Institution: University of Manchester

Unit of Assessment: UoA1 (Clinical Medicine)

1. Unit context and structure, research and impact strategy

UoA1 in the University of Manchester (UoM) covers the research of 222.06 FTE academics working in 12 multidisciplinary research groups. Our research spans the "discovery-to-translation" spectrum, and embraces biomarker discovery and exploitation, trans-disciplinary regenerative medicine, and medical humanities. During REF2021, we have made discoveries that have proved life-changing for patients with cancer, cardiovascular, developmental, genetic and inflammatory diseases (1.6) and have led to adoption of new approaches to care in the NHS (1.2).

Global research impact and reach is enhanced by our collaborative environment (1.1.1B) incorporating: UoM's rich cross-cutting infrastructure that concentrates skills and resource in open-access Institutes, available to us for specialist assistance and advancement of research; our broad and diverse researcher groups across the world; and our industry partners.

An overview of UoA1 is provided in Sections: 1.1: Research Strategy; 1.2: Headline impact; 1.3: Future direction; and 1.4: Unit structure/context, and is elaborated on elsewhere in the return.

1.1 UoA1's Research strategy

During the REF2021 period we have refined our REF2014 statement "*Our aim is to translate basic biomedical discoveries into effective diagnostics and therapies*" into a strategy to generate research of international excellence and impact), aligned to three major challenges:

- Discovering novel disease mechanisms
- Developing new approaches to prevention and early detection of disease
- Taking into clinical practice next-generation, person-centred therapies, interventions and care pathways based on robust, peer-reviewed evidence available for general scrutiny

We are achieving our strategy by implementing programmes that build on our research strengths, enhance partnership and stakeholder engagement, and nurture staff.

1.1.1 Three major principles underpin delivery of our strategy:

A. Greater Manchester's unique healthcare environment as a research platform

The challenges of our health-disadvantaged community (4.2) led Central Government in 2014 to devolve the £6.2bn/year health and care budget (DevoManc) to Greater Manchester (GM) Health and Social Care Partnership (GMHSCP), with UoM as lead academic partner.

GMHSCP has transformed GM's clinical landscape. Supported by pioneering centralised electronic patient record systems, it has established "One Manchester Healthcare" unifying delivery across our primary and secondary healthcare sectors (population 2.8m), and co-ordinated tertiary provision reaching up to 6m people depending on specialty.

Recognising how research drives health improvement and innovation, in 2017 GMHSCP formed Health Innovation Manchester (HInM, Academic Lead **Bruce**). HInM oversees the activities of Manchester's Academic Health Science Centre (MAHSC, 1.5 [UoM core academic partner, Executive Director **Lord**]) and the Academic Health Science Network, enabling synchronous roll-out of clinical research, and accelerating clinical application of new treatments and tests across GM's entire health ecosystem. Within this environment we have built a robust, specialty-agnostic

infrastructure to underpin our research by ensuring re-designation of MAHSC in 2020 and winning NIHR funding for the Manchester Biomedical Research Centre (3.2.1, BRC: £28.5m), Applied Research Collaboration (ARC-GM: £11.3m), Manchester Clinical Research Facility (3.7, MCRF: £12.5m), GM Local Clinical Research Network (LCRN: £22m) and GM Patient Safety Translational Research Centre (PSTRC: £6.7m: one of 3 nationally).

Through GM's delivery of consolidated healthcare, the co-ordinated research and clinical infrastructure and access to a population of 2.8m and their e-records, this environment offers us a unique test bed. It is a microcosm of global health systems allowing outcomes to be tracked against interventions in all major disease areas. As such it empowers: pull-through of UoA1's basic discoveries to clinical translation at scale; and generation of powered, evidenced research, thus advancing our agenda of internationally-relevant healthcare research.

Additionally, our research base within a health disadvantaged population, allows us to generate research that is directly transferable to similar conurbations globally, a pillar of our social responsibility agenda.

B. Turning innovative ideas into clinical value by effective partnering

Within UoM: As part of a 2016 research-focused restructure, UoM merged two of its four Faculties ("Life Sciences"; "Medicine and Health") into the Faculty of Biology, Medicine and Health (FBMH), integrating research at the discovery/experimental medicine interface through multidisciplinary Research Groups.

Across all its scholarship UoM has formed (REF5a.2iii) five "Research Beacons" (4.1.1), examples of outstanding interdisciplinary, pioneering, cross-sector partnerships tackling some of the biggest questions facing the planet; and 26 "Research Institutes and Platforms", that combine disciplines and capabilities, allowing flexibility and delivering research impact in response to contemporary challenges (4.1.2). For instance, as our research is increasingly reliant on analysis of large datasets, we access dedicated specialist skills and resource from the Institute for Data Science and Artificial Intelligence (IDSAI).

Our researchers lead one Beacon (Cancer), and two Institutes (CRUK Manchester Institute [CRUK-MI]; Lydia Becker Institute of Immunology and Inflammation [LBIII]); and are integrated into two Beacons (Advanced Materials, Global Inequalities), and seven Institutes/Platforms (Henry Royce Institute for Advanced Materials (Royce Institute), Manchester Institute for Collaborative Research on Ageing (MICRA), Manchester Institute of Biotechnology (MIB), Christabel Pankhurst Institute for Health Technology (Pankhurst Institute), Digital Futures, Health Policy and Organisation (IHPO), Policy@Manchester).

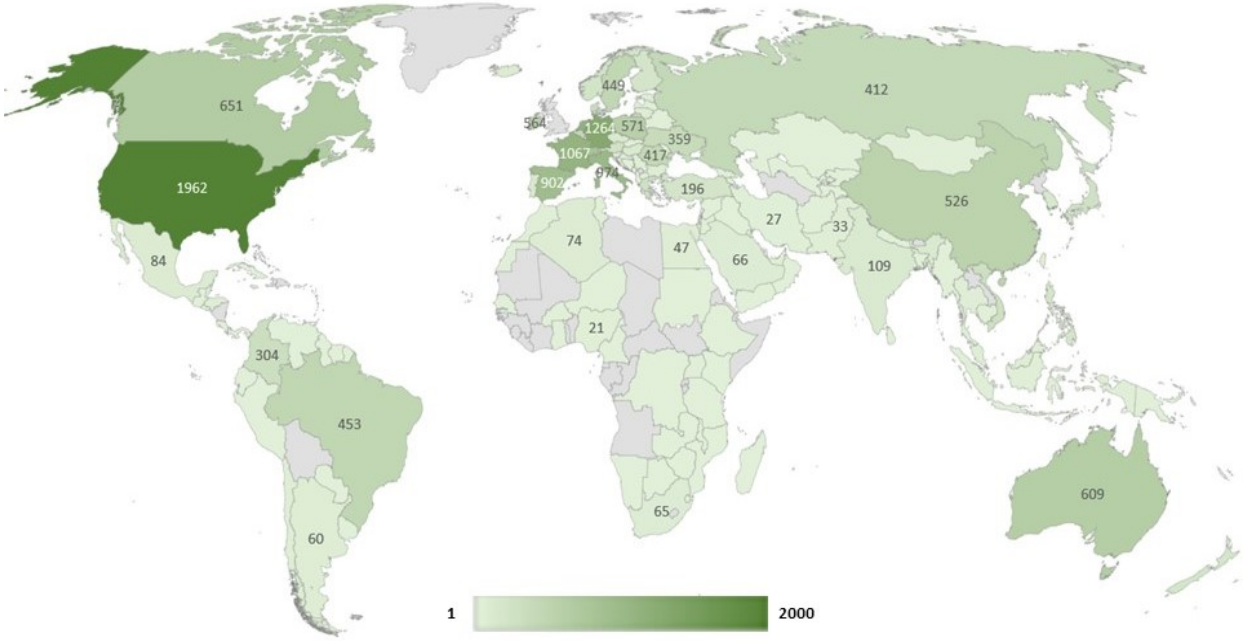
These internal collaborations are particularly important in allowing us to harness advanced, innovative technologies to solve clinical problems.

Outside UoM: Our research culture values external collaborations with Universities and Health Research Institutions (4.6), patient organisations (4.3), and industry (4.4).

As an example of the extent of our collaborations, during REF2021, of our 5,836 primary peer-reviewed publications in Scopus listed journals, ~62% have been published in collaboration with academics and clinicians from 2,792 institutions in 122 countries, who bring to our research: authoritative international expertise; larger patient cohorts for rare diseases, specific treatments, complications and co-morbidities than even our population allows; and extended research skills, knowledge, infrastructure and funding, to bear on globally important clinical questions.

Figure 1 illustrates the reach of our international research collaborations.

Figure 1: Global reach of UoA1's International Collaborations.
The green scale reflects the number of original research articles co-authored with UoA1 Cat A staff (2014-2020) by country. Countries with no collaborative outputs are grey. (N.B. Only countries with >20 co-authored publications are specifically numbered)



C. Fostering research talent and attracting excellent researchers to Manchester

The vitality of our research has been maintained through targeted recruitment and promotion. During REF2021, of the 236 independent researchers returned: 23% were external appointments to targeted prestigious fellowships (2.9) or directly to academic posts (2.8); 24% were promoted (12% to Professor, 4% to Readerships and 8% to Senior Lectureships); 17% are early career researchers (ECRs).

We foster nascent research talent through our PhD (998 students currently), internal fellowship (8), and Academic Clinical Lecturer (ACLs: 22) schemes (2.4) which offer robust, supportive training and mentoring to doctoral students ECRs.

1.2 Headline impact

UoM's institutional statement (REF5a.2) outlines the university's focus on impact. In the 2018 University Impact Rankings UoM was ranked first in Europe. UoA1's research strategy is aligned with UoM's. Evidence of national and international impact across REF2021 is evidenced throughout this document. Headline examples include:

Our 11 REF3 Impact Cases (IC) spotlight established and ongoing clinical and economic impact covering rare genetic disorders, stillbirth, respiratory diseases, acute coronary syndromes and some cancers. When collated, the ICs identify the following health and economic impacts (IC exemplars given by author):

International Impact:

- International roll-out of 10 novel diagnostic/prognostic tests (e.g. VitaloJAK: chronic cough [**Smith**]); four new radiotherapy regimes (e.g. Small cell lung cancer. [**Faivre-Finn**]); and seven new therapies (e.g. Brentuximab vedotin in Hodgkin lymphoma [**Radford**]).

- Therapeutics introduced worldwide (e.g. Voriconazole gaining WHO "Essential Medicine" status for Aspergillosis in 2017 [**Denning**])
- Changed clinical guidance in the UK, across Europe, USA, Canada, China, Japan, Australia, New Zealand, Brazil, India and WHO. (Pan-European Lung Health Checks guidance [**P.Crosbie**])

International/National impact

- Industry partners' revenue increased by >£900m/year (e.g. Biomarin: Vimizim sales for Morquio-A increased by $140m/year between 2017 and 2019 [**Bigger**])
- Potential benefit to ~440,000 UK patients/year and >40m globally/year (e.g. Blood eosinophil-guided treatment reduces acute exacerbations of COPD [global incidence 250m] by ~15% [**Woodcock, Singh**])

National impact

- Potential NHS savings of ~£850m/year (e.g. 1-hour algorithm saves £2,000/patient with suspected acute coronary syndrome [**Body**])

Publications selected for REF2 illustrate preclinical/clinical research impact. Some appear in 1.6 contextualising discovery and impact by individual Research Group.

As markers of research funders'/peer reviewers' assessment of previous and future research impact, since REF2014 we have been awarded 13 new externally funded Research Centres (MRC, CRUK, NIHR, BHF. ~£150m. 3.2.1) and seen eight existing research Centres refunded through infrastructure, programme and project grants (~£100m. 3.2.2)

During REF2021 our research has leveraged NHS/NIHR resource to establish another seven NHS-embedded integrated Treatment and Research Centres led by UoA1 clinical academics:

- 2014: CRUK Major Cancer Centre. (**Bristow** £35m: Christie Hospital: 10,000 new patients/yr)
- 2015: Hyperacute Stroke Centre. (**Smith** Royal Salford NHS Trust: ~2,000 patients/year)
- 2015: Manchester Centre for Genomic Medicine (**Newman** MCGM: serves tertiary population of 3.5m)
- 2017: Manchester Heart Centre (>10,000 new patients/year), incorporating: Acute Cardiac Centre (**Body**); BHF Centre for Magnetic Resonance Research (BCMRR) (**Miller/Naish**)
- 2018: Christie Hospital NHS/NIHR £105m Proton Beam Therapy Centre (**Kirkby**)
- 2019: NIHR £4.4m Centre for Combatting Antimicrobial Resistance (**Felton**)

We have developed robust collaborations. See Figure 1 and Section 4, demonstrating collaboration within UoM (4.1), with our NHS partners (4.2), patient/carer groups (4.3), and industry (4.4), spotlighting collaborative publications and research grants (4.6).

Our Medical Humanities Group (1.6.12): has informed the dialogue between the NHS and the public around responsibility for, and delivery of, "care"; examined the rich history of black and minority ethnic staff in the NHS; and is changing perceptions of animals in healthcare research through the Wellcome Animal Research Nexus.

We have identified value in novel diagnostics and therapeutics through studies sponsored by UK and international industry partners (£60m, 3.1),

1.3 Future research direction and strategy for impact

Our future research strategy develops evidenced successes during REF2021, and will continue to deliver impact through the future research aspirations of our Research Groups (see Future research in each of sections 1.6.1-1.6.12).

We will build on the three principles underpinning our research strategy, using UoA1's research and researchers to collaborate with colleagues in UoM's Beacons and Institutes to develop novel solutions to key clinical questions; work with our research support infrastructure, to ensure we generate the funding needed for our academics to continue accessing high quality infrastructure and research staff; generate outputs and ideas with the quality to consolidate national/international collaborations; and develop our workforce.

Covid-19 has emphasised the need to further develop our research in two specific areas:

- **Directing research to address inequality** in health and healthcare delivery in: **The UK**, supporting GMHSCP's local agenda (4.2), whilst generating research transferrable to equally health-disadvantaged communities world-wide; **Low-income countries** through evidenced healthcare education (Research in Medical Education Group 1.6.12); UKRI Global Challenges Research funding in Cardiovascular Disease (1.6.2); ESRC "Genetics for Africa" funding (1.6.4), and our Aspergillosis research which has global reach (1.6.9).
- **Improving responsiveness to future SARS-associated coronavirus epidemics** building on the research initiatives described in 1.10.

1.4 Unit Context and Structure

UoA1 undertakes research within UoM's strategic research environment (REF5a.2). The structures put in place at Faculty merger facilitate interdisciplinary science. Whilst day-to-day management of academic staff and students is within Schools (Biological Sciences [SBS], Medical Sciences [SMS], and Health Sciences [SHS]), and Divisions (Figure 2), research is focused on trans-disciplinary Research Groups.

UoA1's submission covers twelve Research Groups each spanning discovery to translation, with a shared goal of improving patient outcomes. All 236 independent researchers are returned (**222.06 FTE**). We cluster the Groups by research focus: Specific disease/system (four groups), Inflammation-focused (five groups), Applied technology (two groups) and Medical Humanities (one group) as follows:

Specific disease type/system:

- **Cancer** (Cancer: **Bristow**)
- **Cardiovascular Sciences** (CVS: **Keavney**)
- **Developmental Biology and Medicine** (DBM: **Heazell**)
- **Genetics and Genomics** (Genetics: **Newman**)

Inflammation:

- **Manchester Collaborative Centre for Inflammation Research** (MCCIR; **Hussell**)
- **Respiratory Medicine** (RespMed; **Smith**)
- **Centre for Musculoskeletal Research** (CfMR; **Barton**).
- **Centre for Dermatology Research** (CfDR; **Griffiths**)
- **Infection** (Infection; **Denning**)

Technology:

- **Biomarker Technologies** (BiomTech: **Whetton**)
- **Regenerative Medicine** (RegenMed: **Hoyland**)

Medical Humanities: (MedHum: **Snow**)

Figure 2. Illustrating some of the main elements of the cross-disciplinary environment feeding in to each Research Group from the Divisions within FBMH's Schools

1.5 Contextualising UoA1's research environment

1.5.1: Within UoM. UoM's research environment is predicated on multidisciplinary research (4.1, REF5a.2ii/iii). Hence, whilst core membership of our Research Groups is based on clinical focus, researchers can call upon individuals and teams with generic skills (platform technologists, health economists, data analysts etc.) and specialised facilities (3.5. 3.6. 4.1) from other Groups and Institutes, enhancing trans-disciplinarity without diluting specialist expertise.

