History of research

funded by the MPS Society

"Making a difference"

FOREWORD

Brian Bigger, Professor of Cell and Gene Therapy at the University of Manchester, April 2022

The global pandemic has brought about great change and challenges for everyone, not least those with MPS and related diseases. From a research perspective, months have been lost on important projects, and others have been repurposed for long periods for the COVID testing or treatment effort.

Nevertheless, the MPS Society continues to provide support for important research into MPS and related diseases and new treatments continue to be developed all the time for these rare diseases, largely through the contribution to the research of charities like the MPS Society.

It seems like a long decade since Professor J. Ed Wraith wrote the foreword for the previous history of research document from the MPS Society in 2011. Ed was one of the first beneficiaries of MPS Society funding, starting in 1988, and he built an incredible legacy in research in Manchester as director of the Willink Biochemical Genetics Unit until his untimely death in 2013, almost nine years to the day I write this. He and many other colleagues in Cambridge, London, Manchester and even Poland, New Zealand and Australia have benefited from MPS Society UK funding over the years, helping in many cases to shape their careers.

My career was built on MPS Society funding with a five-year MPS Society funded fellowship in Manchester in 2006, largely driven by Ed, Christine Lavery and the establishment of the MPS Stem Cell research group, bringing myself, a basic scientist together with leading Metabolic disease clinicians including Ed, the bone marrow transplant clinician Professor Rob Wynn, and some years later Professor Simon Jones and his team. Even 16 years later, despite a lab name change, the majority of our work continues to be focused on treatments and outcome measures for MPS diseases.

In the last 10 years the MPS Society funded the initial work on genistein as a substrate reduction therapy for MPS diseases, with a PhD student seconded from Professor Wegryzn's lab in Poland to my lab in Manchester and later an important trial into high dose genistein in Sanfilippo disease together with Professor Jones, that although unsuccessful in treating brain disease, allowed us to move onto other more effective therapies.

One of Ed's lifelong passions, to see stem cell gene therapy become a reality was work supported by the MPS Society, initially in my lab, together with multiple collaborators in Manchester and beyond, that entered a clinical trial for MPS IIIA in 2019 with five patients treated to date by Rob, Simon, myself and colleagues in London and another trial for brain targeted stem cell gene therapy for MPS II starting later this year. A stem cell gene therapy treatment for MPS IIIB was also developed and gene therapy for MPS IIIC.

The MPS Society has also branched out to include Fabry disease research and in the development of more conventional enzyme replacement therapies for MPS IV, for example, the MPS Society was instrumental in getting this and other enzymes accepted as funded treatments by NICE in England.

More recently in 2019, the MPS Society has established a Clinical Scientific Advisory Committee (CSAC) chaired by Professor Bryan Winchester. Although enzyme replacement therapy is a tremendous advance for somatic disease, it has begun to highlight neurological issues in patients with Hunter disease for example, that were hitherto unknown as it is not able to correct this aspect of the disease. Notwithstanding the impact of COVID, this is one reason why the MPS Society's current research focus has been on understanding and improving psychological wellbeing in disease.

Although the gene therapy landscape has been quite remarkable over the last decade with many trials in MPS and related diseases, not all have been successful. In particular, older patients are often not eligible for gene therapy trials and many patients have received one gene therapy intervention but cannot receive another. There remains much to do to provide lifelong treatments for MPS and related diseases and the MPS Society continues to provide critical funding for research into these devastating diseases.

INTRODUCTION

The MPS Society has funded research into treatments, and one day a cure, for MPS and related diseases since 1983. Research makes up one of our three pillars, alongside Support and Awareness, stating our most important aims as a charity and commitment to those we work with. This document has been updated for our 40th anniversary to look back at those many and varied research projects that have been funded thanks to the support of our individual fundraisers and donors as well as grants from philanthropic organisations.

