" (**Herbert**, **Gorman**, **Turnbull**). Our research also underpinned regulatory approvals. Clinical data produced by Newcastle led to EMA and NICE approval for a drug to treat Duchenne muscular dystrophy; ICS "*Ataluren: the first approved oral treatment for Duchenne muscular dystrophy"* (**Bushby**, **Guglieri**, **Straub**).

**1.6 Open Access and Research Integrity**

We encourage wide dissemination of research outputs and data. Colleagues are supported to develop data management plans to ensure effective data sharing, including through the University's Research Data Repository. The University ePrints repository ensures research outputs are made Green Open Access, while we make full use of RCUK/UKRI, COAF, Faculty and Institute funds to increase the proportion of publications made open access. We are actively preparing for Plan S.

The University is a signatory of the Condordat for Research Integrity and appointed Prof Simon Woods (UoA21) as expert convenor on research integrity (REF5a 2.3.2). We have joined the UK Reproducibility Network, subscribe to UKRIO, and are members of the Russell Group's Research Integrity Forum. Research integrity is the remit of our Dean of Research and Innovation.

## 2. People

### 2.1 Overview

Our research excellence and impact is underpinned by recruitment and development of our researcher base at all academic levels. We are committed to developing clinical academics and have recognised institutional success in securing external clinical fellowships. We operate specific programmes for early career funding and mentoring. Members of UoA1 provide national leadership for both clinical and non-clinical training initiatives and award panels.

We have achieved 90 externally funded fellowships, with 13 Professorial (including NIHR Senior Investigator Awards for **Bushby**, **Isaacs**, **Jones**, **Rees**, **Reynolds**, **A.Sayer**, **Simpson**, **Turnbull**, and Wellcome Trust Investigator Awards in Science and Senior Research Fellowships for **Collin**, **Cordell**, **Hambleton**, **Haniffa**, **Veltman**), as well as 47 Post-doctoral and 30 Doctoral awards.

We have appointed 14 internally funded "transition to independence fellowships" through our NU Research Fellowships (NURF) and NU Academic Track (NUAcT, REF5a 3.2.4) schemes, nine of whom have completed the scheme and obtained open-ended contracts or academic appointments. A further 17 strategic academic appointments have been made. We have higher degree studentships funded through our MRC, BBSRC and Wellcome Trust DTPs and by NIHR, UKRI, charity funders and overseas scholarships, together with a Masters of Research (MRes) programme.

In recognition of their research contributions, **Turnbull** was elected to **Fellowship of the Royal Society** and was **knighted** for services to health care research and treatment. **Jones** was made **OBE** for services to clinical training and people with liver disease. **Hambleton**, **Haniffa**, **Herbert**, **D. Mann** and **Plummer** have been elected as **Fellows of the Academy of Medical Sciences**.

### 2.2 Staffing Strategy and Staff Development

#### 2.2.1 Staffing and recruitment policy

Our strategy combines a strong career development pathway alongside targeted recruitment of high-performing academics to grow our international research leadership across our domains. We have retained 80% of staff returned in REF2014 while expanding FTE by 14.8 FTE. New appointments at all levels are to open-ended contracts as part of our commitment to minimising workforce casualisation.

#### 2.2.2 External recruitment

We recruited 12 new professors (6 clinical) as part of our strategy to expand research impact across our research domains, with a further 5 appointments of future leaders at Senior Lecturer/Lecturer level. In **Cancer**, **Rees** was appointed Professor of Gastroenterology, and **Nsengimana** (Senior Lecturer in Biostatistics) enhances our clinical trial design capability across all research domains. In **Long-term Conditions and Ageing** we made appointments to spearhead clinical research in ageing, multi-morbidity and long-term conditions. Chairs: **A.Sayer** (Geriatric Medicine) to bring leadership in translational ageing research, establish new research in sarcopenia and lead the successful Newcastle NIHR Biomedical Research Centre renewal (2017); **Witham** (Trials for Older People) for expertise in specialist clinical trials in older populations; and **Robinson** (Lifecourse & Lifestyle) for epidemiology expertise. To underpin our

longstanding research excellence in nutrition, healthy ageing and exercise physiology, we recruited **Stevenson** (Professor of Sports and Exercise Science), **Hulston**, **Spiers** (Senior Lecturers in Sport and Exercise Science) and **Orange** (Lecturer) and invested £25M in sports and exercise research facilities. Although their work contributes to UoAs 1, 3 and 24, there is not yet the critical mass required for a UoA24 return. **West** was appointed as a NURF and subsequently promoted to Senior Lecturer. In **Regenerative Medicine, Transplantation and Advanced Therapies** we recruited Chairs: **Stellos** (Cardiovascular Medicine & Epitranscriptomics) and **Burt** (Precision and Molecular Pathology to direct the Pathology Node and lead developments in precision medicine). In **Rare Diseases** we made appointments to lead research in genetics (**Veltman** as Jacobson chair of Personalized Medicine and Dean of NUBI) and to strengthen our translational research into neuromuscular diseases (**Diaz Manera** as Professor of Neuromuscular Diseases).

We also made senior appointments from industry. In **Cancer** we recruited two Chairs; **Wedge** (Stratified Cancer Medicine Discovery) from AstraZeneca and **Hickson** (Cancer Drug Discovery) from Janssen to expand our programmes in drug discovery, with **Harris** (Molecular Immunology) from GSK to the **Immunity and Inflammation** domain. **Connon** was recruited to a Chair in Tissue Engineering, bringing commercial entrepreneurial talent to the **Regenerative Medicine, Transplantation and Advanced Therapies** domain and as the Faculty Director of Business Development.

**2.2.3 Clinical Academics and NHS-employed Active Researchers**

Our research strength within UoA1 is built on a highly effective relationship with our two Care Quality Commission “outstanding”-rated partner trusts (NuTH and CNTW). In UoA1, 66 researchers are clinical academics holding honorary contracts with one of the partner trusts. Additionally, we host a further 66 NHS-employed active researchers with honorary University status. All NHS-employed researchers have affiliate membership with one of our Research Institutes or Schools and have access to all University facilities to support their research.

