Translational Research in Joint and Related Inflammatory Diseases
NOCRI simplifies access to the UK’s world-leading clinical research infrastructure
Foreword

Collaborative research accelerates the development of new treatments, devices and diagnostics to tackle complex healthcare needs. Creative engagement between the NHS, universities and industry forms a powerful alliance to drive translational medicine. This alliance is vital. It ensures that advances in basic science progress swiftly into benefits for patients and the economy.

NIHR Translational Research Partnerships are the embodiment of this collaborative approach. Supported by NOCRI, the TRPs accelerate the development of solutions to meet real patient needs. If your early phase programmes are targeted at joint and related inflammatory disease, then contact the NOCRI team to discuss how the NIHR TRPs can help.

Professor Dame Sally C Davies
Chief Medical Officer and Chief Scientific Adviser, Department of Health

This booklet highlights the way NIHR Translational Research Partnerships can help broker early phase collaboration between industry, the NHS and universities to the benefit of all parties. The NIHR Office for Clinical Research Infrastructure (NOCRI) makes this process easier for industry, enabling the generation of new ideas and leaps in research. We have a clear and managed approach to collaborations, including tools to shorten the contracting process and a dedicated Operations Manager. This helps companies to achieve their translational research objectives more efficiently.

Mark Samuels
Managing Director, NOCRI

NOCRI connects the country’s expert investigators, technologies and research facilities to deliver high quality clinical research. If you would like to know more about how NOCRI can help you to establish academic-NHS-industry collaborations, please e-mail the NOCRI Translational Research Partnerships office at trp@nihr.ac.uk, or call +44 (0) 203 328 6744.
Introduction to NOCRI

NOCRI makes it easy to access the UK’s clinical research infrastructure, which includes world-leading scientists in world-class facilities. With 60 million people in the National Health Service, we connect companies to investigators with access to well-characterised cohorts of patients.

NOCRI is a unique resource for the global life sciences industry - improving the quality, efficiency and success of translational research. We achieve this by providing:

- fast and easy access to the UK’s clinical research infrastructure
- rapid connection to expert investigators and cutting edge technologies
- a managed process for collaborative research.

We focus on facilitating successful outcomes, from making rapid introductions through to supporting collaborations to ensure delivery of research.
Introduction to Translational Research Partnerships

The NIHR Translational Research Partnerships (TRPs) were developed at the request of the life sciences industry. The Partnerships combine the finest minds and capabilities from 36 universities and NHS organisations into a single structure. Underpinned by world class NIHR clinical research infrastructure, they create a unique resource to drive translational research in defined therapeutic areas, address unmet medical needs and take on the challenges of an evolving drug, device and diagnostic development model. All participating centres work to a set of unified and streamlined operating procedures that are supported by a dedicated team within NOCRI. Together, this enables us to define, design and deliver research projects better and faster through improved communication with industrial partners and a cost-effective delivery model.

The Translational Research Partnership concept draws strength from the UK’s long tradition of creating breakthroughs in translational and early phase clinical research. In the field of inflammation, the discovery of TNF as a pivotal molecule in the pathogenesis of rheumatoid arthritis by scientists at the Kennedy Institute in London (now in Oxford) has revolutionised the treatment of this condition, and subsequently that of other inflammatory diseases such as ankylosing spondylitis, psoriasis and Crohn’s disease. This is but one example from a long list of achievements held by the UK’s translational and early phase clinical research industry.