CSAC and its role in research

The Clinical and Scientific Advisory Committee (CSAC) is a small committee, made up of four members of the Board of Trustees (Bryan Winchester – chair, Atul Mehta, Fiona Stewart and Gordon Harvey) and one member of the MPS Society senior leadership team (Sophie Thomas) who voluntarily participate in reviewing applications for grants for research projects and recommending them to be funded if appropriate to the Board of Trustees as a whole, who then have the final decision to award funding. This follows a process of internal review, often involving liaising with applicants and clarifying or working on their proposals and if necessary, organising external peer reviews if there are areas of science where specific expertise is needed.

CSAC's mission is to scientifically review research proposals to provide an unbiased recommendation to the Board to fund applications which they deem to have scientific merit, be feasible and deliverable and worth the money, in the hopes that the research the MPS Society supports will benefit the patient community in the future. Over the past year, CSAC has specifically focussed on applications that align with the focus of the MPS Society's spotlight on mental health and wellbeing.

CSAC's funding is provided by the MPS Society and is partly made up of some legacy funds which are restricted for the purpose of contributing towards research projects.

The Board has awarded three applications this year on the recommendation of CSAC. Currently, the MPS Society is looking at ways to replenish the funds available for research grants and CSAC are waiting on applications where the final decision has not yet been made.

About Rare Disease Research Partners

MPS Commercial, now known as Rare Disease Research Partners (RDRP) was established in 2012. It's a wholly-owned, not-for-profit subsidiary of the MPS Society and its social objectives are to reinvest any surplus to support the mission of the MPS Society to transform the lives of patients through specialist knowledge, support, advocacy and research.

Thank you

Thank you to all of our donors over the years who have donated funds to make these research projects possible.

HISTORY OF RESEARCH

2021

Dr Daniel Bailey £84,007:
Brunel

This research involves a study to look at whether physical activity levels and sitting time are linked to mental health (depression and anxiety) and quality of life in adults with Fabry disease. The next stage of the research will develop a programme to help adults with Fabry disease increase their physical activity and reduce sitting time to improve mental health and quality of life. Lastly, the new physical activity programme will be tested in adults with Fabry disease over 3 months to find out their experiences with the programme and what the possible mental health and quality of life benefits could be.

Dr Johnny Kenth £77,399:
Manchester Children's Hospital

This project will use data on individual patients' disease progression and treatment response to help doctors predict future negative outcomes before they happen, thereby allowing treatment decisions to be more informed.They will develop a mathematical (prognostic) model using existing and new, prospectively collected data to calculate the risk of worsening airway and lung problems in people with MPS IVA.

Dr Uma Ramaswami £9,886.75:
Royal Free

This project is a patient survey, which aims to evaluate the impact of Covid 19 on treatment interruption, shielding and the mental wellbeing of LSD patients during the pandemic.

January 2021

The CSAC secretariat established to help aid the process of receiving, reviewing and recommending applications.

2020

Professor Simon Heales £43,162:
GOSH

Evaluation of a Digital Microfluidics Platform for Rapid Assessment of Lysosomal Enzyme Activity in Dried Blood Spots. Unfortunately, Covid has delayed this research project.

Dr Karolina Stepien £9,400:
Salford Hospital

Does Hydrotherapy alleviate pain and improve functional mobility in patients with Mucopolysaccharidosis. Unfortunately, Covid has delayed this research project.

September 2019

CSAC was formally established with the first Board Meeting Agenda Report being delivered at the September meeting. Previously there had been an informal Research committee. The committee consists of 5 members, with Professor Bryan Winchester as chair. CSAC review grants, organising for them to be peer reviewed if necessary and then reports to the Board with recommendations for approval after they have been evaluated.

2017

Dr Ramaswami £15,000:
RFH London

Fabry Pain app.

Dr Wilcox & Dr Sharma £12,000:
Salford Royal Hospital NHS Trust, Manchester

Bio-viability of Genistein.