We pioneered development of the model of a dedicated Clinical Academic Office (CAO), led by the Dean of Clinical Medicine (**Fisher**), which oversees and manages the interface between the University and NHS organisations for both employed and honorary staff. This CAO facilitates integrated Follett joint-appraisal and job-planning to ensure seamless working across the clinical/academic interface. Those with honorary clinical senior lecturer status or above have a University review alongside their NHS Appraisal to ensure that their research commitments are recognised when setting development goals. In addition, the CAO model includes a regular joint Human Resources committee meeting between the NU and NHS partners where strategic and operational issues can be identified and resolved swiftly. The CAO model has been recommended as national best practice by the multi-agency Clinical Academic Training Forum (inaugural chair **Jones**), which reports to the Office for Strategic Coordination of Health Research (chair **Day**) to support clinical academic career development.

Since the award of our AHSC, we have strengthened the integration of clinical academics and NHS-employed active researchers by establishing standing committees in Research and Innovation; Education and Training; and People and Culture. These committees are tasked with delivering greater integration across the AHSC to ensure the University and the 2 largest NHS organisations, together with the local authority, maximise our ability to deliver impactful innovations for patient benefit. A major focus of the AHSC training programme will be to develop

a sector-leading model for clinical academic career support for NMAHPs, building on our already strong track record.

**2.2.4 Development and Integration of Early Career Researchers (ECRs)**

We are committed to the *Concordat to Support the Career Development of Researchers* and actively manage career progression. We have a dedicated Career Advisor and an Organisational Development Specialist at University level who assist our Career Development Working Group to ensure that our Career Pathways Framework and training meet the needs of the Faculty. Consequently, we have retained our *Vitae HR Excellence in Research Award* through multiple reviews since the original award in 2010. Our Skills Academy was launched to consolidate and develop our offer (REF5a 2.5) and we have mentoring schemes at all career levels. Our active Faculty Postdoctoral Committee, with representation across all Institutes and themes, organises an annual postdoctoral conference.

Our Bridging scheme provides short-term funding to retain key skills and researchers between grant awards and contributes to EDI by supporting researchers who might otherwise drop out of a scientific career. The scheme has supported 95 research associates and technicians across the Faculty over this REF cycle, 42% in this UoA.

Our Small Grant Scheme enables researchers to acquire preliminary data to support grant applications. During this REF period we allocated £580K across 76 projects, mainly to ECRs.

Our Broadening our Horizons scheme supports researchers and PGR students by allowing them to present their work at conferences, visit other research groups nationally and internationally to gain new techniques or mentoring. The scheme has supported 135 colleagues since 2014.

**2.2.5 ECR Development to Independence**

We operate a highly successful ECR development programme which enables researchers to realise their ambition of becoming independent academics. We combine proactive identification of talented researchers with direct support from fellowship schemes and small grant awards. Since 2014 we have enabled 24 ECRs to transition to independence.

**2.2.6 Non-Clinical Fellows – Investment in ECR Development**

We invest in 2 non-clinical fellowship schemes, open to internal and external candidates. **Faculty Fellowships** allow early-stage post-doctoral researchers to develop original research ideas, over 2-3 years, to prime external fellowship applications. Fellows have a scientific advisor and a career mentor to guide their development. We introduced **NU Research Fellowships** (NURFs, 2015) as a route to non-clinical academic appointment and this scheme was subsequently extended across the University through the **NU Academic Track** appointments (NUAcT, REF5a 3.2.4). All of our fellowship schemes are extremely competitive (NUAcTs >600 worldwide applicants in 2020).

NURFs, NUAcTs and externally awarded career-level fellows are supported by the Director of Non-Clinical Fellowships (**Higgins**, UoA5) who closely monitors progression against fellowship milestones. Fellows receive academic mentoring via the Faculty PI development programme, which covers grant writing, research group management, budgeting and time management skills. Fellows have access to additional funding streams from institutional awards, allowing them to expand their research portfolio and obtain pump-priming data for larger external grant applications.

These non-clinical schemes are successful: 80% of researchers who have completed our Faculty Fellowship scheme have secured fellowships or academic positions. Of the 12 NURF appointments, to date 9 have transitioned to Lecturer or Senior Lecturer contracts. Two new NUAcTs have been appointed in this UoA since this programme started in 2019 (**Stewart** in **Immunity and inflammation** and **Viñuela** in **Long-term conditions and ageing**), underpinning our REF2014 strategy to build capacity in those areas. Future NUAcT fellowship appointments will align with priority research areas including **Rare Disease**. In **Cancer** we will co-fund at least one university-commercial partnership fellowship to cement industrial linkage in cancer drug discovery.

**2.2.7 Clinical Fellows**

We have a longstanding track-record of developing clinical academic careers and **Jones** is Dean for the NIHR Academy. Our Academic Foundation Programme (AFP) was the first in the UK to offer 8 months of protected research time during the 24-month programme and now forms the basis for programmes across the UK. Our model of cross-professional integration of training support through our CAO has been adopted by the NIHR Academy and we host NIHR Academy Incubators in Methodology (**Teare**, UoA2) and Medical Education (**Vance**, UoA23).

UoA1 has hosted 90 posts on our AFP in collaboration with Health Education England. The CAO supports medical, dental and allied health professional trainees and ensures high quality supervision, support and mentorship. We have hosted 79 Academic Clinical Fellows (ACFs) who are supported to develop externally funded fellowship applications leading to a higher degree (PhD/MD), with 63% having gone on to higher degrees. We host the Wellcome Trust 4ward North Clinical PhD Academy with Leeds, Manchester and Sheffield Universities, providing academic research training for clinical academics across the spectrum of biomedical research.

Our Academic Clinical Lecturers (ACLs) receive bespoke support to complete their clinical training alongside a post-doctoral research career. Over the REF period we have supported 43 NIHR Clinical Lecturers. Particular successes are **Hill** and **Bomken** (MRC Clinician Scientist Fellowships), **Duncan** and **Reynolds** (Wellcome Trust Career Development Fellowships), **Frith** (NIHR Clinician Scientist Fellowship) and **Lamb** (MRC PSMB and Genentech programme grant support).