The TRPs bring together the UK’s leading academics and the life sciences industry, in order to drive translational research.
Building on these successes, the Partnerships bring together some of the world’s best clinical researchers and translational research capabilities, placing us in a unique position to translate pre-clinical data into successful clinical research and development. Our activities span the complete range of translational research, including pre-clinical models, exploratory trials, phase I and II proof of concept clinical drug trials and other studies for medical technology and diagnostic applications. The Partnerships are supported by a dedicated team within NOCRI which acts as a single point of contact and facilitates the set-up of all research projects. Where necessary, NOCRI also works with potential commercial partners to identify suitable public funding schemes aimed at collaborations in translational science and exploratory development. Study design is informed by formidable expertise and capabilities:

- cutting edge expertise in exploratory development protocols, biomarkers, pathophysiology, disease mechanisms and patient selection
- expertise at the interface of pre-clinical and clinical research, including pre-clinical models of disease, human disease tissues and validation and optimisation of biomarkers
- enabling technologies and infrastructure, including advanced imaging, biobanks and dedicated research facilities
- cohorts of well-characterised patients available for clinical development studies.
Structure and key capabilities of NIHR Translational Research Partnerships (PoM: proof of mechanism; PoC: proof of concept)
The Joint and Related Inflammatory Disease TRP is a consortium of nine centres where each centre is formed by a university and its associated NHS organisations, represented by an Academic Lead. The Partnership centres were selected by an international review panel based on their recognised expertise and capabilities in the designated field. A collaboration agreement binds the Partnership together, ensuring that all centres work to common business processes and timelines.

A dedicated TRP team within NOCRI acts as the single point of contact for a commercial partner and coordinates all steps from first contact through to delivery of the signed project, thus ensuring that TRP projects deliver to time and target.

NOCRI enables the quick exploration of research opportunities by facilitating scientific exchange through setup of meetings and assisting in the negotiation of required agreements and contracts. We provide standard templates for non-disclosure agreements (NDAs) and contractual arrangements, including the model industry collaborative research agreement (mICRA), which has been accepted by all participating universities and NHS organisations and endorsed by trade associations such as the Association of the British Pharmaceutical Industry and the UK BioIndustry Association. These templates facilitate rapid sign-off and turnaround. Through our streamlined processes we aim to complete all necessary steps from NDA agreement, to study start within a period of eight months.
In essence, the Partnership aims to act as one institution by providing a single point of contact and entry into the nine centres of excellence. Collectively the centres provide exemplary scientific expertise, strong track-records in working with the life sciences industry and first class clinical research facilities provided by the NIHR Biomedical Research Centres/Units, NIHR and NIHR/Wellcome Trust Clinical Research Facilities and partner Contract Research Organisations. The Partnerships are committed to delivering research faster and better.

For further information on the Partnerships, please e-mail the NOCRI Translational Research Partnerships office at trp@nihr.ac.uk, or call +44 (0) 203 328 6744.

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TRP operational process and milestones for project setup
NIHR Translational Research Partnerships are strongly positioned to ensure scientific ideas are applied to patient need earlier than would otherwise have been possible, by concentrating expertise and fast-tracking ideas.

**Key facts**
The Joint and Related Inflammatory Diseases TRP provides:

- expertise in a range of joint and related inflammatory diseases including amongst others rheumatoid arthritis, osteoarthritis, synovitis, lupus, Sjögren’s syndrome and psoriasis
- experts in experimental medicine with outstanding track records in undertaking clinical research, each of whom have easy access to well-defined patient cohorts and state of the art facilities, including NIHR funded infrastructure
- advice and facilities to conduct first-into-man and first-into-disease projects; suggestions and execution of ex vivo validatory work on human tissue samples and efficient delivery of phase I and phase IIA trials and other well designed studies
- translational expertise to design and undertake early phase studies to deliver data that match a drug target to an appropriate therapy area and establish proof of concept
- the potential to revolutionise drug development by harnessing academic expertise, state of the art clinical and laboratory facilities and applying an original and cost-effective operational model.

The research centres that make up the NIHR Translational Research Partnerships have been selected to work together based on their proven ability to deliver in experimental medicine and translational research. By working together in this way, the Partnerships bring a unique breadth of expertise to industry’s translational research questions.