Figure 2 illustrates how UoA1's Research Groups recruit members from the Divisions of FBMH's three Schools. As an indicator of how cross-fertilisation of ideas and skills contributes to our research, 179 of the 538 REF2 outputs are with members of other UoAs (particularly UoA2: Epidemiologists, Health informaticians, Health economists, and UoA5 Biological Scientists, but also others across UoAs as detailed in 4.1.3)

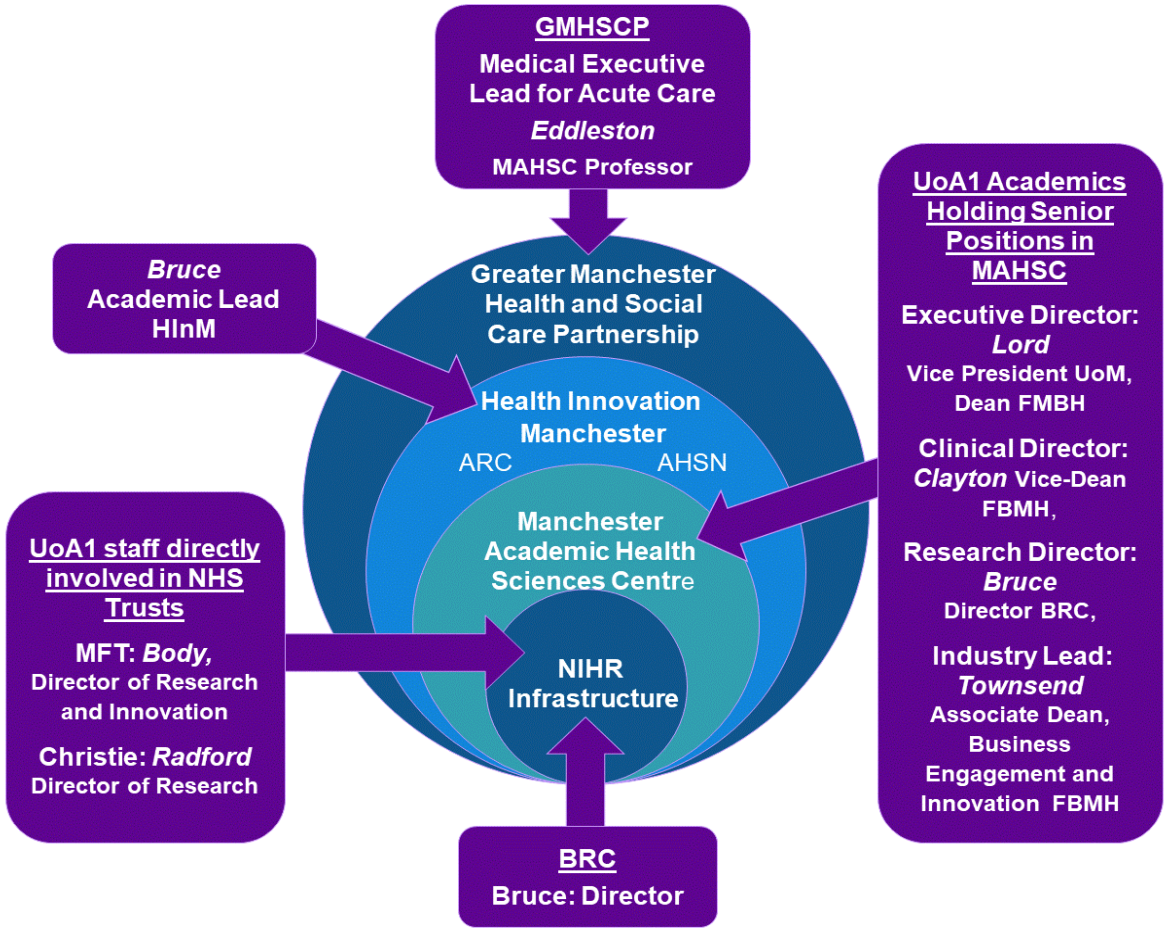
***1.5.2: NHS Environment*:** Research and infrastructure of our BRC, ARC-GM, MCRF, PSTRC and LCRN are integrated within NHS structures at a UoM/NHS interface mission-critical for experimental medicine, to complete the "One Manchester" environment.

MAHSC is key to ensuring smooth operation of research around and across this interface. UoA1 researchers hold major strategic roles in MAHSC (Figure 3) ensuring alignment of UoA1's strategy with that of GMHSCP.

Redesignated in 2020, MAHSC, (one of eight NIHR/NHSE/NHS Improvement AHSCs nationally), strategically aligns NHS organisations and UoM, to facilitate translation, creating opportunities for UoM's academics and NHS clinicians to conduct cross-cutting translational research within GM.

The comments of the redesignation panel emphasise how well MAHSC has delivered this agenda. They stated the: "*volume, breadth, and quality of* [our] *research, education, and strategic plan was strong, with alignment to the NHS Long Term Plan, Life Sciences Industrial Strategy, and goals of the Accelerated Access Collaborative*" and applauded our track record of "*translating scientific advances into patient benefit, system-wide leadership for specific innovative technologies, capacity and plans for contributing to economic growth through partnerships with commercial organisations, and clear route for commercialisation of innovative technologies"*.

Figure 3: Involvement of UoA1 Academics in "One Manchester"



1.5.3 Our wider environment is global, (Figure 1) incorporating other Universities, our community and industry. Discussed in Section 4.

1.6 Activities and Impact of each Research Group

We describe the activities and some key discoveries of our Groups and their themes, illustrating how our research environment has encouraged academic endeavour. We also headline the future research strategies of each Group, and present a sample of REF2/3 outputs to indicate the scope,

range and impact of research within individual Groups. Outputs are embedded in the text as journal citations, consisting of author surname, short journal title with year and unique identifier (example: "REF2IDXX") to enable interrogation of the output in REF2 return.

Other evidence of success is given in document Sections: 2: Fellowships; 3: Major research grants; 4: Collaborative research).

SPECIFIC DISEASE TYPE/SYSTEM CLUSTER

1.6.1 CANCER (Cancer 70.65 FTE)

Background

Cancer is a UoM Research Beacon.

Our environment incorporates UoA1's discovery-focused £40m CRUK Manchester Institute (CRUK-MI: **Marais**), and comprehensive £35m CRUK Major Cancer Centre (**Bristow, Marais**), which with MAHSC's NHS Trusts form the over-arching Manchester Cancer Research Centre (MCRC: **Bristow**). UoA1's cancer research is largely based in our lead cancer Trust - The Christie, Europe's largest single-site cancer centre, seeing >44,000 patients/year. Of ~10,000 new patients in 2019, >2,000 entered clinical trials. The Christie also houses the UK's first NHS high energy proton beam therapy centre (NHS/NIHR: £125m). Research is undertaken by the PRECISE research group (**Kirkby***:* £16m EPSRC/EU/BRC).

During REF2021 MCRC has delivered growth through translation of basic/discovery research into hospital and community healthcare, which in GM, is addressing the NHS long-term goals of earlier cancer detection; precision risk assessment; and increased survival.

This strategy has enhanced our environment through £120m funding of external Centre Awards during REF2021 (3.2) which focus on our research.

Major research themes

Cancer research in Manchester covers nine major themes.

CRUK-MI Discovery (**Marais, Dive**) Spanning the spectrum of basic cancer research, our discoveries prime novel translational and clinical research, CRUK-MI researchers have made important discoveries across molecular oncology (**Viros***,* **Nature.2014:**REF2ID:38898076), translational oncogenetics, cell division, systems oncology (**Bristow**, **Cell.2018:** REF2ID:84676050), cell signalling, cancer immunology (**Zelenay**, **Cell.2015:**REF2ID:39037165), and drug discovery (**Springer**, **Cancer.Cell.2014:**REF2ID:38895404).

Experimental Cancer Medicine (**Krebs, Makin**). ECM aligns genetics (**Astley**, **JAMA.Oncol.2018:**REF2ID:64158134), molecular profiling, biobanking, imaging (**Valle**, **ESMO.Open.2020:**REF2ID:175167302; **Jackson**, **J.Nuc.Med.2015:**REF2ID:116756477), and biomarker discovery (**Krebs**, **Nature.Med.2019:**REF2ID:85366722) allowing patient stratification to deliver effective phase I/II trials (~300 adults and children/year) employing digital technology/science to optimise patient engagement and clinical decision making

Genomics (*Evans, reported in UoA2*)

Prevention & early detection (PED) (**Crosbie, Howell**) Leading the BRC £2.7m PED theme and integrated within CRUK's International Alliance for Cancer Early Detection (ACED), PED has explored and translated novel ways of detecting cancer (**P.Crosbie***,* REF3 Impact Case), and developed clinically-relevant strategies for prevention (**A.Howell**, **Lancet.2019:** REF2ID:158351714) and intervention (**E.Crosbie**, **Int.J.Cancer.2019:**REF2ID:82680279).

Radiotherapy-related research (**Choudhury**) Has made advances in all aspects of radiotherapy research from pre-clinical radiobiology to clinical therapy (**Faivre-Finn**, REF3 Impact Case). Particular discoveries in REF2021 are in the fields of technical radiotherapy (**Taylor**, **Com.Phys.Com.2020:**REF2ID:158179007), radiogenomics (**Choudhury**, **Clin.Canc.Res.2017:** REF2ID:63004429), radiotherapy-immunotherapy combinations (**Illidge, J.Clin.Oncol.2014:** REF2ID:38883666), theranostics and predictors of treatment toxicity and response.

Tumour microenvironment (**Bristow, Malliri**) Our research within the Wellcome Centre for Cell-Matrix Research (UoA5) and CRUK-MI has established novel cell-cell and cell-matrix interactions driving cancer behaviour (**Malliri**, **Cell.Reps.2014:**REF2ID:38897887) that have been harnessed clinically (**Bristow**, **Lancet.Oncology.2014:**REF2ID:84676224; **Illidge**, **EMBO.Mol.Med.2017**, REF2ID:63598214)

Targeted and Immuno-oncology (**Illidge**), Incorporating Innovate UK iMATCH (Innovate Manchester Advanced Therapy Centre Hub), one of only three cell-therapy consortia focused on activity scale-up, safety and delivery in clinical ATMP trials (**Owens**, **J.Immunotherapy.2018:** REF2ID:170772378), has investigated cancer evasion of immune surveillance, and harnessed cellular immunity (**Honeychurch**, **Clin.Canc.Res.2017:**REF2ID:63597969), and antibody-based treatment therapeutically. (**Illidge**, REF3 Impact Case; **Faivre-Finn**, **J.Nat.Canc.Inst.2014:** REF2ID:38779070).

Centre for Biomarker Sciences (**Dive**, reported in BiomTech 1.6.10).

Clinical Oncology (**Radford**)**;** Pulling information from preclinical groups (**Saha**, **Lancet.Haematol.2019:**REF2ID:102909622), industry and experimental cancer medicine (**Lee**, **Ann.Oncol.2019:**REF2ID:131872567) and working with Christie clinicians and international collaborators has benefited patients through changed treatment pathways in chemo- and chemoradiotherapy combinations. (**Radford,** REF3 Impact Case; **Illidge**, **NEJM.2015:** REF2ID:38883662; **Blackhall**, **JAMA.Oncol.2018:**REF2ID:84326687).

Future Research

We will deepen our science in current research areas, building on large CRUK infrastructure awards. Some areas, now evolving out of prescient developments in cancer science, deserve special mention:

Strategic Team Science and New Research Building: The Paterson Rebuild (£150m, 30,0000m^2, Q4-2022 move-in) funded by MCRC partners (UKRPIF £25m, Wolfson Foundation £5m) will radically enhance our environment by co-locating teams of UoM researchers with NHS clinicians, manifesting as “collaborate zones” designed, through interaction, to drive our science into clinical trials and NHS uptake with further pace and scale.

Early Cancer: We will direct activity towards detection and early intervention in pancreatic, lung and hereditary cancers (combines BRC PED theme and CRUK ACED awards) giving new direction to cancer diagnosis particularly “difficult-to-manage” cancers (pancreas, lung, ovary)

Proton Beam and Experimental Radiotherapy: Our £16.5m CRUK Radiation Centre of Excellence grant allows development of the UK’s only National Proton Research Facility with in-vitro and in-vivo experimental beams and development of FLASH microsecond radiotherapy, reducing toxicity. We will also focus on hypoxia- and molecular-targeted therapies and radio-immunotherapy placing the UK at the forefront of proton research.

Cancer Immunology will develop Cancer Immunotherapy, co-creating multi-modality approaches to cancer early interception by exploring immune status in early cancers, designing new solid tumour chimaeric antigen receptor, T-cell receptor, and tumour-infiltrating lymphocyte therapies,

matching novel ATIMPs to relevant cancers, as well as trialling novel antibody-based therapies, leveraging funding from commercial partners (e.g. Gritstone Oncology 4.5).

Digital Cancer Centre will implement new AI-driven trials for elderly patients with comorbidities combining resource from Christie's electronic Patient Reported Outcome Measures and Data Insight programme, new HEE Data Sciences training grant, teams led by UoM's two Health-AI Professors (*Kaski* [UoA11: partnership with Aalto University, Finland]; *Yau* [UoA11: co-Director of the Health Data Research UK-Turing Wellcome PhD Programme in Health Data Science]), IDSAI, and UoM's Digital Futures platform (4.1) to provide more appropriate cancer care for the elderly.

Molecular Proteomics and Biomarkers of Resistance We will develop in-situ proteomics and AI to analyse cancer tissue sections defining novel biopsy-based biomarker signatures in Christie's new Academic Pathology Unit, co-located with the Cancer Biomarkers Centre. This will build on our discovery research, generating novel precision medicine tests employing (ultimately autonomously) machine-learning to guide therapies, predict responses and outcomes, whilst addressing the critical world-wide shortage of histopathologists.

Intelligent Onco-Materials: Collaborating with Manchester Institute of Biotechnology, National Graphene Institute (Graphene Institute 3.5.3) and Royce Advanced Institute, we will develop new nano-oncology programmes exploring nanoparticles to: recognise clinically pertinent protein changes post-radiotherapy; permit early-detection cancer signals; design and develop biosensors and bio-wearables (for instance, to flag early neutropenic sepsis and cytokine storms); and create artificial cancer-associated chromosomal loci expressed in primary cells for novel models of copy number gain.

1.6.2 CARDIOVASCULAR SCIENCES (CVS 28.91 FTE)

Background

Working across cardiovascular physiology and disease, including disease causes (diabetes, hypertension) and effects (acute cardiac syndromes [ACS], stroke), during REF2021 our research impacted the whole discovery-to-translation landscape.

Our clinical environment has been enhanced through formation of an integrated Manchester Heart Centre, allowing us access to a tertiary care population of ~6m.

Major research themes

Integrative cardiac physiology (ICP): (**Eisner** [BHF Chair]) ICP has made significant mechanistic discoveries, incorporating causes, effects and potential therapeutic targets in and of: myocardial hypertrophy (**Kitmitto**, **Nature.Comms.2019**, REF2ID:143030568), heart failure (**Trafford**, **Sci.Rep.2019:**REF2ID:108002857); ion channels and their regulation (**Nelson**, **Sci.Reps.2016:**REF2ID:51338108), cardiac rhythms and dysrhythmias (**Morris**, **Nature.Comms.2014:**REF2ID:38653466); and cardiac dysfunction (**Ray**, **Nature.Comms.2017:** REF2ID:116757117), using laboratory science, in-vitro/in-vivo model systems, and patient studies.

Genetics of cardiovascular disease: (**Keavney** [BHF Chair]) CVS genetics, collaborating with UoA1's Genetics Research Group (1.6.4), using 100,000 genomes data, and gene deletion/silencing technologies (**Cartwright**, **J.Mol.Cardiol.2014:**REF2ID:159757480; **D'souza**, **Sci.Reps.2020:**REF2ID:182172032) has identified new genes/gene-variants underlying cardiovascular conditions, including: atheroma (**Tomaszewski**, **Art.Thromb.Vasc.Biol.2019:** REF2ID:157870719); congenital heart disease (**Black**, **Circ.Res.2019:**REF2ID:157870694), and dysrhythmias (**Venetucci, J.Hum.Gen.2020:**REF2ID:172892859).

Micro- and macro-vascular disease: (**Heagerty**). Has defined vascular homeostatic mechanisms (**Greenstein**, **Science.Signal.2016:**REF2ID:51334938), structural and functional vascular changes in hypertension and diabetes (**Nelson**, **Science.Signal.2014:** REF2ID:38921840), and the role of perivascular fat in causation and reversal of vascular dysfunction (**Heagerty, Sci.Reps.2017:**REF2ID:64529271).

Clinical innovations: (**Tomaszewski**) Has pioneered practical diagnostics (**Miller**, **J.Am.Col.Cardiol.2014:**REF2ID:38899460), treatments and pathways for common cardiac/vascular disorders including: suspected ACS (**Body**, REF3 Impact Case, hypertension (**Tomaszewski, Eur.Heart.J.2019:**REF2ID:158685661), blood pressure management before surgery (**Heagerty**, **Anaesthesia.2016:**REF2ID:51478759), and stroke (**Parry-Jones**, **Ann.Neurol.2019:**REF2ID:135391772).

Future Research

We will continue building on our successes through a programme of future-proofing, diversifying and expanding our researcher base:

Future proofing: £1m BHF Accelerator Award will build stronger cross-disciplinary research collaborations, involving physical scientists and humanities scholars, promoting research innovation and holistic approaches to understanding causes and effects of cardiovascular disease.

Global Challenges Funding (~£800k;MRC/DIFD) will be used to expand the pool of clinicians dealing with cardiovascular diseases in developing countries, reducing global inequality.

Our strong cadre of ECRs and new lecturers, (**Miller, Pinali, D'Souza, Morris**) with funded fellowships complementing the research of our two BHF Chairs (**Keavney, Eisner**) and supported by PhD students on our BHF 4-year PhD programme will extend and futureproof our science in pathophysiology and genetics.

Exploiting HInM's adoption pipeline. HInM's translational route has taken Body's algorithms across GM. It is supporting this and other clinical packages from local adoption to national implementation, for instance: Parry-Jones' ABC-intracranial haemorrhage care bundle (reduces 30-day deaths from 35.5% to 24.2%) and urinary mass spectrometry for antihypertensive metabolites (**Tomaszewski**) increasing compliance up to 50%. Emerging clinical research packages will be directed down this route giving accelerated uptake for patient benefit.

Cardiac Imaging: Launched 11/2020, BCMRR 3T-MRI (£3.1m) will accelerate delivery of experimental medicine and translational cardiovascular and stroke research using imaging biomarkers. Its introduction as part of an expanded programme of Sports Cardiology Research will bring insights into why ethnicity influences cardiac deaths in athletes.

1.6.3 DEVELOPMENTAL BIOLOGY AND MEDICINE (DBM 18.5 FTE)

Background

DBM undertakes research across fetal development, organogenesis, infancy and childhood. It has improved early-life outcomes and increased understanding of stem cells and their uses and the genetic programming of organogenesis. Clinical outreach is through MFT's specialist regional/super-regional clinics.

Major research themes

Tommy's Centre for Maternal and Fetal Health (**Heazell**): Has improved understanding of human placental blood flow and its regulation (**Aplin**, **Theranostics.2017:**REF2ID:59973955) demonstrating how and when it influences: fetal development (**Brownbill**, **J.Physiol.2015:** REF2ID:38655081); and survival. Research has also changed lives: of families with previous stillbirths (**Heazell**, REF3 Impact Case); women with pregnancy complications (**Myers**, **Hypertension.2020:**REF2ID:177316240); following assisted reproductive technology (ART); and of fetuses and infants of epileptic mothers (**Bromley**, **Neurology.2014:**REF2ID:38767339).

Paediatric Growth and Development (**Clayton**) working with national/international collaborators to established patient cohorts at scale, has improved long-term health for children with maternally-induced congenital (**Banka**, **Am.J.Hum.Gen.2016:**REF2ID:51535113) and acquired (**Bromley**, **JAMA.Pediatrics.2014:**REF2ID:38654821) disorders that can significantly impair long-term health (diabetes, cognition, hypertension, obesity [**Clayton**, **JAMA.2018:**REF2ID:84110213], cardiovascular disease, cancer).