**2.2.8 Team Science and the Technicians Commitment**

We are committed to Team Science and ensure that our students, technical staff, technologists, methodologists and professional service staff are acknowledged for their contribution to research and have a stable and rewarding career structure. To promote career development of our technicians, we formed NU TechNet (2016) as a forum to share resources, information and experiences. This initiative was led by Leitch, now the Faculty Deputy Head of Infrastructure, who was shortlisted for THE Technician of the Year (2019). Newcastle was therefore well placed to become a founding signatory of the Science Council Technician Commitment in March 2017, which aims to ensure that technicians working across the higher education and research sectors receive career development, visibility and recognition for their work.

To integrate our technical staff into our research programmes, we created a cross-faculty research theme in Innovation, Methodology and Application which is co-led by senior technicians and academic methodologists. This theme provides an important link between applied technological innovation and research applications. Our Professional Services teams of project and business development managers contribute to, and are named on, funding applications. The vital role of technicians is recognised by co-authorship of outputs and ICS. Our technicians are internationally

recognised and are leaders in international technical societies, are recognised by society awards, undertake journal and grant peer review and sit on specialist external grant panels. Technical staff are co-authors on 35% of UoA1 submitted outputs, while 33% of ICS have underpinning research which include technical staff as authors.

### 2.3 Recognition and Reward

Formal recognition for excellent performance happens via our annual promotions round, an open process which encourages all academics to submit their case for promotion. Achievements are based on quality evaluations and non-contextual citations, not journal names or impact factors. (NU signed the *Concordat to Support Research Integrity* in 2018). Of the 168 academics in UoA1, 44 were promoted during this REF period, five achieved multiple promotions. The impact of personal circumstances during the COVID-19 will be integral to future reward and recognition processes.

### 2.4 Research Students

Our Postgraduate Research (PGR) student community contributes significantly to our research environment, productivity and impact. Since REF2014, 826 PhD (60% females) and 106 MD (37% female) students have solely or partly been supervised by UoA1 researchers. To foster the best possible students, we invest in research-led undergraduate teaching with emphasis on project work in our laboratories. Carefully selected graduates and intercalating medical students proceed to a range of focused PGR Masters (MRes and MPhil) programmes which have supported 1,049 students during this REF cycle. These students spend >6months working on research projects, with 91% reporting overall satisfaction with their programme (PRES 2019). More than 160 papers in this REF cycle can be attributed directly to MRes project work. This training “conveyer” generates a pool of research-motivated postgraduates who can compete successfully for funded doctoral studentships.

#### 2.4.1 Recruitment

The diversity of our doctoral students contributes to our research environment. Almost 25% of our doctoral student body is international, and this is expected to rise with recently-developed joint PhD programmes with Monash, Australia and Universitas Indonesia in Jakarta. One third of the students come from BAME backgrounds, (14% excluding international students). We also foster wider aspects of diversity amongst our home students. To eliminate bias in selection, our largest doctoral training programmes (DTPs) pioneered a system to redact all identifiers during both project selection and student short-listing. We can demonstrate the absence of gender bias and 38% of the PhD students in our BBSRC-funded 2018 and 2019 cohorts are first-in-family at university; this compares favourably with Newcastle’s 37% widening participation rate at undergraduate level and is a powerful indicator of inclusivity and diversity in our PGR community.

#### 2.4.2 Progression, Monitoring and Support

We provide multiple layers of pastoral support to every PGR student, building from supervisors, through annual progress review panels, to PGR co-ordinators, the Postgraduate Tutor and, ultimately, the PGR Dean.

Annual Progress Review for doctoral students is independent of the supervisors and performed by academics drawn from the Faculty. The report is scrutinised by their Research Institute and the PGR Dean to identify and, in almost all cases, rapidly resolve any developing problem. PGR supervisors undertake compulsory training, leading to excellent rates of timely thesis submission

(88% within four years for full-time PhD students) and programme completion (89%). This is also reflected in the 88% of our students who reported overall satisfaction with their doctoral programme (PRES 2019, top of the upper quartile in the Russell Group).

We recognise the vulnerability of doctoral students to the COVID-19 lockdown and have put in place a raft of measures to mitigate the impact wherever possible. These include fee-free extensions and significant investment in a NU COVID-19 Impact Scholarship Scheme to provide additional stipend support.

**2.4.3 Skills Development and Future Career Preparation**

Each student is supported by a Research Student Development Programme which aligns with the Vitae Researcher Development Framework and promotes the development of research-specific and generic skills. Although our UKRI-sponsored DTP students benefit from additional training, we widen access wherever possible to allow non-DTP students to join activities. For example, the student-led NE Postgraduate Conference (one of the largest such conferences in the UK with >600 annual registrants) is largely supported by UKRI DTP sponsorship but allows free participation to all PGR students in the North of England.

We believe that the combination of research enthusiasm engendered by comprehensive student training with the satisfaction produced by supervisory excellence and sensitive support is responsible for the remarkable productivity of the doctoral students within this UoA. 35% of submitted papers in this UoA have doctoral students as authors.

**2.5 Equality, Diversity and Inclusion**

We are committed to values and practices that create a research environment in which colleagues have the freedom and opportunity succeed. Our former Institutes held Athena Swan Silver awards: Cellular Medicine (2013, renewed 2016), Genetic Medicine (2015) and Northern Institute of Cancer Research (2015), which were consolidated into a Faculty Silver Award in 2018. We are committed to equality across all protected characteristics with NU being a member of the Advance HE Race Equality Charter, the Business Disability Forum and is a Global Stonewall Diversity Champion. This commitment is reflected in NU policies and programmes such as our Networks and support schemes. We have built on these at a local level as outlined in s.2.2 above. We also supplement the University Returners Support Programme with Faculty funding, in recognition of the relatively high costs of much of our research.