Dr Brian Bigger / Dr Simon Jones £20,000:
University hospital & RMCH Manchester

A phase III double blinded placebo controlled clinical trial of high dose oral genistein aglycone in MPS III Extension study.

2016

Dr Hiwot £47,650:
Queen Elizabeth Hospital Birmingham

Fabry Cardiac device study.

Dr Brian Bigger / Dr Simon Jones £10,000:
University hospital & RMCH Manchester

A phase III double blinded placebo controlled clinical trial of high dose oral genistein aglycone in MPS III Yr 3 funding.

2015

Dr Simon Heales £34,000:
UCL London
Antibody testing in LSD diseases.

Dr Derralynn Hughes £20,000:
RFH London
Genotype-Phenotype Relationships in Fabry Disease to Stratify Severity and Understand Heterogeneity using Extended Family Pedigrees.

Dr Ghosh & Dr Jones £10,000
Immune tolerance induction regimen in severe MPS I

Dr Brian Bigger / Dr Simon Jones £60,000:
University hospital & RMCH Manchester
A phase III double blinded placebo controlled clinical trial of high dose oral genistein aglycone in MPS III Yr 2 funding.

2014

Dr Brian Bigger / Dr Simon Jones £40,000:
University hospital & RMCH Manchester
A phase III double blinded placebo controlled clinical trial of high dose oral genistein aglycone in MPS III Yr 1 funding.

2013

Dr Brian Bigger £150,000:
University Hospital Manchester
Year three of pre clinical trial for Genistein.

2012

Dr Brian Bigger £150,000:
University Hospital Manchester
Year two of pre clinical trial for Genistein.

2011

Dr Chris Hendriksz £4,000:
Birmingham Children's Hospital, Birmingham, UK
Year three of a three year project looking at new imaging techniques and to develop appropriate assessment scales to measure cognitive decline by use of new psychological methods in children with lysosomal storage diseases.

Dr Brian Bigger £150,000:
University Hospital Manchester
Year one of pre clinical trial for Genistein.

2010

Prof Timothy Cox & Dr Patrick Deegan £31,318:
Addenbrookes Hospital, University of Cambridge, England
Year two of an 18 month extension grant to establish what lies at the core of the difference between two x-linked lysosomal storage disorders, MPSII, Hunter disease, and Fabry disease, by determining why females harbouring one copy of the defective gene for MPSII almost never develop the condition, whereas females carrying a single Fabry disease gene nearly always suffer from the disorder.

Dr Brian Bigger £156,750:
MPS Stem Cell Research Group, University of Manchester, UK
A one year grant to study Genistein and synaptic decline in MPS IIIB. This grant includes the cost of a technician, senior post doc researcher and animals, consumables and equipment and a £4000 travel grant.

Dr Brian Bigger £7,000:
MPS Stem Cell Research Group, University of Manchester, UK
To investigate the hypothesis that brain degeneration in MPS III, Sanfilippo mice is reversible after long-term substrate reduction therapy.

Dr Brian Bigger £6,000:
MPS Stem Cell Research Group, University of Manchester, UK
To investigate the effect of heparan sulphate on stem cell homing and engraftment on MPS I.

Dr David Begley £20,000:
Kings College London, UK
A grant to provide six month's funding to support the cost of maintaining the MPS IIIA and MPS IIIB mice colony and laboratory consumables for research into the involvement of the blood brain barrier in MPS IIIA and MPS IIIB.

Dr James Edmond Wraith, Dr Rob Wynn & Dr Brian Bigger £64,886:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Final year of a five year programme grant to establish the Stem Cell Therapy Group with funding for a Senior Research Fellow at the University of Manchester. The post-holder was to be responsible for establishing and leading a research group in stem cell therapy in inherited disorders of Mucopolysaccharide metabolism.