Developmental Haematopoiesis (**Lacaud**) Has discovered molecular (**Lacaud**, **Blood.2014:** REF2ID:51157594; **Lacaud**, **Develop.Cell.2016:**REF2ID:51157536) and cellular mechanisms controlling haematopoiesis and stem cell homeostasis (**Lacaud**, **Nature.Cell.Biol.2016:** REF2ID:51157535) generating data with the potential to improve marrow transplantation and haematopoietic stem cell generation from pluripotent stem cells (**Batta, Cell.Reps.2014:** REF2ID:38891096).

Human Organogenesis (HO): (**Hanley**) HO has deciphered genomic mechanisms underlying organ and tissue development (**Jennings**, **eLife.2016:**REF2ID:50473112), instructing regenerative medicine; and explaining normal and deranged molecular mechanisms leading to developmental disorders (**Birket**, **Stem.Cell.Reports.2019:**REF2ID:135691559) and cancer (**Hanley**, **Genome.Res.2019:**REF2ID:116757229).

Future Research

In-utero fetal development: Tommy's-funded £2m infrastructure, Heazell's NIHR Clinician Scientist Award, and £2m MRC programme grant underpin research into the major global issues of poor intrauterine growth, stillbirth, and postpartum maternal and child health. It will focus on: placental immunity (with MCCIR); defining biomarkers and therapeutic targets to manage modifiable risk; and perturbed intrauterine growth; improving clinical care of women at risk of stillbirth; and enhancing understanding of the placenta's role in early embryo development.

Maternal effects on post-partem development and disease: The pan-European DohART-NET (UoM £450k) will continue to generate scalable research in rare paediatric disorders, and strengthen studies of parental factors in development of children's lifelong morbidities, promoting pre-natal approaches to disease prevention and novel routes into personalised interventions.

Developmental haemopoiesis: Future research supported through CRUK-MI and collaborations with GM's Manchester Genetics Medicine Centre (1.6.4), will apply epigenomics to: human stem cell differentiation; investigating cellular heterogeneity's influence on differentiation; and decode cell fate decisions, generating clinical value through applying the consequent findings to stimulate in-vivo blood cell production (e.g. in aplastic anaemia), and in-vitro, for bone marrow replacement and transfusable blood production.

Organogenesis: Our future research will continue our work on the genetic basis of organ formation and its regulation. This will inform the research of DBM, and develop novel therapeutic approaches based on ex-vivo stem cell manipulation for use in regenerative medicine.

1.6.4. GENETIC AND GENOMIC MEDICINE (Genetics 15.8 FTE)

Background

Working within GM's Genetic Medicine Centre (GMGMC) UoA1's researchers have discovered new genetic diseases and disease mechanisms, informing clinical management.

GMGMC is a cross-disciplinary NHS/UoM, diagnostic, treatment and research facility led by UoA1's Newman. It intermeshes with GM's Genomics Laboratory Hub in the £28m/year NHS Genomic Medicine Centre serving a tertiary care population of ~3.5m. They are part of a "Genetics Campus" at MFT Oxford Road incorporating purpose-designed buildings (Citylabs) for industry and UoM partners. Proximity to GMGMC and quality infrastructure attract companies such as Yourgene, APIS. (Citylabs1.0) and Qiagen (Citylabs2.0) to site UK/European bases in Manchester.

Genetics' academics support other UoM academics' gene-based research through quality, specialised infrastructure, facilitating phenotyping, genotyping and reverse phenotyping and identifying novel disease genes/genetic diseases. For instance we have reverse phenotyped ~1,000 children recruited to the "Deciphering Developmental Disorders" study and >1,000 individuals with developmental disorders to the "100,000 Genomes" study.

Major Research Themes

Genetic technology: Has developed: new techniques that advance disease gene discovery (**Tassabehji**, **Nature.Gen.2019:**REF2ID:160856730); and new approaches to improve clinical diagnostics (**Black**, **Ophthalmology.2016:**REF2 ID: 50458991).

Ophthalmic Genetics (**Bishop**) through improved understanding of genetic mechanisms (**Manson**, **PNAS.2015:**REF2ID:56432209) has discovered biomarkers (**Bishop**, **Nature.Comms.2020:**REF2ID:158531561) of genetically linked blindness. Pioneering use of gene-therapy has led to successful treatments of hereditary blindness (**Bishop**, **Current.Biology.2015:**REF2ID:38652882; **Black**, **NEJM.2016:**REF2ID:56432208).

Immunogenetics (**Briggs**) has changed understanding of interferonopathies, rare (**Briggs**, **Science.Immunol.2019:**REF2ID:158168536) neurodevelopmental and vascular disorders, causally overlapping with autoimmune diseases (**Crow**, **J.Exp.Med.2017:**REF2ID:83332084), translating findings into clinical outreach (**Crow**, **Nature.Gen.2014:**REF2ID:38659252) through GM's immunogenetic testing centres (one of two in England).

Developmental Genetics (**Banka**) has discovered and characterised novel genetic mechanisms (**Banka**: **Am.J.Hum.Gen.2017:**REF2ID:85195012; **Am.J.Hum.Gen.2017:**REF2ID:85195013; **Am.J.Hum.Gen.2017:**REF2ID:64800873) behind developmental abnormalities to understand syndromic backgrounds (**Roberts**, **Kid.Int.2019:**REF2ID:84828682; **Crow**, **Nature.Gen.2016:** REF2ID:50410335) and stratify patients.

Cancer Genetics (*Evans reported in UoA2*).

Kay N Hinckley Centre for Biomedical Egyptology (KNHCBE)'s aDNA group (**Drosou**), has definitively identified previously highly disputed familial lineages in 3,800 year old Pharaonic Egyptians (**Drosou**, **J.Arch.Sci.2018:**REF2ID:133994639]).

Future Research

We will develop our research by exploiting the platforms and approaches we have built in GMGMC.

Gene therapy. The progress in gene therapy for blindness (**Bishop** MRC £1.45m) in mice and pilots of 24 patients with xeroderma pigmentosa and choroideremia, has opened the way for

translational gene therapy research under our gene therapy licence, further improving outcomes in patients with hereditary blindness and extending into disorders of other systems.

Diagnostics: Success developing a low-cost point-of-care test with Genedrive (UoM-spinout 2007), preventing neonatal gentamycin-induced hearing loss (**Newman** NIHR-i4i £900k, BRC Hearing Theme £3.6m) represents a paradigm for developing near-patient diagnostics for genetically-mediated disorders in any body system. Global translation through existing funding (ESRC £160k) to take genomic medicine into Africa, will leverage further opportunities for deployment of gene-based technologies into low-income countries.

Gene discovery: GMGMC brings understanding to hereditary disorders through genophenotyping and reverse phenotyping. The NHS Genomics Medicine Centre will accelerate translation, advancing pre- and postnatal diagnosis, and patient management

Platform Technologies: Through our genomics platforms and experience of experimental/translational genetic medicine we will input into other groups' genetic investigations (e.g. Cancer, CVS, CfMR) enhanced by continually upgraded research infrastructure (most recently: polygenic risk scoring, multi-omics [with **Whetton** BiomTech], UoM's big data analytics) for advancing personalised medicine.

Ancient DNA: £1.1m funding and access to hard/soft tissue biorepositories (KNH: 360 individuals spanning 5000yr) will be harnessed to study genetic disease development, and micro-evolutional responses to climate change and infections, informing modern global questions.

INFLAMMATION, INFECTION AND IMMUNITY CLUSTER:

UoA1 has major research activity around inflammation and its management, reflected here in five Groups with shared goals, cross-cutting technologies and collaborative research/outputs.

Their common research, brings international leadership in diagnosing and managing Immune-Mediated Inflammatory Diseases (IMIDs) and catalyses development of highly characterised patient cohorts (e.g. through five Manchester-led/co-led MRC Stratified Medicine Initiatives [~£20m during REF2021, 3.2.3]), and Manchester-led biologics registries.

Clock biology is a common research theme across these Groups and one increasingly embraced by Cancer (**Bulfone-Paus**, **OncoImmunology.2015:**REF2ID:38655527) and CVS (**Ray**, **Nature.Comms.2017:**REF2ID:116757117). All our Inflammation Research Groups have researchers working within UoM's Centre for Biological Timing (CBT), the largest clock biology community in Europe (27 PIs, 154 researchers, £56m active grant funding).

UoA1 researchers bring clinical guidance and direction to CBT's research, whilst within this collaborative, skills spanning clock biology, model organisms, and fundamental cellular events are employed by UoA1's researchers to make discoveries of clinical importance (examples in each Group) that impact when and how patients are assessed and treatment given for optimum effect (e.g. Lung inflammation [**Gibbs, Nature.Med.2014:**REF2ID:38792277]; success of lung transplantation, [**Durrington**, **Thorax 2018:**REF2ID:77977672**],** Intervertebral disc degeneration, [**Hoyland**, **Ann.Rheum.Dis.2017:**REF2ID:50943914]).

1.6.5 MANCHESTER COLLABORATIVE CENTRE FOR INFLAMMATION RESEARCH (MCCIR: 10.8 FTE)

Background

UoA1 researchers contribute to MCCIR through overall leadership (Director **Hussell**), and leading 3 of 14 themes: Lung immunity (**Hussell**); Homeostasis and Pathogenesis (**Bulfone-Paus**); Skin inflammation (**Saunders**), and bringing clinical focus across the Centre.

Examples of Research Achievements

During REF2021, UoA1's research in MCCIR has:

- Characterised novel immune mechanisms (**Arkwright**, **Nature.2014:**REF2ID:38652407; **Lord**, **J.Clin.Invest.2019:**REF2ID:134867970) across a spectrum of human diseases (eg. asthma [**Hussell**, **J.Al.Clin.Immun.2017:**REF2ID:61456947], Crohn's disease [**Lord**, **Gastroenterology.2019:**REF2ID:134867985], colonic cancer [**Bulfone-Paus**, **OncoImmunology.2015:**REF2ID:38655527]);
- Changed understanding of allergy **(Mills**, **J.Al.Clin.Imm.2015:**REF2ID:38921447; **Allen**, **J.Al.Clin.Imm.2015:**REF2ID:38651799 and **J.Al.Clin.Imm.2014:**REF2ID:38651803), and its diagnosis and management (**Mills**, **J.Al.Clin.Imm.2018:**REF2ID:64483222);
- Improved clinically-critical understanding of circadian cycles in lung disease (bronchial inflammation [**Gibbs**, **Nature.Med.2014:**REF2ID:38792277; and **J.Clin.Invest.2018:** REF2ID:83321223], lung fibrosis [**Kitchen**, **PNAS.2020:**REF2ID:158703217], pneumonia [**Kitchen**, **PNAS.2020:**REF2ID:158729230] and lung transplantation [**Durrington**, **Thorax.2018:**REF2ID:77977672])
- Defined responses to SARS-Cov-2 (1.10; [**Hussell**, **Science.Immunol.2020:** REF2ID:176556622]).

Future Research

Immune phenotyping and responses to SARS-CoV: With UK-CIC (UKRI/NIHR £6.5m), we will continue to identify risk immunophenotypes in COVID-19 patients, and develop susceptibility testing strategies for future SARS-CoV variant epidemics.

Understanding disease mechanisms in inflammatory lung disease: **Hussell's** £1.7m WI with BRC Respiratory Theme funding, will stimulate discovery of novel immune mechanisms regulating bronchial and alveolar pathology in asthma and COPD, informing changes in disease management.

Food allergy and childhood allergen desensitisation are an ongoing NIHR/MRC (£1.6m) and FSA (£1.8m) funded research programme. **Gibb's** £600k MRC-funded studies of systemic immune-modulation by human microbiomes will bring a new and clinically important perspective to mechanisms underlying food allergy.

Collaborative research: We will bring our expertise to collaborations with other groups: "Tommy's": placental immunology; "RespMed, CfMR, and CfDR, exploring basement membrane integrity in organ-specific immunity; Cancer: examining immune status in early cancer, developing novel anti-cancer ATIMP strategies; Diversify approaches to antimicrobial resistance with Infection (1.6.9) harnessing immune mechanisms for anti-bacterial therapies.

1.6.6. RESPIRATORY MEDICINE (RespMed 10.2 FTE)

Background

Respiratory Medicine is a BRC theme (£2.8m).

Our environment is enriched by undertaking clinical research within the NW Lung Centre (one of England's largest: 40 consultants); and, broad national and international collaborations.

RespMed has led discovery of disease mechanisms, diagnostics, and, through phase I-III trials, designed novel treatments that have improved lives of patients with the respiratory diseases: childhood asthma (**Murray**), chronic cough (**Smith**), chronic pulmonary obstructive disease (COPD) (**Singh, Woodcock**), and cystic fibrosis (**Horsley**)

Major Research Themes

Technological advances/diagnostics aiding patient management: Recognising that technological advance enhances diagnosis and study conduct, RespMed has made innovations in how respiratory disease is diagnosed (**Papadopoulos**, **Nature.Comms.2018:** REF2ID:84378043), measured (**Smith** REF3 Impact Case), and studied (**Whitfield**, **Plos.One.2018:**REF2ID:120890152; **Horsley**, **Eur.Resp.Journal.2016:**REF2ID:50614334).

Childhood asthma (**Murray**)**:** Has advanced understanding of disease mechanisms, including using novel analytical approaches to cohort data (**Murray**, **PLOS.Medicine.2018:** REF2ID:84929282), making diagnoses (**Durrington**, **Lancet.Child.Adolesc.Health.2017:** REF2ID:63507545), defining prognosis (**Murray**, **Clin.Exp.Allergy.2019:**REF2ID:158242127) and practical interventions (**Murray**, **Am.J.Resp.Crit.Care.Med.2017:**REF2ID:64483095)

Chronic cough (**Smith, Woodcock**) Has discovered novel cough mechanisms (**Woodcock**, **Am.J.Resp.Crit.Care.2015:**REF2ID:51284284) and changed the landscape in conducting meaningful clinical trials through the development of an objective "cough test" (**Smith**, REF3 Impact Case), improving the effectiveness of trials of anti-tussives (**Smith**, **Lancet.2015:** REF2ID:38939363).

COPD (Singh): using large Manchester-based and collaborative patient cohorts, has demonstrated the efficacy of new approaches to the use of novel and established drugs, alone and in combination (**Singh, Woodcock**, REF Impact Case) to optimise management of COPD in hospital and the community (**Woodcock**, **NEJM.2016:**REF2ID:50457821), with a particular focus on preventing exacerbations (**Singh**, **NEJM.2019:**EF2ID:158455208) requiring hospital admission.

Cystic fibrosis: has driven personalised medicine through genetically-guided therapies (**Horsley**, **Chest.2014:**REF2ID:38794083 and **NEJM.2018:**REF2ID:82928469) and increased awareness of the scope of pulmonary comorbidities (**Denning**, **PLOS.One.2014:**REF2ID:38662758).

Future Research

Airways disease: The BRC Respiratory Theme will:

- Allow RespMed to grow research in understanding triggers and prevention of acute exacerbations of COPD, through biomarker-led trials within the Manchester-led international DisEntangling Chronic Obstructive pulmonary Disease Exacerbations NETwork (DECODE-NET) giving access to at-scale cohorts.
- Underpin future cystic fibrosis research exploring novel gene-based and gene expression approaches to management, in collaboration with Bigger (RegenMed).

Chronic Cough: Smith's WI Award (£1.6m) enables expansion of mechanistic understanding of cough, feeding clinical trials through the European Respiratory Society's Clinical Research

Collaborative (NEuroCOUGH). Smith's development of an objective cough measuring instrument (**Smith**, REF3 Impact Case) offers unparalleled opportunities for industry-driven anti-tussive collaborative trials informing much needed point-of-care anti-tussive evaluation and validation.

1.6.7. CENTRE FOR MUSCULOSKELETAL RESEARCH (CfMR: 14.25 FTE)

Background

CfMR, a European League Against Rheumatism Centre of Excellence, incorporates two Versus Arthritis Centres of Excellence, Genetics & Genomics (VACEGG, reported here) and Epidemiology (*reported in UoA2*). It hosts the £4.5m BRC Musculoskeletal Theme, and largest rheumatoid arthritis (RA) biologics registry internationally (BSRBR-RA).

Research has driven discovery of the genetic/gene-expression basis of disease and improved lives of patients with musculoskeletal IMIDs (RA, lupus, psoriatic arthritis [PsA]) by bringing the power of: digital epidemiology; modern genomics; and experimental medicine to bear on well-characterised patient cohorts from registries.

Major Research Themes

Advances in gene technologies relevant to IMIDs (**Raychaudhuri**)**:** CfMR academics have developed novel ways of generating (**Orozco**, **Sci.Reports.2020:**REF2ID:177697976) and interrogating DNA and RNA datasets that impact directly both on understanding of autoimmune diseases (**Raychaudhuri**, **Nature.Gen.2016:**REF2ID:62520052) and how personalised treatments are defined (**Barton**, **Ann.Rheum.Dis.2018:**REF2ID:132446682).

Genetic predisposition to IMIDs (**Eyre**): VACEGG academics have uncovered common genetic traits linking autoimmune disorders (**Raychaudhuri**, **Nature.Gen.2015:**REF2ID:38923696; **Eyre**, **Nature.Comms.2015:**REF2ID:38776697).

Rheumatoid Arthritis (**Barton**)**:** Patient stratification based on clinical (**Barton**, **Arth.Res.Ther.2018:**REF2ID:84778509) and genetic measures applied to Manchester cohorts and international Manchester-led registries, brought new understanding of: the role of key genes in the genesis of RA (**Eyre**, **Nature.Gen.2018:**REF2ID:78449349 and **Nature.Comms.2020:** REF2ID:177697963), disease behaviour and treatment response (**Barton**, **Nature.2014:** REF2ID:38652684; **Viatte**, **JAMA.2015:**REF2ID:38652680), and guided patient stratification (**Buch, Arth.Rheum.2018:**REF2ID:78240777)

Lupus (**Bruce**): The lupus group has used registry data and trials of carefully characterised patient groups to enhance outcomes and reduce disease activity, based on improved understanding of underlying disease mechanisms (**Briggs**, **Arth.Rheum.2016:**REF2ID:51322901) and disease presentation (**Bruce, Ann.Rheum.Dis.2014:**REF2ID:38655382); and through carefully targeted trials of novel therapies, particularly biologics (**Bruce**, **NEJM.2020:**REF2ID:164703773).