Our return includes 168 members of staff. 36% are women, 12% Black, Asian & Minority Ethnic (BAME) with two colleagues declaring a disability. We are committed to promoting equality and progressing all academic careers and in the REF period, 33% of internal academic promotions were women, including 35% of those promoted to Reader or Chair. We are actively working to improve this gender balance. We also focus on the challenges for clinical academics balancing NHS, research and personal commitments. 50% of ACFs and 40% of ACLs are women, the latter being higher than the national average. We ensure flexible clinical training for part-time trainees. We are proud that 4 of our 5 academics elected FMedSci since 2014 are women.

**2.5.1 Flexible Accommodation and Working Patterns**

Our physical workspaces are configured for colleagues with sensory and physical access requirements and our buildings have baby changing facilities. Flexible working is accommodated; pre-COVID some colleagues chose to work remotely part of the week or had flexible or

compressed working hours to accommodate their personal circumstances. Meetings and seminars are arranged around flexible work patterns, religious needs and ensure a gender balance of presenters. We also ensure gender balance on our decision-making committees and in seminar programmes.

### 2.5.2 Future EDI Strategy

We monitor gender and ethnicity at each career stage to inform our recruitment and career development activity. We will continue to work on University initiatives to create research cultures, activities and environments where people from varied backgrounds can thrive. Our future EDI strategy therefore focuses on continuing to seek to achieve gender balance across all career stages; encouraging all colleagues, particularly women, to seek promotion; supporting and enabling colleagues to declare disabilities; scrutinising our recruitment processes and improving our accessibility to diverse applicants and thereby addressing our gender balance and the relatively low proportion of BAME colleagues (5%).

To enable critical scrutiny of our recruitment processes, “blind” triaging of NUAcT applications is now undertaken; subsequent monitoring will determine whether this effects meaningful change.

### 2.5.3 EDI in the REF Submission

We have ensured that EDI considerations are embedded throughout our submission. For example, our outputs have been selected through an open process of self-nomination using our Research Management System followed by anonymous evaluation by at least two other senior academics with both an indicative score and reasons. The REF lead moderated the scores across disciplines. Selection of the return was by paper, not author, in line with our code of practice.

## 3. Income, infrastructure and facilities

### 3.1 Income

We have continued to sustain a portfolio of major awards across the research councils, UK government, European, charitable and commercial sectors. Income to UoA1 from research grants and contracts was £270M.

We highlight income from participation in more than 60 European funded projects (FP7, H2020, IMI, COST) where we have coordinated and led on research valued at >€90M (and with a direct income to Newcastle of £24M). Awards for externally-designated research Centres and regional and national infrastructure totalled £71.5M. Highlights include NIHR funding of £45M (Table, s1.2, page 3) and renewal of our Wellcome Trust Centre for Mitochondrial Research (£6.1M). In 2019 we launched the MRC International Centre for Genomic Medicine in Neuromuscular Diseases (**Straub**, £3.2M). Income from commercial studies was worth £26M (323 projects). Our performance (UK top 10) in translational funding from MRC was specifically highlighted in their national evaluation report on Translational Research, 2008-2018.

Staff in UoA1 contributed to the awards of five multi-year DTPs during this REF cycle with a combined value of nearly £21M.

### 3.2 Infrastructure

Our infrastructure supports our academic programmes and enables partnerships with collaborators in industry and healthcare. We have invested in buildings and equipment including the flagship Catalyst Building, a £44M bespoke headquarters for our National Innovation Centres for Ageing (NIC-A) and Data (NIC-D) and the NIHR Innovation Observatory (NIHRIO). We have created purpose-built biomedical and medicinal chemistry cancer research laboratories including the £5.5M Wolfson Childhood Cancer Centre (2016), housing ~90 clinical and non-clinical researchers, and refurbished our Drug Discovery Medicinal Chemistry laboratories in partnership with our Science Faculty. We have also purchased the Campus for Ageing and Vitality (CAV) from NuTH. This is one of our existing clinical research sites, home to our clinical ageing research activities, including the BRC, the Clinical Ageing Research Unit, our Imaging research Hub and CRESTA clinics (s3.3). Developing the CAV site is central to our future strategy (s1.4).

### 3.3 Facilities

Our infrastructure is grouped within Innovation Hubs which combine equipment, facilities and world-leading expertise.

The **Analytics Hub** provides eight core scientific facilities delivering analytical technologies and expertise in Light Microscopy, Electron Microscopy, Flow Cytometry, Proteomics and Protein Production, Genomics & Sequencing, Bioinformatics Support, Bio-Screening and access to the Cat3 laboratory. The Hub also hosts the MRC-funded Single Cell Functional Genomics Unit. The Analytics Hub has 18 core staff aligned to the Innovation, Methodology and Application theme. The Hub technical leads secured funding for Spectral Flow Cytometry for multi-parameter single cell analysis (Wellcome Trust, 2020) and collaborative grants to drive cutting-edge research, including the Human Developmental Cell Atlas. Since 2014, the Analytics Hub has facilitated over 754 publications. Combined investment of >£9.4M has ensured that the Analytics Hub delivers cutting-edge analytical technologies and methodologies.

The **Imaging Innovation Hub** (Centre for In Vivo Imaging, CIVI) is a research-dedicated, multi-disciplinary research centre which leads MRI and PET research. Since 2014 we have expanded our MRI capability investing £1.5M in a second, multi-nuclear clinical 3T scanner with new core research posts. A further £5M investment by the University and the MRC (Clinical Research Capabilities and Technologies Initiative) provided a 3T-PET/MR scanner. The facility has been further strengthened by £1M university investment in the PET Tracer Production Unit to enable clinical-grade PET ligand production by the end of 2021. These facilities have supported >230 projects, leading to >300 papers in this REF cycle. CIVI also operates the UK's only vertical bore non-human primate scanner (4.7T, UoA4) and a 7T preclinical MRI scanner for basic bioscience and translational work in rodents.