Prof Timothy Cox & Dr Patrick Deegan £32,000:
Addenbrookes Hospital, University of Cambridge, England
Year one of an 18 month extension grant to establish what lies at the core of the difference between two x-linked lysosomal storage disorders, MPSII, Hunter disease, and Fabry disease, by determining why females harbouring one copy of the defective gene for MPSII almost never develop the condition, whereas females carrying a single Fabry disease gene nearly always suffer from the disorder.

Dr Brian Bigger £20,000:
MPS Stem Cell Research Group, University of Manchester, UK
Second year of a two year grant for improving enzyme secretion and tracking in lentiviral mediated stem cell gene therapy of MPS III. NOTE: Made possible by a grant from the Irish MPS Society.

Dr Brian Bigger £6,500:
MPS Stem Cell Research Group, University of Manchester, UK
Travel grant to the MPS Stem Cell Group.

Dr Chris Hendrickz £4,000:
Birmingham Children's Hospital, Birmingham, UK
Year two of a three year project looking at new imaging techniques and to develop appropriate assessment scales to measure cognitive decline by use of new psychological methods in children with lysosomal storage diseases.

Dr Blundell £12,000
Develop methods for assessing cognitive ability

2009

Dr Brian Bigger £20,000:
MPS Stem Cell Research Group, University of Manchester, UK
First year of a two year grant for improving enzyme secretion and tracking in lentiviral mediated stem cell gene therapy of MPS III. NOTE: Made possible by a grant from the Irish MPS Society.

Dr Chris Hendrickz £4,000:
Birmingham Children's Hospital, Birmingham, UK
Year one of a three year project looking at new imaging techniques and to develop appropriate assessment scales to measure cognitive decline by use of new psychological methods in children with lysosomal storage diseases.

Professor Elsa Shapiro $49,500:
University of Minnesota in Minneapolis USA
To investigate the cognitive, adaptive, quality of life and psycho-social outcomes of children who are at least one year post Haemopoietic Stem Cell Transplant for MPS IH, Hurler disease. This investigation will build upon the data collected in the Society's previous three year psycho-social research project and result in publications.

Dr James Edmond Wraith, Dr Rob Wynn & Dr Brian Bigger £63,183:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year four of a five year programme grant to establish the Stem Cell Therapy Group with funding for a Senior Research Fellow at the University of Manchester. The post-holder was to be responsible for establishing and leading a research group in stem cell therapy in inherited disorders of Mucopolysaccharide metabolism.

Professor Bob Jolly £2,750:
Massey University, Palmerston, North Island, New Zealand
One year grant to fund physiological principles underlying Intrathecal ERT in lysosomal storage diseases.

Dr Brian Bigger £6,500:
MPS Stem Cell Research Group, University of Manchester, UK
Travel grant to the MPS Stem Cell Group.

2008

Prof Grzegorz Wegrzyn £40,000:
University of Gdansk, Poland

Fourth year extension grant to develop "Gene Expression-Targeted Isoflavone Therapy (GET IT) for Mucopolysaccharidosis Type III, Sanfilippo disease". The hypothesis was based on reducing the substrate, heparan sulphate, that cannot be degraded in lysosomes of affected patients due to a defect in one of the enzymes. NOTE: £20,000 funded by the UK MPS Society and the other £20,000 funded by ten international MPS Societies

Dr James Edmond Wraith, Dr Rob Wynn & Dr Brian Bigger £61,473:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year three of a five year programme grant to establish the Stem Cell Therapy Group with funding for a Senior Research Fellow at the University of Manchester. The post-holder was to be responsible for establishing and leading a research group in stem cell therapy in inherited disorders of Mucopolysaccharide metabolism.

Sarah Long Up to £5,000:
University of Bath, Bath, England

'Tipping the Lens' was a participatory social documentary project enabling young people aged 11 years and over living with MPS IVA, Morquio disease, to develop their own narratives using their own words and visual images. The project involved staging an exhibition at the expert meeting on Morquio disease held in August 2008, writing up the research as part of the researcher's academic studies and producing a DVD.