PsA (**Bowes**): In collaboration with CfDR have used the PSORT cohort to show PsA has a different genetic basis to psoriasis (**Bowes**, **Ann.Rheum.Dis.2015:**REF2ID:63640309), affecting psoriasis long-term outcomes (**Bluett, Nature.Comms.2015:**REF2ID:38652682) and management.

Future Research

We will build international leadership in five areas through linked programmes.

Genetics/Genomics: In collaboration with GMGMC we will align Versus Arthritis (£2m) Genetics and Genomics Centre activity with *Orozco*'s Wellcome SF programme developing functional

genomics/genome editing to identify causal gene signatures in musculoskeletal IMIDs, progressing their individual and shared molecular taxonomy.

Biorepository-based Research: BRC-funded Lupus Extended Autoimmune Phenotype Cohort, BSRBR-RA and NIHR IMID BioResource enable design and execution of experimental medicine, proof-of-concept studies, and trials at scale in selected patient subsets, focusing on shared molecular processes across different IMIDs.

Evidenced therapeutics: Our goal is "targeting the right drugs, to the right patients, at the right time" based on outcomes and data sets from our MRC Stratified Medicine Initiatives. Follow-on phase 2/3 studies will employ adaptive and Bayesian approaches to clinical trial design, thereby improving trial efficiency, enhancing our ability to treat relevant subsets effectively.

Optimising drug adherence: BRC MSK theme funding allows further programme development to optimise therapy adherence, using behavioural psychology and biofeedback interventions coupled with drug level testing, improving disease control across IMIDs.

Digital Epidemiology: underpins inflammatory/non-inflammatory joint disease research. With Centre for Epidemiology colleagues (*UoA2*) we will further develop methodological rigour for digital tools, wearables and routinely collected data in collaboration with UoM's big data and health informatics groups, using these leading-edge technologies to improve understanding of patient-reported outcomes and multimorbidity, facilitating person-centred care; and validated safety of novel IMID therapies.

1.6.8 CENTRE FOR DERMATOLOGICAL RESEARCH (CfDR: 11.55 FTE)

Background

CfDR's research has improved understanding and outcomes in skin disease management by applying basic research technologies to understand underlying pathogenesis and true burden. Close, long-standing collaborations with industry have enabled targeted clinical trials in: psoriasis; photodermatoses; and skin ageing (within Manchester Institute for Collaborative Research into Ageing [MICRA; 4.1]).

CfDR hosts the BRC Dermatology theme (£2.8m) and the world's largest pharmacovigilance register for psoriasis (BADBIR; 20,000 registrations).

Clinical research takes place in dedicated Dermatopharmacology and Photobiology Units in Salford Royal's GM Dermatology Centre (largest in England with 40 consultants).

Major Research Themes

Ultraviolet radiation biology and medicine (**Rhodes**): has uncovered: clinically important cellular (**O'Neill**, **Sci.Reports.2018**:REF2ID:157881800) and immunological changes (**Farrar**, **Clin.Translat.Imm.2020:**REF2ID:158447985) in UV damaged skin; the role of skin type in differential tissue and gene damage (**Rhodes, J.Inv.Derm.2018:**REF2ID:82375603), and the importance of active management of vitamin D prophylaxis in UK latitudes (**Farrar**, **Nutrients.2018:**REF2ID:84663907).

Psoriasis (**Griffiths, Warren**)**:** Has described the global impact of psoriasis (**Griffiths**, **BMJ.2020:** REF2ID:178908742), and heightened awareness of the comorbidities of psoriasis itself (**Young**, **J.Invest.Derm.2015:**REF2ID:38937348; **Kleyn**, **Br.J.Dermatol.2018:**REF2 ID:85216881) and psoriasis treatments (**Yiu**, **J.Invest.Derm.2018:**REF2ID:116756524).

Through clinical trials and registry data it has made a major contribution to the world-wide impact of novel psoriasis therapies (**Griffiths**, **Lancet.2015:**REF2ID:38793134) and their optimal use

(**Warren**, **J.Invest.Derm.2018:**REF2ID:63088344). It has introduced novel care pathways including educating and empowering patients through initiatives such as Psoriasis Shout Out.

Skin ageing (**Watson**): Linking with photobiology and employing FBMH's Core Laboratory Facilities (3.6) has defined key molecular (**Watson**, **Redox.Biol.2015:**REF2ID:38937920) and structural mechanisms (**Watson**, **Mech.Age.Develop.2016:**REF2ID:64766048) behind the appearance and mechanical function (**Sherratt**, **J.Pathol.2020:**REF2ID:177106532) of aged skin, informing development of novel topical therapies.

Future Research

CfDR's future research develops three existing and one new theme:

UV Radiation Effects. Research will investigate UV radiation "best balance for health" expanding Rhodes' UV/vitamin D sufficiency/deficiency (£450k) and Marais' melanomagenesis (£2.1m) studies.

Skin biology and ageing. **Watson's** Wallgreens-Boots-Alliance funded (£3.8m) skin homeostasis research, enriched by the Skin Proteome Study (**Sherratt** £1.5m), a ground-breaking bioinformatics-augmented systematic literature review, will uncover new understanding of skin disease and inform **Saunder's** Wellcome-funded skin inflammation work,

Psoriasis. PSORT (£7m) generated a collaborative which, employing at-scale examination of psoriasis subgroups, using the NIHR Bioresource and BADBIR, will feed into **Yiu's** NIHR-funded Fellowship investigating responses to and adverse effects of biologics; and BRC Dermatology Theme-funded multimorbidity research improving psoriasis sufferers' lives through: personalised medicine. With KCL, we will expand the COVID-19-psoriasis global registries to gain further insight into interplay between these two diseases.

Atopic dermatitis. Building on early basic science (**Arkwright**, **J.All.Clin.Immunol.2020:** REF2ID:178183460), **Saunders**' Wellcome funding (£950k), upcoming clinical trials of novel therapeutics, and participation in the eczema BADBIR-equivalent, A-STAR, we will bring atopic dermatitis into our discovery-to-translation research portfolio.

1.6.9 INFECTION (8.2 FTE)

Background

UoA1's research specifically focused on infection has been largely directed towards fungal infection. In 2020 we extended our research to include: SARS-COV inflammasome for stratification and outcome predictions; (1.6.5, 1.10); and antibiotic stewardship to combat resistance.

Major Research Themes

Aspergillus Research: UoA1 academics in the National Aspergillosis Centre (world's largest fungal respiratory research and treatment centre) have explored the wider epidemiology of aspergillosis (**Rautemaa-Richardson**, **Lancet.Inf.Dis.2018:**REF2ID:75966231), discovered novel mechanisms underlying the behaviour of aspergillus in-vivo (**Bertuzzi**, **PLOS.Pathogen.2014:**REF2ID:38652843; **Denning**, **Nature.Comms.2018:**REF2ID:82649733); and defined drug resistance mechanisms. (**Bromley**, **Nature.Comms.2020:** REF2ID:158591821). By working with industry partners NAC has developed, trialled and translated important monitoring tools (**Kosmidis**, **Antimicro.Agent.Chemo.2020:** REF2ID:178191103), and novel therapeutics, into clinical care, changing Aspergillosis management on a global scale (**Denning**, **REF3 Impact Case**)

Future Research

Bronchopulmonary Aspergillosis: affects >6m people worldwide. Invasive aspergillosis threatens cancer chemotherapy programmes, and solid organ/stem cell transplantation. **Bromley's** basic research on invasion (MRC £560k) and fungal genomics (Wellcome £770k) will inform novel anti-fungal strategies in developed and developing countries.

Antibiotic stewardship Management, combatting resistance: This will bring a second infection theme into the NW Lung Centre. The newly formed (2020) NIHR Centre for Precision Approaches to Combatting Antimicrobial Resistance (£4.4m) will use existing antibiotics better in individualised treatments. It will define patient-specific approaches to antibiotic stewardship by employing big data analytics on patient-derived metrics, infection biomarkers (**Dark** £1.8m; NIHR), and outcome data, to refine anti-bacterial prescribing.

TECHNOLOGY-BASED GROUPS

In collaboration with researchers in UoM's Faculty of Science and Engineering (FSE), we have built two Research Groups that address diagnosis and therapeutics through harnessing technological advances to IDSAI's powerful big data analytics.

1.6.10. BIOMARKER TECHNOLOGIES (BiomTech) (8.2 FTE)

Background

In 2013 MRC described a significant failure to translate MRC-funded biomarker discoveries into clinical products. BiomTech, was formed in response.

Major Research Themes

BiomTech has two discovery arms:

Manchester Centre for Cancer Biomarker Sciences (MCCBS: **Dive**). A CRUK Centre of Excellence (CRUK £3.5m; BRC £700k; AstraZeneca £11m) MCCBS has refined liquid biopsy assays and xenograft models for target validation (**Dive**, **Cancer.Discov.2016:** REF2ID:51171905), optimising patient stratification (**Brady**, **Nature.Med.2016:** REF2ID:51526225), and informing patient management across a spectrum of cancers.

Stoller Biomarker Discovery Centre (SBDC **Whetton**) £12.8m MRC infrastructure funding matched from SCIEX, Stoller Foundation and BRC. Housed in purpose-built facilities in Citylabs1.0, it is the largest discovery proteomics centre in Europe. It has undertaken key research informing: technology behind biomarker discovery (**Whetton**, **Nature.Protocol.2015:** REF2ID:39034142); patient stratification; and therapeutic advances (**Whetton**, **Bioinformatics.2020:**REF2ID:158123299); in cancer (**Whetton**, **J.Proteome.Res.2019:** REF2ID:158123315), inflammatory diseases and psychiatric disorders.

A single-point-of-contact translational pipeline.

Manchester Molecular Pathology Innovation Centre (MMPathIC **Freemont**) established by MRC/EPSRC (£2.9m), facilitates development and clinical translation for academic and industry biomarker discoveries, through: early health economic evaluation (with health economists [*Payne, Thompson, UoA2*] and health informatician [*Geifman, UoA2*]); partnering with appropriate clinicians; assisting with acquiring funding from grant funders and venture capitalists; and navigating testing and regulatory processes, to deliver market-ready products. Robust testing in real healthcare settings is enhanced by co-ordinated roll-out across GM's post-DevoManc landscape.

During REF2021 MMPathIC:

- Facilitated taking 14 new research-derived biomarkers into clinical use (e.g. gene-based brain tumour diagnostics, urinary metabolites of antihypertensives, sensitive methotrexate assay, early bladder cancer cytology diagnostic)
- Assisted seven companies from: UK: APIS Technologies (4.4), and SMEs Gelmetix, Chromition, DeepMed I/O), USA: Singulex, France: Kurma Diagnostics; Australia: Sienna Diagnostics; to identify market niches and commercialise products.

Specific examples: Assessed validated Singulex Ultrahigh sensitivity Troponin-I assay for myocardial injury, and diagnostic platform (**Freemont**); Supported Chromition in grant applications (SBRI, Innovate-UK) securing £2m funding for evaluation of novel multiplexed immunohistochemistry disclosing systems (**Freemont**); with EPSRC funding, patented and developed to clinical trial a graphene biosensor (patent: GB1809160.3) for lung disease breathomics (*Migliorato [UoA12]*);

MMPathIC was described at review by MRC's Stratified Medicine Group as "impressive and successful, has achieved cultural change".

Future Research

We will build on our technology base to drive the biomarker discovery essential for patient stratification and personalised medicine, creating opportunities for novel biomarker discovery-based projects (e.g. ID Liver started Q3 2020 £4.5m Innovate/Industry)

Advances in "omics" technology such as those pioneered by MCCBS, SBDC, Genetics and CfMR coupled to technological advances made in UoM Institutes (e.g. "wearables", nanoscale sensors) will generate unique opportunities to discover and clinically translate novel biomarkers through MMPathIC's adoption pipeline, enabled by HInM, leveraging resource through UoM's £2.4m Wellcome Institutional Translational Partnership, and £25m Pankhurst Institute (4.1).

1.6.11. REGENERATIVE MEDICINE (RegenMed 13 FTE)

Background

RegenMed is the clinically-focused arm of the cross-faculty Manchester Regenerative Medicine Network (91 academics from FBMH/FSE [REF2021 funding: £104m]).

RegenMed made basic mechanistic discoveries that feed in to the clinical use, alone or in combination, of a spectrum of technologies directed towards restoring tissue functionality, crossing disciplines, organs and diseases with the shared goal of technology-driven improvement in patient wellbeing.

Major Research Themes

Stem cell manipulation to restore tissue/organ structure and/or function e.g. myocardium (**Birket**, **Nature.Biotech.2015:**REF2ID:85187571), skeletal muscle (**Cossu**, **EMBO.Mol.Med.2015:**REF2ID:51514383 and **EMBO.Mol.Med.2015:**REF2ID:51514382), kidney (**Lennon**, **Stem.Cell.Rep.2018:**REF2ID:64334356), and brain (**Bigger**, **EMBO.Mol.Med.2020:** REF2ID:159841487).

Gene and biologic therapies. Bigger's research on enzyme replacement, now rolled out with industry partners, has completely changed the lives of children and young adults with mucopolysaccharidosis (**Bigger**, REF3 impact case);

Understanding and managing the disease "niche" (physical, cellular and chemical disease environment) employing technologies including transcriptomics (**Herrick**, **J.Pathol.2018:**

REF2ID:76553857), mechanotransduction (**Richardson**, **Nature.Comms.2019:** REF2ID:131625790) and clock biology (**Hoyland**, **Ann.Rheum.Dis.2017:**REF2ID:50943914).

Advanced biomaterials: With Biomaterials (UoA12) and, latterly, Royce Institute, MIB, and the Graphene Institute, has generated purpose-engineered clinically valuable matrices and scaffolds by designing (**Freemont**, **Soft.Matter.2016:**REF2ID:50401988), clinically trialing ("Polynerve": First-in-man NIHR-funded phase-I trial of a synthetic polymer nerve conduit in patients with digital nerve injury), and safety testing (**Pennock**, **ACS.Nano.2020:** REF2ID:174502187) completely novel biomaterials.

Tissue engineering; using cells, biologics and scaffold to generate new tissues in-vivo (**Biant**, **Health.Technol.Assess.2017:**REF2ID:64760718).

Future Research

Novel niche-specific biomaterials: Recent formation of the >£200m Henry Royce Institute (4.1.2) will bring closer collaboration between RegenMed academics and engineers, delivering novel biomaterials for augmenting, replacing and regenerating failing organs. Commercialisation will be through the £25m Pankhurst Institute guided by upscaling experience from "Polynerve" and Gelmetix (UoM spin-out 2012)

Regulating the disease environment: Through MaRMN we will cross-fertilise innovative methods of regulating disease niches to restore niche biology or slow/prevent progress of diseases, building on our experience of: nanodelivery of biologics (vs Arthritis £1.2m), gene therapy (MRC £600k), stem cell delivery (MRC £1.5m), and model systems (EPSRC £700k) to translate discovery into therapeutics.

Innovation in treating genetic disease: **Bigger's** pioneering mucopolysaccharidosis enzyme replacement and gene therapy is a paradigm for other inherited disorders. Already translating into muscular dystrophies, and renal disorders, we will expand our activities into other systems.

1.6.12. MEDICAL HUMANITIES (MedHum: 12 FTE)

Background

MedHum exemplifies how diversification of research can impact direction and delivery of clinical medicine and instil understanding of the value and critical interpretation of clinical research.

Major Research Themes

Centre for History of Science, Technology and Medicine (CHSTM). UK's largest research group engaged with integrated historical studies of medicine, science and technology. CHSTM enhances UoA1's research through contextualising clinical and experimental medicine within wider historical, social, political and global contexts. CHSTM is a Wellcome Cluster of Excellence. CHSTM has overlapping interests with academics returned in History (UoA28).

CHSTM academics have:

Changed understanding of how historical studies of healthcare can be undertaken, and data analysed and used to change future delivery.

- Employed text mining to enrich data retrieval/analysis from archival material (**Timmerman**, **PLoS.One.2016** REF2ID:156081072)
- Award winning Public Patient Involvement (PPI) research:
  - Examined the NHS' history (**Snow's** ongoing online project "NHS@70", created first oral history of the NHS, and second largest collection in British Library Sound Archive, stimulating the NHS to use historical evidence when developing policy and practice)

- Defined and the role of migration in shaping and enhancing NHS workforce (**Snow Doctors Beyond Borders 2016,** REF2ID:64687762).

- Analysed how industry shaped healthcare and legislation (**Greco Soc.Sci.Med.2015:** REF2ID:134063706)

Contextualised forensic science and criminology (**Burney, Wilson**, Book: **"Murder and the Making of English CSI", 2016:**REF2ID:156080601 (For work in this field Burney was awarded a Guggenheim Fellowship [2019])

Explored the history, value and ethics behind animal-based research, shaping future debate and policy (**Kirk**, **Sci.Technol.Hum.Values.2017:**REF2ID:62519735; **Wilson**, Book: **Making of British Bioethics 2014:**REF2ID:46405056)

Evaluated and critiqued external events that have changed science, medicine and health; e.g. climate change (**Jankovic Weather.Climate.Society.2017:**REF2ID:50935639)

Research within Medical Education (RME) uses its own research and that of others to develop student understanding of designing and analysing healthcare research using qualitative and quantitative techniques. RME academics have:

- Altered understanding of psychological and physical impacts of healthcare environments on healthcare workers and students (**Hart**, **Med.Education.2014:**REF2ID:38793691) and measured and evaluated the impact of health education on healthcare delivery in low-income countries (**Byrne-Davis**, **J.Nurs.Ed.Pract.2015:**REF2ID:38657045).
- Have influenced UoM's medical students to initiate and undertake their own research:
  - Manchester Medical Research Student Society won Academy of Medical Sciences Inspire Awards in 2014, 2018 and 2020;
  - Manchester's Madagascar Medical Expeditions (MADEX, founded 2014 and run by medical students [and now graduated MADEX students]) through annual expeditions maintains ongoing research programmes studying Malagasy children living with schistosomiasis. For his research, founder Stephen Spencer was awarded a SEE's Rivers Foundation Explorer Award and RCP Turner-Warwick lectureship (2019 Yearbook)

Future Research

CHSTM: The societal and political background to NHS delivery has been brought into sharp focus by Covid-19. There will be lessons learnt to improve healthcare delivery that CHSTM researchers are uniquely placed to contextualise. This research potential was recently (8/20) spotlighted by **Snow's** team's award of £1m AHRC grant "NHS voices of Covid-19". They, in partnership with the NHS, patients, wider public, and British Library, will examine: how the pandemic has altered public attitudes to the NHS; what "care" means; and who provides "care".