Our **Clinical Research Hub** provides comprehensive resources for interventional trials. We lead the Research Design Service NE & North Cumbria (**Hancock**) and trial design is enhanced by our strong academic Methodology Research Groups. The 20 members of the Biostatistics Research Group have expertise in the design, conduct, analysis and reporting of clinical trials, including advanced adaptive trial design (**Wason**, UoA2), of central importance to our Rare Disease research. **Witham** provides specific expertise for studies in Ageing populations. The Health Economics and Evidence Synthesis Groups (both UoA2) bring essential expertise to support translational research and underpin programmes across this UoA (DPFS, EME, HTA, IMI funding).

Research also benefits from the only NIHRIO in the UK which horizon scans for medical technologies that are up to 10 years from becoming publicly available, and tracks progress as they evolve. The observatory has three core activities: technology briefings, advanced horizon scanning tools and patient involvement.

The UKCRC-registered Newcastle Clinical Trials Unit has supported 107 trials over this REF period. The current portfolio comprises 33 trials spanning infectious disease, cancer and mental health (by classification: 16 CTIMPS; 2 ATMPS; 2 device trials; 3 surgical; 23 RCTs, 3 adaptive trials, 1 stepped wedge and 7 cohort studies). The total value of trials during the REF period is £95.2M and of active trials is >£30M.

We co-manage four Clinical Research Facilities (CRFs) across the city with NuTH. In addition to our NIHR CRF, they are the Clinical Ageing Research Unit (CARU) which focuses on investigations in older people and is equipped with specialist gait assessment facilities; the Sir Bobby Robson Cancer Trials Research Centre at the Northern Centre for Cancer Care which carries out all phases of cancer trials, including paediatric studies; and a Dental CRF. Adjacent to CARU are our innovative CRESTA clinics (*Clinics for Research and Service in Themed Assessments*) which are one-stop, multi-disciplinary, research-integrated clinics centred on the needs of older patients with complex multiple disorders.

The **Pathology Hub** is built around the MRC/EPSRC Newcastle Molecular Pathology Node (recently renamed NovoPath). It combines expertise in molecular and cellular pathology, computing and engineering to develop novel molecular pathology tests, with an emphasis on *in vitro* diagnostics and biomarker identification for disease stratification in chronic and rare diseases. Work is complemented by the NIHR Newcastle MedTech and In Vitro Diagnostics Co-operative (MIC) providing high-quality evidence to demonstrate the potential value of new *in vitro* diagnostic tests. The combination of the Node, MIC and NIHRIO is a unique resource in the UK. The success of our infrastructure is illustrated by project awards totalling £22M supported by the Node and £14.5M to the MIC. The Newcastle MIC (with Leeds, Manchester and London MICs) is providing national evaluation mechanisms to accelerate promising diagnostics to real-world use through a Diagnostics and Technology Accelerator COVID-19 platform (CONDOR).

Our researchers have access to extensive well-characterised human tissue samples in the Newcastle Biobank, which incorporates over a dozen registered and NHS-approved tissue banks held within the University. These include specialist collections in cancer, mitochondrial disease, neuromuscular diseases and orthopaedic conditions. The MRC-funded Newcastle Brain Tissue Resource collects and manages human tissue for research into neurodegenerative diseases. Our researchers also have access to the entire NuTH surgical pathology archives through the Cellular Pathologies Biobank. The Wellcome Trust-funded Human Developmental Biology Resource, co-hosted in Newcastle and London, collates embryonic and foetal tissue for functional genetic and cell-based research. This resource is critical to the international community and closely collaborates with the **Human Cell Atlas Initiative**.

The Transplant and Regenerative Medicine Laboratory operated by NU in the NHS Newcastle Blood Centre provides a dedicated organ perfusion facility for pre-clinical human and large animal organ studies. Research focuses on techniques for organ maintenance and resuscitation prior to transplantation and develops processes for ex vivo delivery of advanced therapeutics to cells, organoids and whole organs. The associated MRC-funded Quality in Organ Donation (QUOD)

Expand Programme (s1.3.5) has additional human tissue banks derived from donor human pancreas, heart and lungs. This repository of fixed tissue, in parallel with perfused organs, precision-cut viable tissue slices and primary cells provides a unique resource with the goal of enhancing transplant outcomes, accelerating translation of advanced therapy organ replacement and ultimately enabling endogenous organ regeneration.

**3.4 Diagnostics North East and Therapeutics – Engaging with External Partners**

Our combined facilities between NU and NuTH provide one of the most comprehensive sets of diagnostic infrastructure in the country, spanning basic science, development, evaluation, adoption and horizon scanning, incorporating expertise in all elements of clinical diagnostics. We promote these under the banner of Diagnostics North East (DxNE), with the MIC and NovoPath at the core. DxNE provides a clear entry point and pathway for engagement for academic and commercial partners. Molecular diagnostics and precision medicine is central to our AHSC strategy and delivery plan: to deliver novel diagnostic and prognostic tests incorporating cell and molecular biomarkers, computational pathology and in vitro diagnostics.

Therapeutics in Newcastle represents a further strong partnership between NU and NuTH. Advanced therapies infrastructure provides bespoke GMP clean manufacturing facilities, supporting research including gene therapy medicines, somatic cell therapies and tissue engineered products. Since 2014, we have invested in additional cryopreservation facilities and a negative pressure isolator to accommodate a growing portfolio of gene therapy commercial trials. A GLP tissue culture facility (2019) and flow cytometry (2020) facilitates the critical technology transfer of cellular therapies from research lab to GMP.

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

**4.1 Overview**

We lead national and international research consortia and work closely with industry to bring our research to patients and the market. We support research funding assessment and distribution by governmental and charitable bodies. Selected examples highlighting the range of contributions our academics make are described below.