Jenny Noble £16,000:
Lysosomal Storage Diseases New Zealand

A one-off grant to host an international consensus meeting for bone diseases in lysosomal storage diseases on the use of bisphosphonate therapy in Oligosaccharides held in Christchurch, New Zealand, 19-20 November 2008.

Dr Brian Bigger £33,625:
MPS Stem Cell Group, University of Manchester

Year three of a three year grant fund a technician and part time PhD student to investigate non-myeloablative bone marrow transplantation for mucopolysaccharide diseases.

Dr Brian Bigger £20,000:
MPS Stem Cell Group, University of Manchester

Year three of a three year grant to fund the costs of a PhD student to work on making cord blood transplant a safer way to treat those with MPS I Hurler and to develop methods in which the bone marrow can be used as a vehicle to transport missing genes into the bone and brain.

Dr Brian Bigger £30,000:
MPS Stem Cell Group, University of Manchester

Matched funding with the University of Manchester towards a strategic studentship developing a lentiviral vector to deliver the missing enzyme to cells transplanted into mice with MPS III.

2007

Prof Timothy Cox & Dr Patrick Deegan £89,202:
Addenbrookes Hospital, University of Cambridge, England

Final year of a three-year grant to establish what lies at the core of the difference between two x-linked lysosomal storage disorders, MPSII, Hunter disease, and Fabry disease, by determining why females harbouring one copy of the defective gene for MPSII almost never develop the condition, whereas females carrying a single Fabry disease gene nearly always suffer from the disorder.

Prof Grzegorz Wegrzyn £50,000:
University of Gdansk, Poland

Final year of a three-year project to develop "Gene Expression-Targeted Isoflavone Therapy (GET IT) for Mucopolysaccharidosis Type III, Sanfilippo disease". The hypothesis was based on reducing the substrate, heparan sulphate, that cannot be degraded in lysosomes of affected patients due to a defect in one of the enzymes.

Dr Brian Bigger £8,000:
MPS Stem Cell Group, University of Manchester

Travel grant to the MPS Stem Cell Group.

Dr Brian Bigger £20,000:
MPS Stem Cell Group, University of Manchester

Year two of a three year grant to fund the costs of a PhD student to work on making cord blood

transplant a safer way to treat those with MPS I Hurler and to develop methods in which the bone marrow can be used as a vehicle to transport missing genes into the bone and brain.

Dr Brian Bigger £30,000:
MPS Stem Cell Group, University of Manchester

Year two of a three year grant fund a technician and part time PhD student to investigate non-myeloablative bone marrow transplantation for mucopolysaccharide diseases.

Dr James Edmond Wraith, Dr Rob Wynn & Dr Brian Bigger £60,418:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year two of a five year programme grant to establish the Stem Cell Therapy Group with funding for a Senior Research Fellow at the University of Manchester. The post-holder was to be responsible for establishing and leading a research group in stem cell therapy in inherited disorders of Mucopolysaccharide metabolism.

2006

Dr Brian Bigger £111,750:
MPS Stem Cell Group, University of Manchester

The identification of stem cell populations with a capacity to compliment the major deficiencies in MPS diseases.

Dr Brian Bigger £20,000:
MPS Stem Cell Group, University of Manchester

Year one of a three year grant to fund the costs of a PhD student to work on making cord blood transplant a safer way to treat those with MPS I Hurler and to develop methods in which the bone marrow can be used as a vehicle to transport missing genes into the bone and brain.

Prof Timothy Cox & Dr Patrick Deegan £70,912:
Addenbrookes Hospital, University of Cambridge, England

Year two of a three-year grant to establish what lies at the core of the difference between two x-linked lysosomal storage disorders, MPSII, Hunter disease, and Fabry disease, by determining why females harbouring one copy of the defective gene for MPSII almost never develop the condition, whereas females carrying a single Fabry disease gene nearly always suffer from the disorder.