RME: COVID management and outcomes also emphasise the significance to clinicians of evidenced health policy and healthcare provision and delivery, further consolidating **Byrne-Davis** and **Hart's** research (£400k) illustrating the need to empower clinicians to objectively evaluate clinical data using a breadth of techniques.

1.7 Animal Research: Embracing 3Rs Principles

Kirk (MedHum) researches the contextual and moral landscape of animal research from within Wellcome's Animal Research Nexus: "Changing Constitutions of Science, Health and Welfare".

All UoA1 researchers work within an award-winning animal research environment. In 2016 UoM's animal research website, which publishes ethics committee minutes, welfare policies, governance information, infographics on number/species of animals, and studies on medical advances arising

from animal and 3Rs research, received an Openness Award from Understanding Animal Research (UAR), the judges concluding: "*Information is accessible and appropriate to a wide range of audiences, layered and easy to navigate. Material was extensive and of an excellent standard, and infographic and Q&A sections particularly impressive*."

The website contributes to UoM's engagement activities with local schools, media, patients and the public that in 2018 received the National Centre for Public Engagement Gold Watermark Award. In 2019, UoM was in UAR's top 10 organisations for animal research.

1.8 Research Openness

We work within UoM's Open Research Environment (REF5a.2v): see subsections: 1.6.12, 1.7 (animal research); 3.9 (Library-based researcher training); 2.4.4 (medical education): 4.3 (PPI)

UoM makes **Open Access (OA)** funds available from UKRI (£1.2m) and Wellcome (£170k) block grants and UoM's OA Fund (£300k). The Library has arranged OA memberships and agreements with several publishers securing reduced or waived APCs.

The University-wide Open Research Working Group, arranges training events and workshops around Open and Reproducible Research, and feeds directly into the UK Reproducibility Network

1.9 Best Research Practice

Contributing to, and managing research, comes with responsibility to ensure its probity, quality and ethical base. UoM governs standards, fostering the highest levels of research integrity within a research culture that values knowledge-creation for: its own sake; potential benefits to humankind; and enrichment of higher learning (REF5a.2v).

UoA1's research governance is remitted by UoM's Research Governance Team (RGT) which also supports researchers undertaking NHS-based research.

Acting for UoM as Research Governance Sponsor, RGT ensures researchers and UoM meet the UK Policy Framework for Health and Social Care Research's requirements. RGT works closely with individual researchers, providing practical advice and sign-posts researchers navigating NHS research regulations.

Within UoM, RGT works with the Research Governance, Ethics and Integrity Team ensuring alignment with the principles in Universities UK's Concordat to Support Research Integrity.

1.10 Research Response to Covid-19

55% of UoA1 researchers are clinicians. Whilst the Covid-19 pandemic pressured clinical services, it brought opportunities to demonstrate the agility and innate collaboration in our research ecosystem when faced with major healthcare issues. Examples include:

- National Medicines Discovery Catapult at Alderley Park became one of three national "Lighthouse" Covid mega-testing laboratories. CRUK-MI scientists accelerated its launch by volunteering genomics skills. **Klapper** (Professor of Clinical Virology) is an advisor.
- 3D printing of PPE (collaboration with School of Architecture [**Clayton**])
- Formation of "Covid-19 Rapid Response Research Group" (**Bruce** Chair): brokered by BRC, channelled research activity of scientists, clinical academics and MAHSC clinicians towards understanding the disease, and developing reliable tests and treatments. Key outputs include:

- **Hussell:** Longitudinal immune profiling reveals key myeloid signatures associated with COVID-19 **Science.Immunol.2020:**REF2ID:176556622
- **Felton**: Dexamethasone in hospitalized patients with Covid-19. **NEJM.2020:** REF2ID:178170381
- **Klapper:** International external quality assessment for SARS-CoV-2 molecular detection and laboratory preparedness during Covid-19 **Euro.Surveill.2020:**REF2ID:178171255

- Accelerated diagnosis and testing (**Body** co-PI CONDOR, £1.3m NIHR) national research programme, evaluating coronavirus tests in clinical settings.
- **Snow** (CHSTM), awarded £1m (AHRC) to explore how patients' attitudes towards the NHS have been changed by the pandemic
- UK Coronavirus Immunology Consortium (**Hussell**, Theme Lead) awarded £6.5m from UKRI/NIHR investigating immune system-SARS-CoV-2 interactions.
- Following an appeal, £500k philanthropic donations received by FBMH for Covid-related research funds 10 pilot projects.
- GM Mass Testing Expert Group (MTEG) (**Bruce** co-Chair) includes UoA1 academics and NHS consultants/GPs to inform GMHSCP's roll-out of testing technologies/programmes.
- Redmond (Emeritus Professor of International Emergency Medicine, Founder of UK-MED) led the medical team staffing Manchester's 750 bed Nightingale Hospital
- Our BRC through **Hanley** is part of the MRC/NIHR Post-hospitalisation COVID-19 study (£8.4m Leicester) and UK Interstitial Lung Disease Post-COVID19 Fibrosis (MRC £2.4m Nottingham) consortia, investigating the debilitating effects of "Long Covid".

Publications. Within 12 weeks of first lockdown, we had contributed to improved sector understanding of Covid-19's healthcare impacts. 32 publications included: 4 basic science (Covid-19-induced inflammasome); 10 new descriptions of Covid-19 presentations in specific disease settings; and 18 management guidelines (**Papadopoulos J.All.Clin.Immunol.2020:** REF2ID:178171547), all with national and/or international collaborators, assisting clinicians safely manage Covid-19 in contexts as diverse as cardiac catheter laboratories, allergy clinics, childhood asthma , IMIDs, psoriasis and lung cancer.

UoA1 published a further 59 papers on Covid-19-related issues from July-December.

2. People

2.1 Staffing Strategy

UoA1 academics work within a supportive, structured, people-focused environment defined by UoM (REF5a.3). Briefly:

2.1.1 Recruitment, development, and retention: During REF2021 we have recruited 129 new staff through external appointments and targeted fellowships, and appointment to internal fellowships and the NIHR ACL scheme. We fully encompass the Researcher Development Concordat (UoM holds the EU HR Excellence in Research badge, retained since 2011), continuously updated by staff input through research staff networks and biennial Staff Survey.

2.1.2 Equality and Diversity: UoA1 recruits the best candidates based on merit.

UoM has the bronze Race Equality Charter Mark, and is signatory to the Disability Confident Scheme and Stonewall Diversity Champions Programme. In FBMH Athena Swan and Project JUNO dedicated roles are embedded across research management.

SBS/SMS have Athena Swan silver status (2018), the assessors reporting: "*The submission demonstrated commitment and engagement in the process from all levels…. The panel considered it to be a clear and reflective submission…it was clear how staff were communicated with throughout the process of restructuring. Good use was made of the "Further Information" section to discuss…support available to staff and students following the Paterson fire".*

There are flexible return-to-work programmes for those returning from long-term parental and sickness leave, including tapered return and short-term reduction in teaching activities.

Of our 12 Research Group Leads five are women. This positive change from REF2014 (no female leads) is part of an upward trajectory, further evidenced by increasingly gender-balanced Chair promotions (13% female REF2014 to 45% REF2021). 11% of academics have a BAME background; double that at REF2014 (5.5%). Those with reported physical disabilities increased from 1 to 2.

2.1.3 Continuous staff development enhances careers through: the "Researcher Development Framework", guiding career development and training; annual Performance and Development Review through face-to-face interview with trained principal investigators; >1000 comprehensive training programmes; "Investing in Success" (funds innovative career development); and "Inspiring Leaders Programme".

2.1.4 Recognition and reward come through the annual promotions processes. Staff are supported in building promotion cases through workshops, School/Divisional promotion champions, and shared online experiences, leading to year-on-year increases in promotion success (e.g. for UoA1 between 2015 and 2019 successful applicants increased from 81% to 88%). Critically the process accommodates career-breaks and part-time working.

2.1.5 Careers of researchers on short/fixed-term contracts. Including our 22 ACLs, 48 Research Fellows and 115 postdoctoral researchers, researchers on short/fixed term are supported by UoM's sector-leading, open-ended contract policy carrying additional benefits after 4yrs continuous service, including: 3 months' salary beyond statutory notice periods; development opportunities (additional training, job shadowing); 6mths redeployment, bridging gaps in funding; Extended Access Policy (applauded in feedback on UoM's HR Excellence in Research award renewal 2017) providing 12mths access to email and e-resources after contract termination.

2.2. Staff Support and Development Structures

Institution-wide support (aquamarine in Figure 3) includes: staff and student mentorship programmes; Staff Learning and Development Unit; Award-winning University Careers Service; Library-based researcher information including researcher profiles and key altmetric data.

In addition FBMH has responsibility for staff development, supporting/mentoring at all career stages through its Researcher Development Continuum (RDC). It adds to the University programmes support tailored to the specific needs of its staff. Key to delivering this are specialised Support Services including:

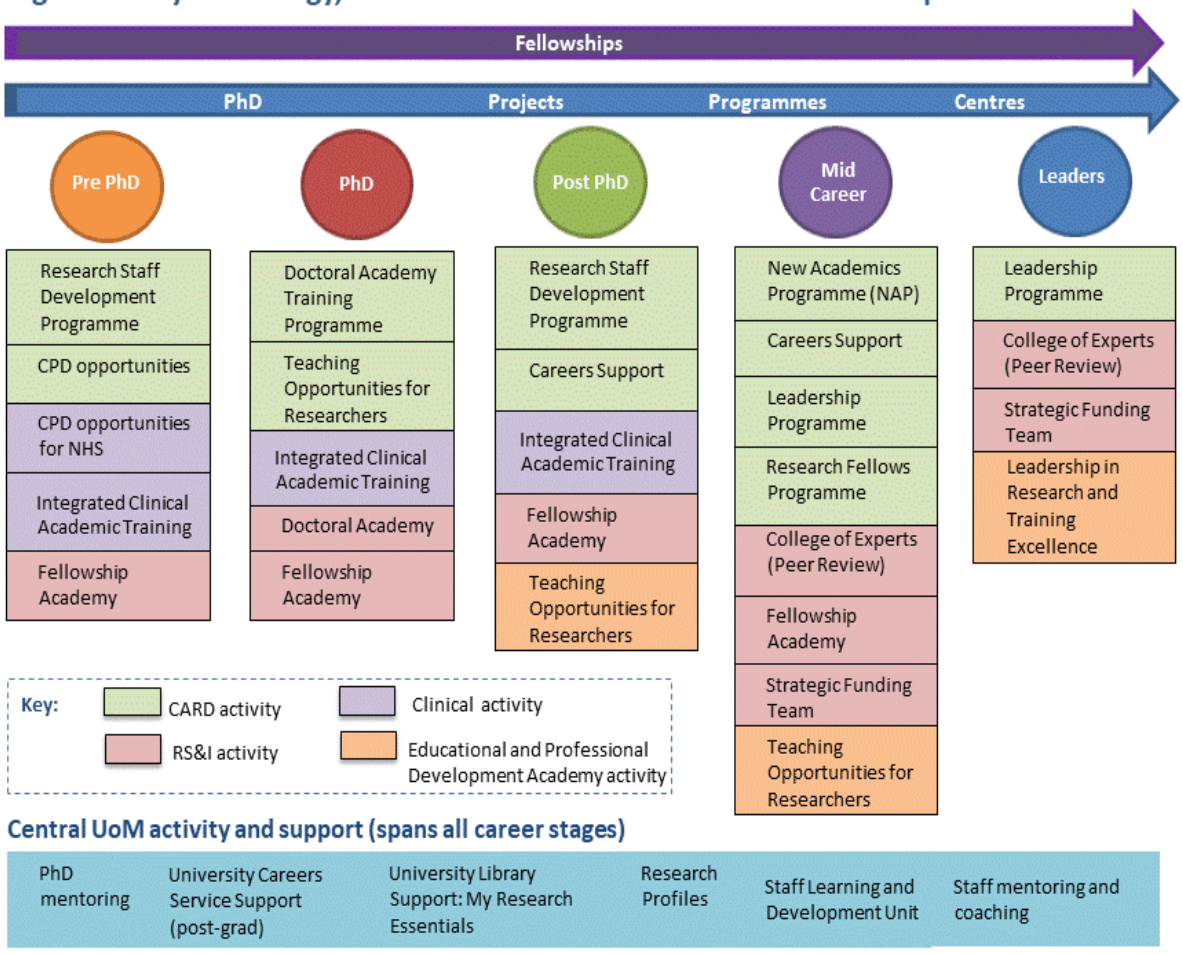
- **Research Strategy and Innovation Team** (RS&I, 3.4)
- **Centre for Academic Researcher Development** (CARD)

- Three teams support research students and ECRs, **Doctoral Academy** (DA), **Fellowship Academy** (FA): and **Integrated Clinical Academic Training (**ICAT**) Team.**

2.3. Research Development Continuum RDC)

RDC is the overarching support framework for all UoA1 researchers from students to senior academics. It offers different support programmes specifically designed to take into account the seniority of individual researchers and their immediate and future needs. Figure 4 shows when and how specialist support is offered and how it complements UoM-wide support. FBMH's Researcher Development Group co-ordinates development provision, ensuring equality of access and opportunity delivered through Schools/Divisions and CARD.

Fig. 4 Faculty of Biology, Medicine and Health – Researcher Development Continuum



CARD delivers coaching and mentoring to UoA1 researchers, students and honorary staff, enabling personalised professional development. It includes:

- **New Academics Programme (NAP)** for all new staff below Professor. Accredited by Advance-HE, NAP is flexible, dovetailing with academics' career aspirations and prior experience, supporting research, teaching, learning and leadership. Successful completion leads to HEA Fellowship.
- **Faculty Leadership Programme**. A two year programme promoting exceptional academic leadership through example and education, enhancing research capability, teaching and learning best practice, leadership and management capacity, personal effectiveness, and strategic career management.

- With DA, provides **training support at key stages of postgraduate degrees** ensuring timely completion, and generic skills development.
- **Researchers Development Programme** provides intermediate level training maximising outputs and impact, developing transferable skills and independent research careers, proactive career management, CV development, interview skills, and academic/non-academic career planning.
- Administering UoA1's **Academic/Research Staff mentoring programme**, enhancing performance and fulfilling potential for individual researchers through 12 months mentoring.
- Convening **FBMH's Research Staff Representatives Forum** a network of 30+ Research Staff Representatives who promote the interests of 1060+ FBMH researchers.

2.4. Developing Tomorrow's Researchers

We place particular emphasis on recruitment and retention for the future, through three specialist support units.

2.4.1 ICAT (Lennon)

ICAT works closely with NIHR's Trainees' Coordinating Centre, overseeing 'Integrated Academic Training'. ICAT is currently supporting 85 ACFs/ACLs.

Full monitoring of career progression is conducted with NW Deanery. Since inception, 65% of ACFs have progressed to PhD programmes or take up ACL posts compared with a reported 47% nationally (2015 data).

With Bristol, Leeds and Newcastle, ICAT is undertaking systematic evidence review to understand why women are lost from clinical research careers.

2.4.2 Fellowship Academy (Hanley, White)

FA supports researchers to obtain external fellowships. From 2016-2019 externally funded "junior" fellowships increased from 7 to 13/year. Researchers access: "CV clinics", bespoke advice and peer review, mock interviews, pump-prime funding, and Institutional Fellowship awards including: ECR Development Award; Dean's Prize for Clinicians; and Presidential Fellowships.

Post-award, fellows are closely mentored within Divisions, clinical Fellows by at least one clinical academic from her/his Research Group. Career guidance is provided through dialogue with senior colleagues, formalised Faculty-level objective setting and mid-term review.

FA manages the "Fellows Network" providing peer support, networking and collaboration opportunities.

2.4.3 Doctoral Academy

DA, managed at Divisional level, ensures: students have comprehensive academic and pastoral support; provides online training (particularly attractive to part-time students) in core skills (£5m UoM funding); promotes wellbeing initiatives; manages successful "PGR Parents' and Partners" groups, providing peer support for students and their families (particularly appreciated by international students); and "Student Representative Network", promoting integration with peers and key postgraduate staff; offers conference and society membership funding; actively supports outstanding undergraduates to enter masters and doctoral programmes; hosts public engagement activities and external speakers, enhancing student networking.

2.4.4 Research Students

Medical Undergraduates (UG): A research ethos is embedded in UoM's medical undergraduates (~2400 across all years) from day one. 10% of the programme is timetabled for "skill-driven research", students learning generic research skills (critiquing publications, producing posters etc.) whilst engaged on research projects with academics.

Annually: ~100 students present at major conferences; ~20 publish in Medline-indexed journals, ~170 students intercalate (choosing from a pool of 39 Bachelor/Masters level programmes, offering students new skills and a robust foundation for academic careers); and ~25 take up Academic Foundation Posts.

2019/2020 awards from CRUK and the Kennedy Foundation will fund five innovative **MB-PhD** studentships/year starting in 2021, supporting aspiring clinician scientists to obtain PhDs in cancer or musculoskeletal/inflammatory diseases between years 3-4 of their UG studies.

Postgraduate Taught Students. We manage and/or deliver teaching in 22 MSc, MRes and MPhil programmes. In PRES 2019 our students' overall satisfaction was 82.4% up 2.9% from 2017.

Postgraduate Research (PGR) Students: Within DA's framework, from 2014-2020, we supervised 736 doctoral students to successful degree award (interdisciplinary supervision equates to our being credited with 549.62FTE). We currently supervise 998 doctoral students.

During REF2021 we have been awarded new, externally funded programmes supporting 35 students/year:

- Multidisciplinary 4 year PhD programmes: **Wellcome**: 4ward North Clinical PhD Academy; Immune-matrix interactions: **EPSRC-funded DTCs**: Tissue Repair and Regeneration; Advanced Biomedical Materials; **BHF:** Cardiovascular Sciences: **BRC**: Trans-discipline studentships
- **DClinSci** programme managed through Manchester Academy for Healthcare Scientist Education (MAHSE). Launched in 2016, MAHSE's Higher Specialist Scientist Training (HSST) Programme includes five-year workplace-based training, incorporates a Doctorate in Clinical Sciences, and, where appropriate, Royal College qualifications. Currently there are 81 UoA1-supervised students.

Recruitment: Standardised selection processes include project and supervisory team assessment by DA, and panel interviews. We place particular importance on meeting healthcare professionals' expectations and needs.