**4.2 National, International Partnerships**

We have a recognised international research profile, particularly in Europe. Our research has been central to 11 EU programmes and we have been Coordinator for eight. These programmes have significant commercial links, including two IMI2 consortia. Our leadership of LITMUS (**Anstee**) brings together a global alliance of 33 academic and 23 commercial partners whose research and products aim to diagnose, risk stratify and monitor NAFLD/NASH progression and fibrosis stage. The programme continues to expand, as new commercial partners engage with the comprehensive and robust biomarker evaluation programme leading towards regulatory qualification. We lead IDEA-FAST (**Ng**) to identify digital metrics for evaluation and monitoring of patients with neurodegenerative or immune-mediated inflammatory diseases such as Parkinson's disease, Rheumatoid Arthritis, Primary Sjögren's Syndrome and Inflammatory Bowel Disease. IDEA-FAST has 15 academic and 32 commercial partners, including Biogen, Roche, Pfizer, Sanofi and AstraZeneca. A feature of our international programmes (e.g. LITMUS, SCOPE-NMD, VISION-DMD, SKIP-NMD) is engagement with healthcare regulators (FDA, EMA, MHRA) through which we lead and articulate international opinion on use of new diagnostics for patient evaluation

and as trial outcome measures to accelerate drug discovery. **Hilkens** is co-founder of a Cooperation in Science & Technology (COST) EU tolerogenic cell therapy network (Action to Foster and Accelerate Cellular Tolerogenic Therapies, AFACTT). **Dickinson** is a member of the COST network EUROGRAFT, and the COST Action Integrated European Network on chronic graft-versus-host disease (GvHd), which includes use of advanced therapies for treatment of GvHd. **Straub** led the MYO-MRI COST Action on the use of advanced imaging in neuromuscular diseases, which spawned an international biennial conference (**Blamire**, **Straub**), now organising its 3rd meeting. The MRC International Centre for Genomic Medicine in Neuromuscular Diseases (**McFarland**, **Straub**, **Turnbull** with UCL and Cambridge) has links with 10 partner Centres in LMIC countries (Brazil, India, South Africa, Turkey, Zambia) to expand accurate genetic diagnosis and build international patient cohorts for trials in neuromuscular diseases. We contribute to the TREAT-NMD Advisory Committee for Therapeutics (TACT, **Straub**), an innovative approach to advise industry and de-risk orphan drug development in neuromuscular diseases. **Haniffa** (joint appointment with Wellcome Sanger Institute), is a leader of the international Human Cell Atlas (organising committee member).

NU has a Strategic partnership with Monash University, Australia developing translational health and life science projects in Neuroscience, Infection and Immunity, Metabolism and Nutrition and Drug Discovery (recently awarded Research England I3 funding). The partnership supports student and ECR exchange and NUAcT positions.

Nationally, we are part of the NIHR Musculoskeletal Translational Research Collaborative (TRC) (**Isaacs**), the MRC-Versus Arthritis Centre for Integrated research into Musculoskeletal Ageing (CIMA, **Loughlin**) with Sheffield and Liverpool and the NIHR Diet and Activity Research Translation (DART) Collaboration (**Robinson**, **Stevenson**). **Jones** leads the MRC Stratified Medicine UK-PBC consortium (**Kirby**, **Oakley**) with Birmingham, Cambridge, Imperial and commercial partners which led to FDA and EMA licensing and NICE approval of Ocaliva for PBC. **Simpson** is a work-package lead for the MRC-funded SHIELD Antimicrobial Resistance Consortium with Edinburgh and Sheffield. Our NIHR Blood and Transplant Research Unit in Organ Donation and Transplantation (**Fisher**) is a joint project with Cambridge. Our Node (**Burt**, **Reynolds**) is part of the National Pathology Imaging Cooperative supported by the Industrial Strategy Challenge Fund (with Leeds, Manchester, Oxford, Sheffield, Liverpool). We are part of the Dementias Platforms UK (DPUK) imaging network with Edinburgh, Manchester, Cambridge, Imperial College and researchers in UoA1 also work closely with the NIHR Dementia TRC (led by Burn, UoA4). **Blamire** is on the UK Biobank Expert Imaging working group.

Our Doctoral Training Programmes (DTPs) are multi-centre consortia building cross-HEI cohorts, including two BBSRC DTPs (with Durham and Liverpool), our MRC DTP ('Discovery Medicine North', with Sheffield, Liverpool and Leeds); and a Wellcome Trust Clinical PhD Academy (with Manchester, Sheffield and Leeds).

**4.3 Commercial Partnerships**

The translational focus of UoA1 supports an array of commercial interactions. We foster strategic partnerships in key areas including research into PBC and NAFLD with Intercept Pharmaceuticals (**Anstee**, **Day**, **Jones**); a 10-year drug-discovery partnership with Astex Pharmaceuticals (**Wedge**) including annual research support of £1M and access to in-house expertise; and with Gyroscope Therapeutics (**Harris**, **Kavanagh**), an innovative ocular gene therapy company with whom Harris has recently started a secondment, with the aim of transferring skills in cutting-edge adeno-

associated virus technology and experience in clinical trial design back to NU upon her return in 2021.

As co-lead of the Northern Alliance Advanced Therapies Treatment Centre (NAATC, **Shaw**) we are developing the systems and infrastructure required to support advanced therapy delivery, increasing patient access with partners including Miltenyi, Datatrial, Cytiva, and Autolus. Our expertise also supports commercial contract advanced therapy research including manufacture of CD34+ stem cell therapy post-myocardial infarction (Cell Prothera), anti-CD362 antibody enriched mesenchymal stromal cells to treat acute respiratory distress syndrome, and autologous stem-cell based tissue engineered treatment for bronchopleural fistula (Videregen and the Royal Papworth Hospital). Gene therapy industrial partnerships now extend to 15 different companies including Autolus, Pfizer, Avexis, Achilles, and Chiesi.

Our commercial collaborations in Transplantation are truly international and include XVIVO Perfusion (Sweden), MyCartis (Belgium), Athersys (USA) and Betalin Therapeutics (Israel). Key regulatory groundwork required to translate innovative research in organ transplantation into the clinic is being pursued in tandem with the Cell and Gene Therapy Catapult, and regulatory bodies (MHRA/HTA).