The head of each NIHR Joint and Related Inflammatory Diseases TRP centre outlines their establishments’ capabilities on the following pages.
The NIHR Biomedical Research Unit in Musculoskeletal Disease at Central Manchester University Hospitals NHS Foundation Trust and the University of Manchester; Manchester Academic Health Science Centre

Disease Expertise

Manchester is internationally recognised for work on the epidemiology and genetics of rheumatic diseases which enables stratification of patients into relevant subsets.

Research Capabilities

We host an NIHR Musculoskeletal Biomedical Research Unit. We have internationally recognised expertise in the study of cardiovascular complications of rheumatic diseases and the neuroimaging of pain. We have major programmes in systemic lupus erythematosus and other connective tissue diseases (systemic sclerosis and inflammatory myopathies) as well as early arthritis, juvenile arthritis and psoriasis. Manchester Academic Health Science Centre also hosts ongoing mechanism-based trials in osteoarthritis.

We have excellent infrastructure for early phase work across the full age spectrum in all three of our NIHR Clinical Research Facilities. We also host cutting edge imaging facilities and genomics platforms.

Patient Cohorts

We have large, well phenotyped patient cohorts in the full spectrum of rheumatic diseases including systemic lupus erythematosus and other connective tissue diseases, rheumatoid arthritis, seronegative arthropathies and we are an international hub for all aspects of psoriasis research.
University Hospitals Birmingham NHS Foundation Trust, Sandwell and West Birmingham Hospitals NHS Trust, Dudley Group NHS Foundation Trust and the University of Birmingham

Disease Expertise
Birmingham’s capacity in rheumatoid arthritis and systemic lupus erythematosus is complemented by specific expertise in primary sclerosing cholangitis, autoimmune hepatitis and stromal cells.

Research Capabilities
Our teams work across rheumatological diseases with a strong cross-disciplinary focus on translational inflammation research, and are active in associated themes such as gastroenterology, hepatology and endocrinology. Within our NIHR/Wellcome Trust Clinical Research Facility, our Good Manufacturing Practice (GMP) cell and gene-therapy suites highlight the translational research platforms available for early phase clinical research. Our imaging and ultrasound guided synovial biopsy capability demonstrates some of our leading technology.

We host the NIHR Birmingham Liver Biomedical Research Unit, MRC Centre for Immune Regulation, MRC-ARUK Centre for Musculoskeletal Ageing Research, ARUK Experimental Arthritis Treatment Centre and the NIHR Surgical Reconstruction and Microbiology Research Centre. We have a Human Tissue Authority-licensed human tissue biorepository and an extensive range of genomic, proteomic and immunology-based capabilities for biomarker development. There is extensive expertise in trials methodology.

Patient Cohorts
Clinics include inflammatory arthritis, early synovitis, systemic lupus erythematosus and Sjögren’s syndrome, as well as inflammatory bowel disease, ulcerative colitis and ankylosing spondylitis.

Professor Christopher Buckley
Arthritis Research UK Chair Of Rheumatology, School of Immunity and Infection, University of Birmingham
The NIHR Biomedical Research Centre at Guy’s & St Thomas’ NHS Foundation Trust and King’s College London; King’s Health Partners Academic Health Science Centre

Disease Expertise
Our expertise in Rheumatology includes rheumatoid arthritis, systemic lupus erythematosus and ankylosing spondylitis.

Research Capabilities
We host an NIHR Biomedical Research Centre, NIHR Guy’s & St Thomas’ Clinical Research Facility and a UKCRC accredited Clinical Trials Unit. We have state-of-the-art imaging facilities, underpinned by the Imaging Sciences Division at King’s College London, providing high resolution ultrasonography, MRI (including functional MRI to evaluate pain pathways at the Institute of Psychiatry) and PET. We have strong expertise in basic science which includes several pre-clinical models of disease and high throughput genotyping and next generation sequencing to support work in pharmacogenetics. Our centre has access to high resolution ultrasonography for assessment of synovial inflammation and vascularity which is available in an outpatient clinic departmental setting. In addition, we have extensive expertise in screening tools, including liver fibroscan, for identifying metabolic syndrome in patients with chronic inflammatory disease. We are leaders in T-cell and monocyte biology and host state-of-the-art genomics and immune monitoring core facilities, a GMP cell therapy suite. Quintiles has a formal partnership with NIHR Guy’s and St Thomas’ Biomedical Research Centre, to bring together Quintiles expertise in commercial early phase clinical trials with our access to patient cohorts and academic and clinical resources.