Recognising challenges in recruiting non-medical graduates into clinical research our BRC and ARC support 6-week 'taster' sessions for NHS professionals to experience research environments. Of the first 19 (2018-20), six are currently seeking funding opportunities.

Student progress and monitoring: PGR students undertake online progression monitoring, providing clarity on critical milestones, and record evidence of engagement with training, progress and personal development. This ensures continual supervisory feedback, and timely thesis submission and degree completion.

Experience and Careers: UoA1 students are advised by UoM's award-winning Career Service, specialising in bespoke careers training, CV writing workshops and networking events with industry.

Through DA, PGR students, assess performance against publication quality (not number), give presentations at pan-School Research Showcases and obtain grounding in disseminating and communicating research to the wider community.

"Student of the Year" awards, give peer recognition of research excellence.

Professional Training: We play key roles in discipline-specific professional postgraduate training and delivery of key national clinical education programmes (4.8)

2.4.5. Early career researchers (ECRs)

UoA1 ECRs' career progression is facilitated through: NAP; CARD; supervision; mentorship; and reduced teaching/management responsibilities for 4yrs, ensuring a sound research base and clear direction. Returning 39 ECRs (17% of eligible staff) reflects the vitality of our research environment.

2.5 Metrics of Recruitment and Retention Success

Key metrics evidence the success of our staffing strategy over REF2021 in attracting and retaining quality researchers. For instance:

- External esteem (4.8) (20 prestigious awards [FRS, FMedSci, OBEs, NIHR-SIs); 46 visiting professorships, 101 grant panel members, six presidents of International Societies)
- Research income: (13 new externally funded research centres; grant expenditure/year/FTE increased 19%);
- 114 external Fellowships/personal Awards (2.9);
- ECR recruitment (17% of returned academics);
- Research driving change in hospital/community healthcare delivery. (Based on our clinical research, during REF2021, NHS/NIHR has established and funds six new integrated research and treatment centres (1.2)
- Output quality (examples in 1.6.1-1.6.12).

In the Times Higher Education (THE) Sustainable Development Goals (SDG) Impact rankings 2020, for SDG3: Good Health and Well-being measures UoM ranked 26th globally and 3rd in UK.

2.6 Integration between clinical and basic scientists

The number of clinically qualified and basic scientists is balanced across Research Groups optimising complementary skill sets. In UoA1 55% of researchers are clinical scientists and 45% basic scientists.

2.7 Consultancy

Academics may undertake up to 10% of their contracted time on consultancy duties, allowing them to increase research activity through interactions with industry partners (4.4) and University spin-outs (4.5). There has been a 30% increase in industry funding/FTE/year since REF2014, and between REF2014 and REF2021 an increase in filed patents from 16 to 102 and licence agreements from 6 to 54.

2.8 Recruitment during REF2021

21% of UoA1 researchers have been external appointments, either directly to senior academic posts (senior lecturer and above), or targeted prestigious Fellowships (included in 2.9)

Senior External Appointments into UoA1:

Chair: **Bristow***:* Director MCRC (Toronto University/Princess Margaret Cancer Centre [PMCC] 2017); **Burnet***:* Proton Clinical Oncology (Addenbrookes 2018); **Kirkby***:* Richard Rose Chair in Proton Therapy Physics (Surrey University 2015); **Morris***:* Statistical Genetics (Liverpool University 2020); **Lord:** Dean, FBMH, Vice President, UoM. (Kings College London 2019); **Papadopoulos**: Clinical Allergy (Athens University 2014); **Springer:** Director CRUK Drug Discovery Unit (ICR 2017); **Tomaszewski:** Molecular Cardiology (Leicester University 2017); **Van Herk:** Radiotherapy Physics (Netherlands Cancer Institute 2015); **Wedge***:* Cancer Genetics (Oxford University 2020)

Reader: **Biant:** Clinical Regenerative Medicine (Edinburgh 2017)

Senior Lecturer: **Aznar:** Radiotherapy (Niels Bohr Institute, Copenhagen 2017); *Blaikley*: Respiratory medicine (Toronto University 2014); **Barriuso***:* (Salamanca 2019); *Cook; (*PMCC 2015); **Lindsay** (Roussy Institute, France 2017)*;* **Mcnamara:** (PMCC 2014): Clinical Experimental Oncology; **Daniels:** Cardiology (Oxford University 2019)

2.9: External personal awards made during REF2021

Senior Research Awards

- **BHF Chairs**: Eisner; Keavney (£2.5m)
- **BHF Senior Research Fellow**: Trafford (£1.1m)
- **MRC Clinician Scientist:** Blaikley (previously Wellcome Fellow) (£950k)
- **Wellcome Senior Fellows**: Lennon; Orozco (£3.2m)
- **Wellcome Investigator Awards in Science:** Hussell, Smith (£3.1m)
- **Wellcome Senior Investigator:** Kirk (£900k)
- **NIHR Senior Investigators:** Barton; Bruce; Illidge, Lord, Smith; (£380k)
- **CRUK/NIHR Advanced Clinician Scientist Fellow**. O'Connor (previously CRUK CSF) (£1.1m)
- **Bloodwise Clinical Scientist Fellow:** Wiseman (£500k)
- **NIHR Advanced Fellowship:** Crosbie (from NIHR CSF) (£690k)
- **NIHR Clinician Scientist Fellowships:** Heazell; Horsley; Kirwan; Miller; Myers; Parry-Jones; Stivaros (£8.7m)
- **ERC Advanced Award:** Myers (£1.8m)

Intermediate Research Fellows

- **Breast Cancer Now**: Ucar (£420k)
- **BHF**: Cottrell; D'Souza; Morris; Pinali (£2.6m)
- **Wellcome:** Viros ((£490k)

Research Fellowships

- **MRC:** Al-Janabi, Athwal; Bluett; Butler; Clark, Dilworth; Dyball, Goenka; Gwinnutt; Hunter; Iestyn; Jalali; Kitchen; Martin; Ormesher; Pearmain: Reid; Rodziewicz, Ryan; Rutkowski, Shuttleworth; Taylor; Worton, Xu. (£12.2m)
- **BBSRC**: Konkel; Schmidt; Shaw; Swift (£1.9m)
- **UKRI**
    - **Rutherford Fellow**: Whitfield (£210k)

- **Future Leaders**: Fustin; Krasovec; (£1.8m)
- **Wellcome**: Fu; Penny; Sankar; Stefaniak; Su; Wan (Total: £8.2m)
  - **Sir Henry Wellcome**: Miller
  - **Sir Henry Dale**: Hepworth; Lopez-Castejon; Lovegrove; Mann; Saunders; Woolner
  - **Humanities and Social Science:** Greco
- **CRUK:** O'Connor; (£380k)
- **EMBO:** Bonavita (£120k)
- **Leverhulme:** Burney (£55k)
- **BHF**: Ainsle; Denham; Hutchings; Mahadevan; Morris; Pius; Robinson; Taylor; Venetucci; (£5.7m)
- **Versus Arthritis**: Gibbs; Lee; Martin; Oldroyd; Sampath; (£1.2m)
- **NIHR :** Cook; Bromley; Briggs; Body; Mahoney; Watson; Yiu; Aggarawal; Hays; Morley; Singh (£8.1m)
- **Marie Curie:** Kondowe; Largeot (£380k)
- **Others**: Roberts (Kidney Research UK); Ellingford (HEE); Higgins (Action Research); Durrington (Asthma UK); Keenan (Fulbright Fight-for-sight); Torres-Ayuso (Ramon Arecas Foundation); Barriuso (ENETS); Valpione (Harry Lloyd); Kitson (Wellbeing of Women); Parry-Jones (Stroke Association) (£3.7m)
- **Kay Kendall Leukaemia Fund**: Williams; Romero-Camerero (£310k)

Destinations of award holders

During REF2021:

- All academics holding “senior” research awards, are returned in UoA1.
- Of 49 Research Fellows completing in period, 6 hold higher fellowships in UoA1, 25 are baseline-funded UoA1 researchers and two in UoA2; 3 hold research positions outside UK, 15 hold clinical NHS positions.

2.10. Category C staff and MAHSC Professors

Close collaboration with NHS colleagues optimises clinical impact. NHS staff are offered honorary contracts for significant contributions to education or research (In clinical medical specialties this exceeds 2,000) and we support through partnership clinicians wishing to adopt a research career track through MRC Clinical Academic Research Partnerships (e.g. Clair Higham: Bone Toxicity following Pelvic Radiotherapy: understanding, predicting and preventing radiotherapy related insufficiency fractures; 10/2019-09/2022)

Through the flagship “MAHSC Professors” scheme, FBMH appoints NHS consultants with exceptional collaborative research track records and international recognition for clinical leadership and innovation, to MAHSC Professorships, with honorary chair status. In addition to 33 MAHSC Professors already researching within UoA1’s Research Groups, 28 new UoA1-associated MAHSC Professors were appointed during REF2021. **Cancer:** Bloor; Brennan; Cowan; Crellin; Handley; MacKay; Mansoor; O’Dwyer; O’Reilly; Sangar; Saunders; Shackley; Wardley; **CVS**: Bowling; Ventateswaran; Vohra; **DBM:** Banerjee; Mughal; **IIR:** Bentley; Booton; Jones; Leonard; Limdi; Poulton; Ustianowski; **RegenMed**: Shah; **BiomTech**: Keevil; Kelsey. Although not included directly in our return, their contribution is evidenced through our REF2 and REF3 outputs.

3. Income, infrastructure and facilities

3.1. Grant Expenditure

During REF2021 UoA1's REF-Eligible researchers increased from 215.09FTE to 222.06FTE whilst REF4b/REF4c expenditure increased by 19%/FTE/year

Overall expenditure by source:

Research Councils: £47m

Research Charities: £238m

UK Government: £57m

EU Government: £15m

All Industry: £60m

Other: £4.4m

In-kind research income (REF4c): £36m

3.2 Significant Externally Funded Research (all funding given as award values)

3.2.1. New Externally Funded Research Centres Established 2014-2020

- NIHR Manchester BRC *(***Bruce***:* £28m). UoA1 research is supported by all seven Disease/System Themes (Musculoskeletal, Cancer Precision Medicine, Hearing Health, Respiratory, Advanced Radiotherapy, Dermatology, Cancer Prevention and Early Detection), 2 of 3 cross-cutting themes (Biomarker Platforms, Rapid Translational Incubator) and Patient-Public Involvement.
- CRUK Major Cancer Centre *(***Marais, Bristow** £35m*)*
- Movember FASTMAN Prostate Cancer Centre of Excellence. (**Marais, Bristow, Clarke** [with Belfast] £6.5m)
- CRUK Lung Cancer Centre of Excellence *(***Dive** [with UCL] £7.5m)
- CRUK Radiotherapy Centre of Excellence (**Illidge** £16.5m*)*
- CRUK Cancer Biomarker Centre (**Dive** £15m)
- BHF Manchester Centre for Heart Magnetic Resonance Research (BCMRR) *(***Miller, Naish** £3.1m*)*
- NIHR Centre for Precision Approaches to Combatting Antimicrobial Resistance (**Felton** £4.4m)
- Versus Arthritis Centre for Genetics & Genomics *(***Barton** £2m*)*
- Stoller Biomarker Discovery Centre: *(***Whetton** £16m [£12.8m MRC]*)*
- Manchester MRC/EPSRC Molecular Pathology Innovation Centre (**Freemont** £2.9m*)*
- Proton Beam Research Centre (**Kirkby** £6m)
- Innovate UK TSB: iMATCH: Innovate Manchester Advanced Therapies Centre Hub (**Illidge** £1.2m)

3.2.2: Existing Centres re-funded in REF period through infrastructure and grants

- CRUK Manchester Institute (**Marais** £40m)
- Wellcome Centre for Cell-Matrix Research (**Kadler** UoA5 £5m). Infrastructure supports UoA1's RegenMed and Cancer Tumour Microenvironment academics (£7.5m grants).
- Maternal and Fetal Health Research Centre (**Heazell** Tommy's £2m; £8.5m grants)
- KNHCBE: Lineage of Pharaonic Egyptians (**Drosou** £1.1m philanthropic donation)
- Centre for History of Science Technology and Medicine (**Snow** £3.6m grants)
- Manchester Collaborative Centre for Inflammation Research (**Hussell** £5.1m grants)
- Centre for Musculoskeletal Research (**Barton** BRC £4.5m, £23.5m grants)
- Centre for Dermatology Research (**Griffiths** BRC £2.8m, £7.5m grants)

3.2.3 Underpinning Grant Awards during REF2021 by Research Group:

This section collates major support grants (Centre and Programme Grants, fellowships and grants >£500k), to evidence where research areas funders and their peer reviewers perceive we generate impact. (N.B: examples of large collaborative grants reported separately: 4.6.2)

Cancer

- Discovery Science: £35.1m (CRUK, Wellcome, EU);
- Experimental Cancer Medicine: £10.9m (CRUK, EU, Research Charites [RCs], Industry);
- Prevention & early detection: £7.9m (CRUK, NIHR, RCs);
- Radiotherapy-related research (excluding proton therapy): £22m (CRUK, NIHR, EU);
- Tumour microenvironment: £3.5m (CRUK);
- Targeted and Immuno-oncology: £18.4m (CRUK, NIHR, Innovate UK, Wellcome);
- Clinical Oncology: £31.1m (CRUK, NIHR, RCs, Industry)
- Proton therapy: £16m (EPSRC, CRUK, EU, RCs);
- CRUK Clinical Academic Training Programme Award. £6.5m;

Cardiovascular Sciences

- Integrative cardiac physiology: £3.5m (BHF, MRC);
- Genetics of cardiovascular disease: £1.6m (BHF);
- Micro- and macro-vascular disease: £2.8m (BHF, Research Charities);
- Clinical innovations: £4.7m (BHF, NIHR, MRC);
- Equalising opportunities, MRC/DFID African Research Leader Award BHF: £750k; Expanding the workforce: £1m (BHF Accelerator Award);
- Cardiac Imaging £3.1m (BHF, NIHR, MRC, RCs);
- BHF PhD studentship programme £2.6m (BHF);
- Funding includes two BHF and one MRC programme grants

Developmental Biology and Medicine

- Tommy's Centre for Maternal and Fetal Health £11.4m (Tommy's, MRC, NIHR, RCs, EU, BHF);
- Paediatric Growth and Development. £1.1m (MRC, NIHR);
- Developmental Haematopoiesis £1.2m (CRUK);
- Human Organogenesis. £1.75m (MRC, Innovate UK)

Genetics and Genomics

- Genetic technology: £1.1m (NIHR, BBSRC);
- Ophthalmic Genetics: £2m (NIHR, MRC, RC);
- Diagnostics £2.4m (NIHR); Immunogenetics £1.1m (NIHR, MRC);
- Developmental £1.7m (NIHR, Industry);
- aDNA £1.1m (Philanthropic donation)

MCCIR ***(UoA1's researchers only)***

- Regulation of immunity: £2.9m (MRC, Wellcome);
- Clinical Allergy: £3.4m (NIHR, MRC, UK Government);
- Clock Biology: £4.5m (MRC, Wellcome);
- Covid UK-Coronavirus Immunology Consortium: UKRI/NIHR (Hussell), (£6.5m across consortium)

Respiratory

- Childhood asthma: £1.5m (NIHR, RCs);
- Chronic cough: £1.4m (Wellcome); COPD: £2m (MRC, NIHR);
- Cystic fibrosis £900k (NIHR);
- Technological advances/diagnostics £800k (NIHR):
- Detecting lung transplant rejection: £550k (RCs)

CfMR

- Advances in gene technologies relevant to IMIDs: £550k (NIHR, EU);
- Genetic predisposition to IMIDs: £4.1m (NIHR, Versus Arthritis, Wellcome, EU);
- Rheumatoid Arthritis: £3.7m (NIHR, Wellcome);
- Lupus: £3.1m (NIHR, Versus Arthritis);
- PsA, JIA, Myositis £4m (NIHR, MRC)
- In addition four MRC Stratified Medicine Initiatives (MATURA [RA], MASTERPLANS [lupus], CLUSTER [JIA], MYO-PROP [myositis]) £15m.

CfDR

- Ultraviolet radiation biology and medicine £1.2m (NIHR);
- Psoriasis: £5.3m (NIHR, Wellcome);
- Skin ageing £5.7m (Industry);
- Drivers of atopic dermatitis: £1.2m (Wellcome, NIHR).
- MRC Clinical Pharmacology Research Training Programme. £3.4m.
- MRC Stratified Medicine Initiative in Psoriasis (PSORT) £7m

Infection

- Aspergillosis: £1.3m (MRC, Wellcome);
- Antibiotic Stewardship: £6.2m (NIHR)

BiomTech

- Manchester Centre for Cancer Biomarker Sciences: £18.3m (CRUK, NIHR, Industry);
- Stoller Biomarker Discovery Centre £16.3m (MRC, RCs, Innovate);
- MMPathIC £5m (MRC, Innovate, EU, Industry)

Regenerative Medicine

- Basic and preclinical studies: £7.1m (Wellcome, MRC, EPSRC, Industry).
- Improving patient outcomes: £10.3m (RCs; NIHR, Industry [includes Orchard Therapeutics. A phase I/II clinical trial of haematopoietic stem cell gene therapy (OTL201) in patients with MPSIIIA. £7.1m, and Oxford Electricals. Electrical enhancement of wound healing. £2.4m]).

Medical Humanities

- CHSTM: £3.6m (Wellcome, Heritage Lottery, AHRC [£1m NHS Voices of Covid]);
- RME: £400k (RCs)

3.3. Securing Future Funding

Our future funding will build on REF2021 successes, align with our future research strategy, and the aspirations of individual Groups. The principles that will drive future funding are:

- Exploiting the unique resources within Manchester to access and translate bioinformatic and digital insights, into clinical care and personalised medicine. We will harness:
  - Hospital-based Clinical e-records;
  - GM's Integrated Care Records across primary, secondary and tertiary care;
  - NIHR Health Informatics Collaboratives
  - UoA1's polyomics, and polyomic data sets from our Research Groups (SBDC, Genetics etc.), and those in the public domain
  - The power of UoM's big data analytics (e.g. IDSAI and Digital Futures Platform)

  to mine data from all these sources at scale and speed, enabling identification of novel biomarkers, and therapeutic targets, and to power personalised medical innovation with genuine global relevance.
- Working within UoM, lead and/or participate in cross-cutting, trans-Faculty strategic initiatives, to view medical problems and their solutions from new angles.
- Maintaining competitive streams of ECRs, doctoral students and fellows, to bring us challenging ideas and ensure seamless succession.
- Renewing our BRC with more funded Themes, building on its successes, and incorporating emergent clinical research areas that would benefit from a BRC's integrated support environment.
- Using DevoManc; HInM; our local government's vision; new infrastructure delivered by MSP, UoM, and NHS; and our in-house discovery-to-clinical implementation pipelines to attract new industry partners to work with us, and locate to Manchester.
- Enabling our NHS-embedded treatment and research centres to succeed through integration of vision and resource, co-ordinated through MAHSC and HInM.
- Ensuring we offer all researchers a supportive and stimulating research environment.