**4.4 Spin-Outs**

**Trenell** spun out "Changing Health" (2015) delivering the national digital behaviour change platform for NHS England, including for T2D, used by more than 600,000 patients. Our melanoma research led to formation of AmLo Biosciences (**Lovat**, 2017) delivering new diagnostic testing to market in 2021, securing ~£2.5M of investment and creating 4 new biotechnology jobs. In partnership with NuTH and our science faculty, we created ScubaTx (**Scott**, ECR) to commercialise technologies for persufflation for organ preservation. This followed the granting of 5 patents, 4 of which were licensed to ScubaTX. We continue to work closely with Alcyomics (**Dickinson**, Skimune, ICS UoA5) whose business is testing the safety of cellular therapies, including tolDC, using a skin explant model. In tissue regeneration, we created 4 further spin-outs; Newcells Biotech Limited (**Armstrong**, **Lako**) which now employs >30 staff members and has raised >£10M in funding since its creation in 2015; Atelerix Limited, 3D Bio-Tissues Limited and CellulaREvolution (**Connon**) to which NU patents have been licensed. Hydrogel research with Atelerix Ltd led to a commercial partnership with world leading 3D bio-printing company CellInk to enable the transport and storage of 3D bio-printed tissue constructs. This research also led to improvements in corneal stem cell accessibility in collaboration with leading Indian eye hospital, the LV Prasad Eye Institute (Hyderabad) offering potential to treat many more patients.

**4.5 The Wider Impact of our Research**

Our research changes the health and wellbeing of patients and improves clinical training and practice. In addition to our UoA1 ICS, we have developed a range of treatments and diagnostic tools, e.g. NU research led to the FDA approved Erdafitinib with Astex (**Irving**, **Newell** MolCancerTherap2011) the "best-in-class" pan-fibroblast growth factor receptor inhibitor to treat metastatic bladder cancers (ICS UoA5). We improved the diagnosis of paediatric musculoskeletal problems (**Foster** PediatrRhemOnline2016) and made clinical diagnostic tools available internationally through an online resource (PMM) with 262,000 users worldwide and endorsed by international professional bodies including NICE, the Royal College of Nursing and Paediatric Rheumatology European Association. The integrated NHS pancreatic islet transplant programme was founded on our research (**Shaw**, DiabetesCare2020) which established safe and effective

cell shipment protocols and is now the largest such programme world-wide. In collaboration with NuTH (**Heslop** NHMAP, **Burns** Breathe2019) we found that cognitive behaviour therapy was both clinically- and cost-effective for anxiety and depression in patients with COPD, with online therapy as effective as face-to-face, We created online courses for patients and respiratory nurses.

We also develop tools to support drug development, developing precision cut slices (PCSs) (**Borthwick**, **J. Mann**, **D. Mann**, **Oakley**) to improve the predictability of drug action on fibrotic tissue ex vivo, leading to the spin-out company FibroFind and with NU spin out Alcyomics Ltd, Skimune (**Dickinson**), a skin based assay for predicting adverse immune reactions to novel chemical and pharmaceutical compounds (both UoA5 ICS).

**4.6 Responsiveness to National and International Priorities**

We have played key roles in the national COVID-19 response. **Jones** led the national approach to co-ordinating clinical academic trainees returning to support clinical NHS service. **Allen** (ECR), **De Soyza**, **Simpson** and **Witham**, and are on the NIHR Urgent Public Health Panel supporting national decision making (most contributors from a single HEI). **Duncan** led Newcastle's major contribution to the Oxford/AstraZeneca vaccine clinical trial and co-chairs the Immunomodulators group of the UK COVID-19 Therapeutics Advisory Group, for the Royal College of Physicians producing rapid evidence summaries to promote safe, evidence-based use of immunomodulators in COVID-19, influencing NHSE guidance. **Simpson** is on the UK COVID-19 Therapeutic Advisory Panel (CTAP) Immune-Inflammatory subgroup. **Duncan**, **Filby**, **Fisher**, **Hambleton**, **Haniffa**, **Harris** and **Kavanagh** are participants in the UK COVID-19 Immunology Consortium. **Duncan** and **Payne** are co-investigators within the DHSC-funded PITCH study documenting T cell immunity to SARS-CoV2 longitudinally among infected and/or vaccinated healthcare workers.

**4.7 Engagement Activities**

We are leaders in Patient and Public Involvement and Engagement (PPI/E) with VOICE (Valuing Our Intellectual Capital and Experience) being our world-leading network and associated online digital platform. Established in 2007 as a small regional panel, it has grown significantly and now sustains a large network of 'research active citizens', supporting >1000 research projects. It is a coordinating mechanism for public engagement and is the PPI/E mechanism for our NIHR infrastructure as well as NIC-A and NIHRIO. VOICE is connecting other Universities engagement activity together (e.g. in 2019 partnering with Imperial College London to develop VOICE in the London region). This empowers researchers to access, involve and engage members of the public from different geographical locations and to increase diversity and inclusion. It is also developing an international presence, establishing chapters in Singapore, China and East Coast US.

In addition, our researchers host varied and thriving PPI/E Groups. For example, in Organ Donation and Transplantation (**Fisher**), research is vetted by a dedicated panel as early in the development process as possible and active co-production is encouraged. We were recently commissioned by NIHR to identify strategies for better engagement of the BAME community in consenting to organ donation (**Exley** (UoA3), **Fisher**). We worked closely with the PBC Foundation, a UK-based organisation of 14,000 members, to change the name of PBC to primary biliary cholangitis. Although a small change, the new name removes the cirrhosis stigma and is now accepted around the world (**Jones**, ClinResHepatolGastroenterol2015). **Hedley** and **Straub** led Rare 2030, a panel of over 200 rare disease experts, a quarter of whom were patients or patient advocates. Using Foresight methodology, this generated comprehensive policy recommendations, guiding European activities for people living with a rare diseases. In Cancer,

we work closely with Newcastle-based organisations including Perspectives and The Young Person's Advisory Group. We have established diverse and active PPI groups to advise on several major programmes (e.g. COLO-SPEED, SWEET), and patient groups are regularly co-applicants on funding applications.