Patient Cohorts
We support large cohorts of patients with rheumatoid arthritis, spondyloarthropathies, psoriatic arthritis, psoriasis, connective tissue diseases, osteoarthritis and osteoporosis.
The NIHR Biomedical Research Centre at Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge

Disease Expertise
Our work in rheumatology includes capability in ankylosing spondylitis, psoriatic arthritis, connective tissue disease and vasculitis.

Research Capabilities
We host an NIHR Biomedical Research Centre and the NIHR/Wellcome Trust Cambridge Clinical Research Facility. Within rheumatologic disease we host themes with specific focus on metabolic bone disease, nephrology and vasculitis. We are the East of England hub for rapid DNA sequencing and have strong expertise in proteomics, metabolomics and in vitro immunologics assays.

Cambridge hosts the NIHR BioResource, a repository of genotyped patients and controls. Our immunophenotyping facility, involving slow cytometry and microarray analysis is state of the art, as are our PET-CT imaging facilities.

We have well developed links with regional hospitals thereby ensuring that we have access to a large patient population for clinical trials.

Patient Cohorts
Our clinics treat the range of inflammatory arthritis as well as osteoporosis, Sjögren’s syndrome, myositis, antiphospholipid syndrome, juvenile idiopathic arthritis, vasculitis and ankylosing spondylitis.
The NIHR Biomedical Research Centre at Imperial College Healthcare NHS Trust and Imperial College London; Royal Brompton and Harefield NHS Foundation Trust

Disease Expertise
In addition to rheumatoid arthritis, we have specific expertise in vasculitis, psoriatic arthritis and systemic lupus erythematosus.

Research Capabilities
We are leaders in macrophage and endothelial cell research. Our experimental capabilities include complement and vascular biology plus intra-vital microscopy of thrombosis and leukocyte trafficking.

We host an NIHR Biomedical Research Centre and the NIHR/Wellcome Trust Imperial Clinical Research Facility which provide dedicated facilities for experimental medicine and clinical trials.

We have access to several pre-clinical models of disease, including lupus, complement deficient mice and experimental models of inflammation in human skin.

Patient Cohorts
We host clinics in both rheumatoid and psoriatic arthritis, scleroderma, systemic lupus erythematosus, vasculitis and Behcet's syndrome.

Professor Dorian Haskard

Head of Immunology and Inflammation, Department of Medicine
Head of Vascular Sciences, National Heart and Lung Institute, Imperial College London
The NIHR Biomedical Research Centre at Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University

Disease Expertise
We are a European League Against Rheumatism Centre of Excellence with translational capabilities across the range of rheumatic diseases, particularly in relation to rheumatoid arthritis, osteoarthritis, Sjögren’s syndrome, systemic sclerosis and juvenile idiopathic arthritis.

Research Capabilities
Newcastle hosts an impressive team of clinical and non-clinical investigators whose research interests span the breadth of rheumatologic disease. We have a strong track record in proof-of-concept and experimental medicine studies, including biomarker development and cellular therapies. We provide a major theme to the NIHR Newcastle Biomedical Research Centre in Ageing and Chronic Disease and are an Arthritis Research UK (ARUK) Experimental Arthritis Treatment Centre. We also host the NIHR/Wellcome Trust Newcastle Clinical Research Facility, ARUK’s Centre of Excellence in Tissue Engineering, and the MRC/ARUK Centre for Integrated Musculoskeletal Ageing.