3.4. Research Support

FBMH's RS&I facilitates our research by enabling interdisciplinarity; disseminating strategic funding intelligence; analysing datasets to inform strategic developments; and supporting partnering, research projects, consultancy, knowledge exchange, and facility-sharing.

3.5 Trans-sector Infrastructure and Facilities Used by UoA1 Researchers

UoM's investment strategy focuses resource, knowledge and skills in Beacons, Institutes and Platforms, specialist facilities and strategic units that can be accessed by all academics. This empowers collaborative, quality research, and is highly resource efficient (REF5a). This strategy is embraced by our NHS and local government partners resulting in multi-funder initiatives such as the new Paterson Building (3.5.3).

3.5.1 UoA1's research is based in 4 UoM campus buildings and 3 Hospital Trusts.

UoM, MFT and Manchester Science Park are co-located along the "Oxford Road Health and Life Sciences Corridor" (ORC) a 1sq mile Local Economic Partnership (LEP)-designated innovation quarter. In addition to UoM, MFT and the Science Park, ORC contains 50% of Manchester's Life Science businesses, and is amongst Europe's largest clinical academic campuses.

UoA1 researchers work within the heart of this environment in: four inter-connected UoM buildings (AV Hill, Michael Smith, Stopford, Core Technology Facility [**MCCIR**, **RegenMed**, **MedHum]**); and MFT "Oxford Road" (4 Hospitals with dedicated clinical and laboratory research facilities: Manchester Royal Infirmary [MRI: **Genetics**, **CVS**, **CfMR**], St Mary's Womens' Hospital, Royal Manchester Children's Hospital [RMCH] together hosting **DBM**, and the Royal Manchester Eye Hospital [**Ophthalmic Genetics**]).

The remainder of our researchers are within five miles of the ORC in specialty-specific, purpose-built, integrated research and clinical facilities within NHS Trusts:

- Christie campus (**Cancer**): Christie Hospital (dedicated research, biobank, and radiotherapy facilities); Oglesby Building; new Paterson Institute.
- MFT "Wythenshawe": Specialist NW Lung Centre (**RespMed, Infection**)
- Salford Royal Hospitals: Specialist GM Dermatology Centre: (**CfDR**)

3.5.2: Manchester Science Partnership (MSP)

MSP, a strategic partnership (UoM, MFT, Bruntwood [major local construction and business premises management company], MMU, and Manchester, Salford and East Cheshire Councils) focuses on growing Manchester's knowledge economy by providing specialist laboratory and office environments and support services purpose-designed for science and technology along ORC.

MSP has significantly enabled UoA1 by bringing hi-tech business to Manchester and siting them in proximity with UoA1 researchers in state-of-the-art buildings on the Science Park, and "Citylabs" in MFT.

In 2014 MSP acquired the life science campus at Alderley Park. Currently undergoing £247m investment, it offers high specification lab space; range of scientific services; and an accelerator delivering comprehensive programmes of business support for start-ups/scale-ups. It is home to a fast growing community of >60 established and 150 pre-start-up companies.

3.5.3 Headline examples of infrastructure investment since REF2014:

New Build (completed)

- **Oglesby Cancer Research Building**: Houses 150 MCRC scientists and 100 support staff in state-of-the-art cancer research laboratories (£38m: CRUK/UoM/UKRPIF).
- **National Graphene Institute** (£61m; £38m EPSRC, £23m EU). A trans-faculty collaborative facility for sector-leading research on 2D materials where UoA1 researchers, in collaboration, develop ground-breaking biomaterials and biosensors.
- **Citylabs1.0** (£25m). Brings together UoA1 researchers, NHS, and industry. Houses MMPathIC, SBDC and industrial partners including APIS and Yourgene.
- **BCMRR** (£3.1m). MFT Wythenshawe site within NW Lung Centre

New Build (under construction)

- Paterson Redevelopment Project*:* Following the 2017 fire that destroyed CRUK-MI's Paterson Building, a new, larger £150m Research Centre is taking shape on the Christie site, accommodating biomedical research laboratories, consultant workspace, collaboration spaces, and support facilities, and promoting collaborations between cancer researchers and clinicians.

Refurbishment

- **Vaughan House***:* Campus listed building refurbished (£2.4m MRC) for Manchester Health Informatics Hub of the Northern England Health eResearch Centre. Promotes cutting-edge research consolidating e-health records and apposite research data.
- **5th floor AV Hill**: The 9,700m² AV Hill building was future-proofed, leaving the 5th floor shelled. Reflecting UoA1's increasing research, in 2015 it was populated with modern laboratories, write-up rooms and office accommodation (£2.8m).
- **Alderley Park:** Built by AstraZeneca, this complex, extensively refurbished by MSP, now houses UoA1 spin outs, other start-ups, larger organisations (Medicine's Discovery Catapult, Infex Therapeutics) and (currently) CRUK-MI.
- **Microbiology/Virology Laboratory Suite:** on the Science Park site provides high quality laboratory space for use by infection researchers, and has fed into antibiotic stewardship and Covid-19 research. (£1m)

3.6 Core Research Facilities Enabling Discovery Research

FBMH's Core Laboratory Facilities (CLFs) maximise the effectiveness of our discovery research through skilled technology-specific Experimental Officers (EOs).

FBMH's Research Technology Development Group oversees nine CLFs: Bioimaging; Biological Mass Spectrometry; Biomolecules; EM; Flow Cytometry; Genomic Technologies; Genome Editing; Histology; Proteomics.

CLFs have grown since 2014 through >£15m institutional/grant investment in established and emerging technologies, staff increasing from 33 (2014) to 49 (2020). Researcher-perceived value is reflected in turnover (<£2m (2013/14) to ~£3.5m (2019/20). Increased impact through investment is exemplified by Genome Editing, historically focused on transgenic animals, but through Wellcome ISSF funding now incorporates CRISPR technology.

To ensure CLFs meet researchers' needs, horizon scanning through Groups, and researcher feed-in informs strategy.

FBMH has preclinical Core Imaging Facilities (CIFs) and shares clinical CIFs with NHS partners, offering preclinical and clinical PET, MR and PET-MR imaging. Clinical research imaging is located in NHS partners (Christie, MFT Oxford Road, MFT Wythenshawe) and UoM's Wolfson Molecular Imaging Centre (on the Christie site) which also houses specialist preclinical PET, MRI and CT facilities.

3.7. Manchester Clinical Research Facility (NIHR MCRF)

UoA1 researchers supported by FBMH's £18m NIHR/CRUK grant-funded Clinical Trials Unit undertake trials in the NIHR MCRF (£12.5m. Director: **Smith**) comprising 4 experimental medicine units embedded within Christie Hospital and MFT (MRI, RMCH, Wythenshawe).

Offering outpatient and 24/7 inpatient services, MCRF includes: dedicated pharmacy, laboratories, imaging suite, minor procedure suite, human performance laboratory, and, for children, play, multi-sensory, and "chill-out" rooms.

Research studies increase year-on-year. Between 2017/8 and 2018/9 studies increased from 563 to 688 in 2018/9, and phase I/II studies from 269 to 317, including: 24 from 5 BRC themes, phase-I study assessing safety/tolerability of a novel synthetic nerve repair conduit; TARGET trial: ctDNA informs stratification to cancer treatment trials.

3.8. Biobanking Resources

As well-characterised clinical material drives stratified/precision medicine research, we have expanded biobanks during REF2021. Examples include:

MCRC Biobank collects fresh cancer samples from MAHSC Trusts. Holds >14,000 fully documented and consented tissue samples of human neoplasms, and pre-operative blood/urine. It also allows researchers to access thousands of stored histology samples through GM's Pathology Network.

MRC Immune-Mediated Inflammatory Disease Biobanks-UK (IMID-Bio-UK: £1.7m lead McInnes, Glasgow [UoA1 leads **Griffiths, Bruce, Freemont**]), links UoA1's CfMR and CfDR biobanks with others nationally (in RA, lupus, psoriasis, primary biliary cholangitis, autoimmune hepatitis, Sjögren's), through a single analysable dataset available to academic and industry researchers. This allows at-scale studies to: define disease mechanisms and drug actions; design improved clinical pathways; and identify therapeutic targets; across the IMID spectrum.

Through BRC, UoA1 feeds into the **NIHR Bioresource** where Manchester leads the IMID Common Disease BioResource as well as a number of rare disease modules including neurofibromatosis-1 and -2, congenital hyperinsulinaemia and hereditary pulmonary fibrosis.

Each MAHSC Trust (e.g. MFT Biobank) offers sample collection and banking services and UoA1 researchers maintain specialist **in-house Biobanks** (e.g. ManARTS [respiratory/allergy]; Scleroderma and Raynaud's; Placental blood and tissue)

MMPathIC has developed initiatives for post-test samples (liquid and formalin-fixed paraffin-embedded tissue), routinely stored by NHS Trusts to be available to industry partners.

UK Biobank (UKBB): UKBB Co-ordinating and Assessment Centre is located within GM. UoA1 researchers work with UKBB (e.g. GWAS identifies novel chronotype loci in 100,420 individuals from UK Biobank. **Ray. Nature.Comms.2016:**REF2ID:51435206) through the Manchester UKBB Community, a researcher network for all using UKBB resources.

3.9 University Library, Key Underpinning Role in UoA1's Research

UoM's Library's extensive digital collection is amongst the Russell Group's largest print and e-resource collections for biomedical sciences. This significant investment gives us seamless access to comprehensive discipline-specific collections, on and off campus.

The Library supports our researcher journeys through Academic Engagement Librarians; research data management planning, Open Access compliance and managing online academic development pathways.

3.10. Impact of Funding and Resourcing initiatives on UoA1's Research

Investment in infrastructure by UoM, UKRI, Research Charities, NHS and MSP has had profound, positive effects on: UoA1's research environment; recruitment and retention of excellent researchers; impressions given to potential industry partners; and, thereby the amount and quality of UoA1's research and its outputs.

UoM's strategy focusing on multidisciplinary research buildings and facilities and collaboration with partners, ensures key complex research activities can be professionally overseen by academics, EOs and technicians equipped with specialist knowledge, skills and physical resource, streamlining research and ensuring dependable results. This has proved to be cost- and time-effective, underpinning reliable, quality data.

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

4.1. Changing Approaches to Healthcare Research though Collaborations within UoM

UoM has a research infrastructure that facilitates multidisciplinary research. In addition to UoA1's cross-disciplinary research groups made possible through Faculty restructure, research ideas, skills and facilities are available to all academics through a network of University Research Beacons, Institutes and Platforms.

4.1.1 University Research Beacons embrace academic research and social responsibility by bringing together the best minds from different disciplines to address major modern world issues around Cancer, Advanced Materials, Global Inequalities, Energy and Industrial Biotechnology. UoA1 researchers lead Cancer and contribute clinical experience to Advanced Materials and Global Inequalities.

4.1.2 University Institutes and Platforms concentrate skills and infrastructure in specialist areas. Constituent academics and their teams conduct their own research, whilst also acting as accessible sources of authoritative advice and specialised facilities that can be tapped by other researchers, ensuring grant applications are authoritative and realistic and research delivery optimal and efficient.

We lead two (CRUK-MI and LBIII), and are integrated into eight more, as follows:

CRUK Manchester Institute (CRUK-MI)

Research in UoA1's CRUK-MI underpins development of novel translational and personalised cancer medicine through discovery of key biological mechanisms, made available to cancer researchers world-wide.

Lydia Becker Institute for Immunology and Inflammation (LBIII)

Led by UoA1's researchers, LBIII brings UoM's immunology and inflammation researchers together, allowing multiple perspectives and approaches to be harnessed into unique

collaborations. LBIII has 104 PIs/RFs (35% clinicians) and 191 PG students. Our Inflammation researchers benefit from LBIII's discovery skills, whilst providing LBIII with clinical direction. We participate to Institute leadership through: **Hussell** (Director); Research Area Leads (**Zelenay:** Cancer; **Kitmitto**: Cardiovascular/multi-morbidities; **Arkwright:** Life course) and clinical immunology leads (**Griffiths, Crosbie**).

Manchester Institute for Collaborative Research on Ageing (MICRA)

Situated in the UK's first city-region to achieve WHO age-friendly status, MICRA is an information hub, linking academics from any discipline that promotes ageing research. UoA1's researchers in skin ageing, multimorbidity, cancer, cardiovascular disease etc. interface with experts in architecture, economics, engineering, and sociology to develop novel holistic solutions for issues facing the elderly.

Manchester Institute of Biotechnology (MIB)

Contains over 40 science and engineering research groups that collaborate in pioneering research, advancing knowledge and uses of biotechnology. UoA1's researchers guide strategic development of pharmaceuticals and advanced materials for clinical application.

Henry Royce Institute (Royce Institute)

The EPSRC-funded UK National Institute for Advanced Materials Research and Innovation is a partnership of seven Universities (Manchester, Cambridge, Imperial College, Liverpool, Leeds, Oxford, Sheffield), National Nuclear Laboratory, and UKAEA. It hubs from Manchester (Chief Scientist: *Withers*, Regius Professor of Materials [UoA12]). The Biomedical Materials theme, led from Manchester (*Cartmell* [UoA12]), gives our researchers unprecedented access to the most advanced ideas and technology and we bring clinical expertise into UK-wide materials sciences.

Christabel Pankhurst Institute for Health Technology (Pankhurst Institute)

Recently launched, the Pankhurst Institute, a £25m partnership between UoM, MFT, HInM, business, and local government, promotes needs-led health technology innovation, spotlighting UoM's rapidly expanding health technology portfolio. It is an important part of GM's health innovation ecosystem, complementing MMPathIC, by optimising interactions between healthcare innovators, the public and commerce.

Institute for Data Science and AI (IDSA)

UoA1 researchers call on the expertise of IDSAI, which covers the complete data science life-cycle from information management, through analytics, to practical applications, joining methodologists with translational scientists, identifying practical applications of data science. This creates a distinctive virtuous circle, where challenging real-life problems drive methodology research, whilst providing a clinical route to exploiting new algorithms and methods.

IDSAI, is only part of the digital ecosystem in Manchester, with expertise embedded in NHS and industry partners. UoM's **Digital Futures Platform** pulls together these communities to build critical mass in new and emerging research areas. We are integrated into the "Health and Care" research arm, identifying clinical value and scope from co-ordinated approaches to unifying and widening access to digital technology.

Institute for Health Policy and Organisation (IHPO)

IHPO researches novel approaches to funding and delivering effective health care, nationally and internationally, breaking paradigms (central planning, hospital-centred care, market-oriented reform) and championing evidenced opportunities (technological advance, devolved decision making). Our research contributes through: exploration of patient perspectives (**Snow's**

NHS@70/Voices of Covid research); use of technology to update patient management (MMPathIC's value proposition-driven biomarkers), and new approaches to disease prevention (**Howell**: Breast cancer prophylaxis **Lancet.2019:**REF2ID:158351714), earlier diagnosis/rule-out (**P.Crosbie***:* community-based cancer screening, **Thorax.2018:**REF2ID:84588550; **Body**: ACS rule-out **Ann.Int.Med.2017:**REF2ID:64544379), and novel interventions (**E.Crosbie** bariatric surgery lessening uterine cancer risk, **Int.J.Cancer.2019:**REF2ID:82680279).

Policy@Manchester

UoM's sector-leading policy engagement institute, connects researchers with policy makers and influencers, nurtures long-term policy engagement relationships, and enhances stakeholder understanding of pressing policy challenges.

A recent success from UoA1's involvement with Policy@Manchester is NICE guidance DG42, "Testing strategies for Lynch syndrome in people with endometrial cancer". Published in 2020 it uses our research demonstrating links between Lynch syndrome and uterine cancer (**E.Crosbie**, **Canc.Prevent.Res.2016;**REF2ID:50562356). In 2018, Policy@Manchester partnered with cancer charity *The Eve Appeal*, raising awareness of Lynch syndrome and cancer screening practices through *#LetsTalkLynch Campaign*, which, through short videos outlined and explained our research, profiling real stories of women and families affected by Lynch-related cancer.

4.1.3 Collaboration evidenced through cross-UoA REF2 outputs and REF3 Impact Cases

REF2 outputs illustrating collaborations between UoA1 researchers and academics returned in different UoAs

- **Barton. Arth.Res.Ther.2018:**REF2ID:84778509: ***UoA2***: Symmons, Hyrich, Verstappen, Sergeant
- **Aplin. Science.Advances.2016:**REF2ID:51497456 ***UoA3*****:** Tirelli, Harris
- **Bigger. EMBO.Mol.Med.2020:**REF2ID:159841487 ***UoA4*****:** Pinteaux, Boutin, Brough
- **Crow. Nature.Gen.2016:**REF2ID:50410335, ***UoA4:*** Kasher; ***UoA5*****:** Pavitt, O'keefe, Griffiths-jones
- **Hussell. Nature.Immunol.2019:**REF2ID:132447452. ***UoA5*****:** Sutherland, Grencis, Thornton, Cook, Macdonald
- **Ray. Nature.Comms.2016:**REF2ID:51435206 ***UoA2*****:** Emsley, Dixon, Russter; ***UoA4*****:** Kyle, ***UoA5:*** Loudon, Bechtold
- **Bowes. Nature.Comms.2018:**REF2 ID:84780542. ***UoA2*****:** Berzuini, Guo; ***UoA5*****:** Talavera.
- **Rhodes**. **J.Invest.Dermatol.2018:**REF2ID:82375603, ***UoA2***: Vail ***UoA7(Earth Systems*****)**: Webb
- **Body. Ann.Int.Med.2017:**REF2ID:64544379 ***UoA8(Chemistry)***: Munro
- **Kitmitto. Nature.Comms.2019:**REF2ID:143030568, ***UoA5:*** Humphries; ***UoA9(Physics)****:* Zhang
- **Stivaros. Molec.Autism.2018:**REF2ID:85282118 ***UoA2***: Emsley, Evans; ***UoA4****:* Green, Montaldi, Parkes, Garg; ***UoA11 (Computing)*** Keane
- **Timmermann PLoS.One.2016:**REF2ID:156081072 ***UoA11:*** Mcnaught, Ananiadou, Batista-navarro
- **Freemont. Soft.Matter.2016:**REF2ID:50401988 ***UoA12***: Saunders, Kinloch

We have made significant contributions to 10 REF3 Impact Cases reported in other UoAs.