**4.8 Strategic Voice**

We contribute to shaping the research agenda in the UK, the NHS and Europe. Our expertise and leadership are recognised through our strategic advisory roles in healthcare research and government policy.

**Day** is Chair of the Independent Office for Strategic Coordination of Health Research, **Jones**, **A.Sayer** and **Hancock** (2016-17) are NIHR Strategy Board members, while **Trenell** advised the ESPRC Healthcare Technologies Panel and **Isaacs** the NIHR Global Health Research Group. **A.Sayer**, **Witham** and **Burn** have contributed to House of Lords Science and Technology Committee (HoL-STC) inquiries on Ageing and the Science of COVID-19 respectively. **Burn** is also a Specialist Adviser for the HoL-STC Genomics & Genome-editing Inquiry and serves on the Scientific Advisory Committee for Genomics England. **Bushby** served on the EU Committee of Experts on Rare Diseases advising the European Commission on rare disease policies. We have also contributed to HEFCE and Research England actions through shaping and delivering the REF process (**Blamire** REF2014, REF2021, **Jones**, **Stevenson**, **B.Walker** REF2021, **Vormoor** REF2014). **Connon** contributed to the Parliamentary Office of Science and Technology briefing on 3D Bio-Printing. From 2021, **Straub** is the UK representative to the European Cooperation in Science and Technology.

Our NHS partnerships are strong, now under the AHSC umbrella, and driven locally by the 66 clinical academics returned in UoA1 who deliver frontline clinical care, with a further 66 "Category C" honorary NHS staff whose research is closely integrated into the Faculty. Our academics contribute to NHS policy and leadership. **Burn** is Chairman of Newcastle upon Tyne Hospitals NHS Foundation Trust. **Shaw** chairs the UK Islet Transplant Consortium and represents Newcastle on the NHS Blood and Transplant (NHSBT) Pancreas Advisory Group. **RW.Taylor** is the Scientific Director of the Yorkshire and North East Genomic Laboratory Hub.

In line with our strong portfolio of research funding from NIHR we also contribute back to their evaluation processes and to NHS and NICE assessments. Twelve of our clinical academics have contributed to the work of NICE providing expert input for NICE guideline development and **O'Brien** is Chair of a NICE Technology Appraisal Committee.

**4.9 Research Councils, Charities and Other Funding Bodies**

We recognise the importance of engaging with research funders to provide peer review for grant awards and fellowships. All of our academics are actively engaged with peer review appropriate to their seniority and research area. We contribute to grant panels:

MRC

- DPFS: **Isaacs**
- Experimental Medicine: **Plummer** (Chair)
- II Board: Hambleton, Mellor
- PSM Board: **B.Walker** (Chair), **A.Sayer**
- FLF Panel: **B.Walker** (Chair)

- Regen Med Panel: **Connon**

BBSRC
- Committee C: **Lako**

EPSRC
- HTP: **Blamire**

NIHR
- EME Programme Committee: **Plummer**, **Simpson**
- Expert Review Panel on Multimorbidity: **M.Walke**r

HTA programme committees
- Prioritisation Committee: Integrated Community Health and Social Care: **Witham**
- Prioritisation Committee: Hospital Based Care: **de Soyza** (Chair), **Frith**
- Programme Funding (Commissioning): **Heer**

Wellcome Trust
- Science Interview Panel: **Hambleton**
- Expert Review Group Immunology and Inflammation: **Haniffa**
- Expert Review Groups Genetics, Genomics and Population Research: **Cordell**, **Veltman**.
- Seed Award Science Committee: **Haniffa**
- Multi-user Equipment and Technology Development Committee: **Filby** (Technologist)

Our national leadership of clinical and biomedical training is demonstrated through contributions to national boards and are particularly influential in terms of policy and practice in clinical academic training with **Jones** as National Training lead for NIHR Infrastructure and Dean of the NIHR Academy. **Jones** was awarded an OBE in 2019 in recognition of his contribution to the development of clinical training (and people with liver disease).

- NIHR Integrated Academic Training Panel: **Jones** (Chair)
- MRC Clinical Training and Career Development Panel: **Simpson** (Deputy Chair)
- MRC Non-Clinical Training and Career Development Panel: **Endicott** (Deputy Chair)
- MRC Clinical Academic Research Partnership (CARP) panel: **Jones**, **Simpson**
- Versus Arthritis Fellowships panel: **Hilkens**
- BHF Fellowship Committee: **Arthur**
- CRUK New Investigator Committee: **Clifford**
- Versus Arthritis Fellowships Advisory Group: **Isaacs**

In line with our international leadership in translational cancer research, drug discovery and clinical trials we contribute to strategy and direction for CRUK

- New Agents Committee: **Plummer** (Chair)
- Small Molecule Expert Review Panel: **Wedge** (Vice-Chair)
- Science Committee: **Endicott**, **Plummer**
- Experimental Medicine Expert Review panel: **Bomken**

UoA1 researchers contributed to 59 other panels across the charity spectrum.

Of the 169 academics in our return 75 have contributed as Editor or Deputy Editor to 123 peer-reviewed journals.

### 4.10 Prizes and Recognition

UoA1 researchers delivered numerous invited presentations, of note being the Harveian Oration, Royal College of Physicians (**Burn**, 2019). Important prizes include the William Farr Medal (**Witham**, Worshipful Society of Apothecaries 2018), the Michael Mason Prize, (**Ng**, British Society for Rheumatology 2015), the King Faisal Foundation International Prize for Medicine (**Veltman**, 2016). **Haniffa** received the Lister Institute Research Prize Fellowship (2016), the European Federation of Immunological Societies ACTERIA Prize (2018) and the Foulkes Foundation Medal for biomedical research (2019). We particularly highlight prizes awarded to our ECRs; the LEO Foundation Future Leader Award (**Amarnath**, 2019) the British Society of Gastroenterology President's Medal (**Lamb**, first time awarded to a junior doctor, 2014) and the L'Oreal UNESCO "For Women in Science" Rising Talent Award (**Pickett**, WT Career Re-entry fellow, 2020).