Our research is underpinned by a cutting edge array of enabling technologies. We have:

- state-of-the-art imaging, including research-dedicated 3T Magnetic resonance imaging (MRI) and Magnetic resonance spectroscopy, Positron emission tomography (PET), ultrasound and Dual-energy X-ray absorptiometry
- arthroscopic and ultrasound-guided synovial biopsy
- a Human Tissue Authority (HTA)-accredited biobank
- GMP facilities that provide excellent capacity for development and production of cellular therapies
- superb laboratory facilities with access to cutting edge technologies.

Patients Cohorts
We have a broad spectrum of relevant patient cohorts including inflammatory arthritis, osteoarthritis, osteoporosis, Sjögren’s syndrome, scleroderma, systemic lupus erythematosus and juvenile idiopathic arthritis.
Academic Director and Arthritis Research UK Professor of Rheumatology, University College Hospital London

Professor David Isenberg

The NIHR Biomedical Research Centre at University College London Hospitals NHS Foundation Trust and University College London; Royal Free London NHS Foundation Trust

Disease Expertise
We are recognised leaders in the study of patients with systemic lupus erythematosus, Sjögren’s syndrome, myositis, anti-phospholipid antibody syndrome and rheumatoid arthritis. We have an impressive pedigree of introducing new drugs to patients, including rituximab and tocilizumab for rheumatoid arthritis.

Research Capabilities
A brand new experimental model facility hosting a variety of arthritis models enables us to undertake top class pre-clinical studies.

We host an NIHR Biomedical Research Centre and NIHR/Wellcome Trust Clinical Research Facility. We have led the development of assessment tools for systemic lupus erythematosus, Sjögren’s and myositis. Our recently-opened Clinical Research Facility backed by outstanding imaging facilities and a new clinical research laboratory allows us to perform well-supported clinical trials and translational research.

Patient Cohorts
Our clinics host autoimmune rheumatic disease patient cohorts, plus an early onset synovitis clinic. We hold substantial serum samples from patients.
Barts and the London NHS Trust and Queen Mary University of London

Disease Expertise
Our centre’s principal focus is rheumatoid arthritis with special interests also in Sjögren’s syndrome and osteoarthritis.

Research Capabilities
We have pioneered the use of minimally invasive ultrasound-guided biopsy from large and small joints from patients with inflammatory arthritis to enable early-phase trials with target validation / modulation pre- and post-treatment in diseased joint tissues.

We host a full set of pre-clinical models including the unique human synovium-SCID mouse transplantation model, superb ultrasound imaging technologies for quantitative evaluation of synovitis / erosions, functional genomics with Illumina next generation sequencing platform and phospho-proteomics.

We host an HTA approved Human Tissue Resource Centre with over 500 well characterised synovial, cartilage and salivary gland biopsies that can be utilised for both academic and commercial studies.

Patient Cohorts
We host large inflammatory arthritis cohorts (rheumatoid and psoriatic) and have established a number of research-focused sub-cohorts that represent a unique bio-medical resource with high density clinical and imaging data plus associated tissue.
The NIHR Biomedical Research Centre and NIHR Biomedical Research Unit in Musculoskeletal Disease at Oxford University Hospitals NHS Trust and the University of Oxford

Disease Expertise
Our centre’s major specialist interests are in inflammatory arthritis including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis.

Research Capabilities
We host a NIHR Biomedical Research Centre and NIHR Musculoskeletal Biomedical Research Unit which provide dedicated facilities for experimental medicine and first-in-disease trials. We have expertise in early-phase trial design and a long heritage of working with industry partners.

We have access to several pre-clinical models of inflammatory arthritis and have expertise in ex-vivo disassociated synovial cell culture.

Within our centre for musculoskeletal trials we host quantitative MRI and ultrasound imaging, including ultrasound guided synovial biopsies. We have access to state-of-the-art biomarker capability including cell biology, genetic, proteomic and epigenetic technologies.

Patient Cohorts
In addition to our primary areas of disease interest, we host cohorts of patients with osteoarthritis, Sjögren’s syndrome, vasculitis, antiphospholipid syndrome and inflammatory bowel disease.