UoA2: Transforming WHO fungal disease policy (**Denning**); Biologics registers: improving outcomes in IMIDs (**Bruce**)

UoA3: Smart Inhaler improves treatment inherence in childhood asthma (**Murray**)

UoA4: Worldwide reduction in fetuses exposed to antiepileptics (**R.Bromley**)

UoA5: Improved Kenyan cervical cancer outcomes (**Hampson**); Transforming management of inherited disorders. (**Sergouniotis**); Improved infection awareness, prevention and treatment in hard-to-reach groups (**Pennock**); Aspergillus drug resistance, enhancing diagnosis and therapy (**Denning**)

UoA7: Changing Public Health vitamin D and sun exposure policy (**Rhodes**)

UoA9: Establishing UK's first high-energy proton service (**Kirkby**)

4.2. Engagement with GM's Healthcare Systems

GMHSCP has unified healthcare delivery and patient records GM-wide, giving us unprecedented access to patients and patient data. This is a symbiosis, our research changing health across our city-region which, within England, has: highest premature CVS deaths; second highest cancer rates and infant mortality, and where deaths from lung disease, and the prevalence of arthritis, back pain and hip fractures are above the national average.

Our research maps onto GM's areas of population multi-morbidity, but impact reaches further, being directly transferable to deprived conurbations and communities world-wide.

Through co-ordinated healthcare and the overarching role of HInM in clinical research: we have seen: a stepped increase in patient recruitment to NIHR Clinical Trials (31,927 in 2017/8 to 66,727 in 2018/9): targeted innovations undergo effective, streamlined evaluation processes, enabling adoption at pace and scale across GM (e.g. Polynerve, T-MACs algorithm, and ABC care bundles) and drives innovative approaches to accessing and helping patients e.g. improving lives of Crohn's and colitis patients: MY-IBD portal (**McLaughlin**); and Psoriasis Shout Out (**Cordingley**).

HInM also facilitates collaborations that enhance research effectiveness across UoM and NHS Trusts, through progressive alignment of research offices, a common approach to costing and grant peer review, access to infrastructure, and unified researcher training; with the goal of completely seamless research infrastructures across MAHSC partners by 2030, optimising future clinical research access and scope.

4.3 Patient and Carer Involvement

Involvement of patients, the public and carers in decision making permeates our clinical research. Through interactions with patient societies, patient experts and patient focus groups. Examples of our interactions with the wider public as sources of research information and as participators in outputs are highlighted by the "Voice of NHS" series (MedHum), and participation in collaborative grants in 4.6.2,. Our partners websites detail how they work with patients and carers to bring added value to our joint activities: BRC; MAHSC partners; HInM; GMHSCP; ARC-GM. Of particular note is "Vocal" a joint UoM, MFT not for profit organisation that bring together people from all walks of life, and connects them with health research.

4.4. Improving Healthcare and Economies through Industry Collaborations

UoM's Business Engagement & Knowledge Exchange team, Masood Enterprise Centre; Innovation Factory, Manchester Institute of Innovation Research and direct involvement with industry, ensure we can access entrepreneurial advice and industry introductions. UoA1's established industry partnerships are at three levels.

4.4.1 Strategic research agreements

As an example, in 2018, because of UoA1's genetics research, GM's Genetic Campus, the NHS/NIHR clinical and diagnostic facilities in MFT, and the physical infrastructure offered through MSP, **Qiagen** (international gene-based diagnostics company), formed a partnership with UoM, MFT, MSP, HInM and Manchester City Council to create a Global Genomics Campus in Manchester, for innovation, life sciences, translational science and molecular diagnostics. The partnership's vision brings together the city-region's entire spectrum of public, academic and clinical resources to develop world-leading genomics in the heart of the Oxford Road Health and Life Sciences Corridor.

In 2019 the partnership funded (£25m) and launched APIS Assay Technologies, sited on the Genomics Campus in Citylabs1.0. Through the partnership, APIS is driving commercialisation of innovative molecular diagnostics assisted by MMPathIC.

In 2020, completion of the physical co-location of the partners took place with Qiagen re-siting ~300 staff into MSP's new Citylabs2.0, on the MFT site. This is now Qiagen's purpose-built single-site European Centre of Excellence for Precision Medicine and hub for diagnostics development.

Other examples include:

AstraZeneca: works closely with Cancer on ongoing programmes of anticancer drug discovery/evaluation and biomarker discovery (2016: £11m investment in Manchester Centre for Biomarker Sciences [**Dive**]).

Walgreens-Boots-Alliance, long-standing partners in dermatological research with CfDR (2018 £4m refunding), recently invested £1.7m to launch the Manchester Skin Proteome Study.

GlaxoSmithKline, a partner with UoM and AstraZeneca in forming MCCIR. In 2017, GSK invested a further £2m in MCCIR as a pre-competitive industrial collaborator.

4.4.2 Industry support for individual projects, mainly through funding discovery and trials of diagnostics, technologies and therapeutics has generated ~£60m of funding for UoA1 during REF2021.

4.4.3 Memoranda of Understanding with industry partners characterise most of our major research initiatives. E.g: BRC (38 strategic and 37 SME industry partners), and MRC Stratified Medicine Initiatives (PSORT, MATURA and MASTERPLANS with 10, 9 and 9 industry partners respectively).

4.5 Entrepreneurship

Through UoM's consultancy policy during REF2021, UoA1 researchers:

- **Registered four spin-out companies:**
  - **Skinbiotix** [**O'Neill**]: skin health;
  - **Complement Therapeutics**: [**Bishop, Unwin**] Targeting complement to treat dry age-related macular degeneration;
  - **VREvo Limited** [**Payton**] Virtual reality for healthcare professional training,
  - **Gritstone Oncology** [**Lord**], develops immunotherapies for cancers and infections. Raised >$300m VC funding, NASDAQ listing 2019 (current market-cap ~$1bn)
- **Were granted 102 patents**, filing a further 86

- **Made 54 royalty bearing licenses**. Most notably a £62m worldwide license agreement with AVROBIO, USA-based clinical-stage gene therapy company, for clinical development of lentiviral gene therapy for mucopolysaccharidosis type II.

4.6. Impact on our research though collaboration with overseas and UK Universities

Our collaborations are described above and in Figure 1. Here we give supporting metrics and examples, spotlighting scope and impact.

4.6.1 Publications evidencing collaborative research

During REF2021, UoA1 researchers have published:,

- With academics and clinicians from 2,792 institutions in 122 countries
- ~3,750 peer-reviewed publications with academics from 26 Universities appearing in the top 20 of one or more of the three leading World University Rankings (THE WUR, ARWU Shanghai, and QS WUR).

  They are: Columbia, Cornell, Duke, ETH Zurich, Harvard, Imperial College, John Hopkins, MIT, NTU Singapore, NU Singapore, Stanford, Berkley, University College, UCLA, UC San Diego, UC San Francisco, Cambridge, Chicago, Edinburgh, Michigan-Ann Arbor, Oxford, Pennsylvania, Tsinghua, Toronto, Washington, and Yale.

Examples evidencing the geographic and clinical scope of collaborative publications

Genetics of rheumatoid arthritis contributes to biology and drug discovery. **Barton. Nature.2014:** REF2ID:38652684: 95 authors from 12 countries: USA, France, China, Canada, Netherlands, UK, South Korea, Australia, Japan, Spain, Sweden, Estonia.

Association of Gestational Diabetes With Maternal Disorders of Glucose Metabolism and Childhood Adiposity. **Clayton. JAMA.2018:**REF2ID:84110213: 23 authors: eight countries: Ireland, Barbados, Israel, Thailand, USA, UK, Canada, China.

Association analyses of >140,000 men identify 63 new prostate cancer susceptibility loci. **Burnet. Nature.Gen.2018:**REF2ID:133783384: 187 authors, 16 countries: Finland, Denmark, Germany, Belgium, Norway, Poland, Portugal, Malaysia, USA, France, China, Netherlands, UK, Spain, Sweden, Australia.

Multi-ancestry GWAS of 21,000 cases and 95,000 controls identifies new risk loci for atopic dermatitis. **Curtin. Nature.Gen.2015:**REF2ID:38659421: 152 authors: 14 countries: Switzerland, Czech Republic, USA, China, Netherlands, UK, Spain, Sweden, Australia, Japan, Germany, Denmark, Finland, Ireland.

Trial of Anifrolumab in Active Systemic Lupus Erythematosus**. Bruce NEJM.2020:** REF2ID:164703773: 11 authors: seven countries: UK, Australia, USA, Japan, France, South Korea, Sweden.

Association analyses based on false discovery rate implicate many new loci for coronary artery disease**. Keavney; Nature.Gen.2017:**REF2ID:64395816: 62 authors: 12 countries. Greece, Austria, Lebanon, Saudi Arabia, UK, Germany, USA, Estonia, Sweden, China, Finland, Canada.

4.6.2 Examples of major collaborative awards with universities, industry, professional bodies and/or patient groups, demonstrating collaborative scope and spread.

- **CRUK International Alliance for Cancer Early Detection** (**Bristow** £3.2m)
  - Universities: UCL, Cambridge, Stanford, Oregon
- **Co-developing Medical Humanities with China** (Wellcome: **Kirk** £1.2m)

  Universities*:* Fudan; Shanghai Academy of Social Sciences.
- **EU Horizon 2020-MSCA-ITN-2018 DohART-NET grant**. (**Clayton**.£450k)
  - Universities: Cambridge; Southampton; Munich; Brussels; Rotterdam; Austrian Academy of Science,
  - Industry: BioTalentum, Hungary; MWM Biomodels, Germany; IVI, Spain.
- **UKRI Global Challenges Research Fund in Cardiovascular Disease** (**Keavney** £1.4m): Research portfolio with overseas Universities/Health Institutes to develop research careers and capacity build
  - Cape Town: Zuhlke (MRC-DFID African Research Leader 2019-2024);
  - North West, South Africa: Pieters (Newton Advanced Fellow 2017-2019): Affordable, societally acceptable interventions, for rheumatic, congenital, and HIV-associated paediatric heart disease in sub-Saharan Africa.
  - Malaya: Choy (early career researcher support) detect, genomically characterise, and effectively treat, primary Aldosteronism.
- **MRC IMID-BIO-UK** (McInnes Glasgow £1.7m)
  - Universities: Newcastle; QMUL, UoM, Cambridge.
  - Industry: Abbvie; Janssen; Novartis; QIAGEN.
  - Patient-led Charities: British Sjogren's Syndrome Association; Lupus UK; National Rheumatoid Arthritis Association; PBC Foundation; Psoriasis Association;
- **MRC Stratified Medicine Consortia**:
  - MATURA: (**Barton** [Co-lead] £5.9m)
    - Universities*:* Cardiff, Glasgow, UCL, QMUL, Newcastle, Oxford, Birmingham, Hertfordshire, Leeds, KCL, Edinburgh.
    - Industry*:* Roche/Genentech, Pfizer, AbbVie, MedImmune, Janssen, Beijing Genome Institute, Qiagen, Protagen, Avacta Life Sciences.
  - PSORT (**Griffiths** £7m)
    - Universities*:* Liverpool, Newcastle, KCL, QMUL
    - Industry*:* Abbvie; Becton-Dickinson; Celgene; GlaxoSmithKlein; Janssen; MedImmune; Novartis; Pfizer; Qiagen; Sanquin;
    - Professional organisations: British Association of Dermatologists; Royal College of Physicians;
    - Patient group: Psoriasis Association.
- **The Animal Research Nexus**: Wellcome Collaborative Award, (**Kirk** £460k)
  - Universities*:* UoM, Exeter, Nottingham, Oxford, Southampton.

4.7. Economic impact of our research

Local government has developed an infrastructure that facilitates intellectual and economic growth in GM, and UoM has transformed its organisation to allow academics to contribute. Within this environment, from during REF2021 UoA1 increased grant income by £193m. This represents an increase in grant income/FTE/year of 19% which, through direct research and indirect service posts, contributing to the employment growth in the ORC by 11% from 2015 to 2019.

Through entrepreneurship and our translational pipelines, new start-ups (e.g UoA1 spin-outs [4.5]; APIS), relocation of major companies (e.g. Qiagen), and growth of existing SMEs (e.g. Chromition) has been enabled by UoA1 academics, contributing to the 61% business growth in ORC from 2012-2018.

At a wider geographical level we have assisted job creation and economic growth (e.g. Our: REF3 Impact Cases record that research as stimulating >250 new UK industry posts, and >£900m/year increased revenue for UK/international businesses; grants such as UKRI Global Challenges Research Fund directly support new posts in overseas health research). We work with UK and international companies to give added value to their products, which brought £60m into GM during REF2021. Internationalisation of our IP also generates overseas income for UoM (e.g £62m agreement with AVROBIO).

4.8 Contribution to Medical Science and Wider Society.

UoA1 academics contribute significantly to National/International medical research and research leadership, knowledge transfer, and education.

During REF2021 UoA1 researchers have:

- **Received prestigious awards** recognising exceptional contributions to medicine including:
  - Fellowship of the Royal Society, **Marais**;
  - Orders of the British Empire, **Dive** CBE, **Black** OBE, **Griffiths** OBE,
  - Fellowships of Academy of Medical Sciences, **Black, Bristow, Crow** (now former staff), **Dive, Hussell, Lord, Radford;**
  - Fellowship, American Academy for Advancement of Science, **Morton**;
  - Membership, National Academy of Sciences, **Nelson**,
  - Guggenheim Fellowship, **Burney,**
  - L'Oréal UK and Ireland Fellowship for Women in Science, **Briggs,**
  - NIHR Lifetime Achievement Award, **Radford,**
  - Distinguished Leader Award, International Society for Heart Research, **Eisner**;
  - AstraZeneca Prize for Women in Pharmacology, and Johan Anton Merck Award, **Dive;**
  - NIHR Senior Investigators: **Barton; Bruce; Illidge; Lord; Smith**
- **42 held visiting Professorships** in overseas Universities
- **115 have performed editorial roles**, e.g. Molecular Cancer Research, **Bristow**; EMBO Molecular Medicine, **Cossu**; Viral Immunology, **Hussell;** International Journal of Molecular Epidemiology and Genetics, **Keavney**; Scientific Reports, **Morris**; Clinical Oncology, **West;** Stem Cell Research, **Whetton;** and 3 were Editors-in-Chief*:* Journal of General Physiology,

and Journal of Molecular and Cellular Cardiology, **Eisner;** Experimental Dermatology, **Paus**; Dermatology and Therapy, **Warren**

- **101 have served on grant panels.**

  International examples: Global Action Fund for Fungal Infections, **Denning**; European Research Council and Italian National Research Council, **Cossu**; World-wide Cancer Research, **Malliri;**

  At the REF2021 census date the following were members of prestigious national research grants panels: **CRUK*:* Bristow** (Chair, Clinical Research Committee), **Choudhury**, **O'Connor**, **Blackhall, Hughes, Somervaille**: **UKRI**: **Lord** (Chair, Future Leaders Fellowship Panel); **MRC: Lord, Malliri, Morris**: **Wellcome*:* Smith**, (Chair, Physiology in Health and Disease Expert Review Group), **Lord** (Chair, Clinical Interview Committee), **Hagan, Wilson, BBSRC: Mclaughlin** (Expert Pool); **UK Blood Cancer*:* Somervaille** (Chair, Research committee); **Versus Arthritis**: **Buch, Orozco**; **EPSRC**: **Freemont** (College of Experts)
- **87 have contributed to running academic societies**, nine taking leading international roles:
  - **Eisner:** Presidents of: European Federation of Physiological Societies; International Society for Heart Research; Physiological Society
  - **Dive:** President: European Association for Cancer Research
  - **Boulton**: President: Worldwide Initiative for Diabetes Education
  - **Hanley:** President: Association of Physicians, GB & Ireland
  - **Morton:** President: American Society of Human Genetics
  - **Tomaszewski:** President: International Society of Hypertension
  - **Newman:** Chair Education Committee: European Society of Human Genetics
  - **Clayton:** Secretary-General: European Society for Paediatric Endocrinology
  - **Griffiths:** Executive Board member: International League of Dermatological Societies
- **119 had major roles in organising conferences**; 127 gave plenary/keynote presentations; 28 gave named lectures e.g. **Eisner*:*** Peter Harris Distinguished Scientist Award, International Society for Heart Research; **Denning*:*** Edouard Drouhet Medal, European Confederation of Medical Mycology; **Woolf*;*** De Wardener Lecturer, Renal Association.
- **Service on WHO/UN science bodies**: **Woodcock:** Co-Chair, UN Technology and Economic Assessment Panel to the Montreal Protocol; **Rhodes***:* UN Environmental Effects Assessment Panel; **Green:** WHO International Agency for Research into Cancer's Scientific Council, **Denning**: WHO SEARO Task Force on Antimicrobial Resistance.
- **NICE**: 27 gave evidence to NICE or were panel experts; **Hamdy:** Interim Vice Chair MTAC**, Freemont, Dark** served on NICE committees; 48 were involved in drafting National Guidelines.
- **Training**. 85 clinical academics were directly involved in formal training programmes for clinical trainees, 23 serving on education/training committees of Royal Colleges**.**

4.9. Social Responsibility through Education and Clinical Impact

Social Responsibility is one of UoM's three Core Goals, sitting equally alongside world-class research and outstanding learning and student experience. UoM is signatory to the National Co-ordinating Centre for Public Engagement's Manifesto for Public Engagement, and in 2018 was awarded a Gold Engage Watermark.

Opportunities offered by our local clinical research environment, focus UoA1's research strategy at problems endemic in our local community. By addressing local healthcare needs our research is also directly pertinent to other UK and wider global communities.

UoA1 researchers engage with our public both in the form of specialist patient groups (e.g. partners in PSORT), and public engagement activities. During REF2021, 179 shared our research with the community from children to members of public-facing learned societies, public lectures, local and national Science Weeks etc.