Prof Grzegorz Wegrzyn £50,000:
University of Gdansk, Poland

Year two of a three-year project to develop "Gene Expression-Targeted Isoflavone Therapy (GET IT) for Mucopolysaccharidosis Type III, Sanfilippo disease". The hypothesis was based on reducing the substrate, heparan sulphate, that cannot be degraded in lysosomes of affected patients due to a defect in one of the enzymes.

Dr James Edmond Wraith, Dr Rob Wynn & Dr Brian Bigger £59,008:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year one of a five year programme grant to establish the Stem Cell Therapy Group with funding for a Senior Research Fellow at the University of Manchester. The post-holder was to be responsible for establishing and leading a research group in stem cell therapy in inherited disorders of Mucopolysaccharide metabolism.

Dr Brian Bigger £30,000:
MPS Stem Cell Group, University of Manchester

Year one of a three year grant fund a technician and part time PhD student to investigate non-myeloablative bone marrow transplantation for mucopolysaccharide diseases.

2005

Prof Timothy Cox & Dr Patrick Deegan £71,521:
Addenbrookes Hospital, University of Cambridge, England

Year one of a three-year grant to establish what lies at the core of the difference between two x-linked lysosomal storage disorders, MPS II, Hunter disease, and Fabry disease, by determining why females harbouring one copy of the defective gene for MPS II almost never develop the condition, whereas females carrying a single Fabry disease gene nearly always suffer from the disorder.

Prof Grzegorz Wegrzyn £60,000:
University of Gdansk, Poland

Year one of a three-year project to develop Gene Expression-Targeted Isoflavone Therapy (GET

IT) for Mucopolysaccharidosis Type III, Sanfilippo disease. The hypothesis was based on reducing the substrate, heparan sulphate, that cannot be degraded in lysosomes of affected patients due to a defect in one of the enzymes.

Cheryl Pitt & Christine Lavery £40,000:
The Society for Mucopolysaccharide Diseases, UK

Final year of a three-year investigation into the psycho, social outcomes of bone marrow transplantation in MPSI, Hurler disease.

2004

Dr David Begley £45,959:
King's College Hospital, London, England

A one-year grant to research the involvement of the Blood-Brain Barrier in MPS IIIA and B, Sanfilippo disease, by comparing and quantifying the Blood-Brain Barriers (BBBs) permeability to solutes of defined molecular weight and physico-chemical characteristics in two mouse models of MPS IIIA and MPS IIIB and in wild type mice.

Cheryl Pitt & Christine Lavery £40,000:
The Society for Mucopolysaccharide Diseases

Year two of a three-year investigation into the psychosocial outcomes of bone marrow transplantation in MPSI, Hurler disease.

Dr Bryan Winchester & Dr Clare Beesley £75,000:
Institute of Child Health, London, England

Final year of a two-year project to identify putative biomarkers in MPS disorders and investigate at a molecular level the secondary effects of GAG storage, recognising that biomarkers could be a useful tool to monitor the effectiveness of treatments.

2003

Cheryl Pitt & Christine Lavery £40,000:
The Society for Mucopolysaccharide Diseases

Year one of a three-year investigation into the psychosocial outcomes of bone marrow transplantation in MPS I, Hurler disease.
Bone marrow transplant (BMT) is considered the treatment of choice for the more severe form of MPS I, Hurler disease. However, the treatment is not a cure, is high risk, and has its limitations. The main limitations of BMT are that it cannot reverse neurological damage already caused by the disease prior to treatment, and it cannot prevent joint and bone problems that are characteristic of MPS I, from developing. Children with MPS I, Hurler, who have had a BMT therefore go on to experience various degrees of learning difficulties and physical disabilities. Over time their mobility is likely to decrease and they are likely to experience a forced dependence on their families. However, the psychosocial and development of these children had been neglected as a topic of research. The MPS Society therefore undertook an ethically approved research project to explore the psychological and social outcomes of BMT for this group of patients.

Dr Bryan Winchester & Dr Clare Beesley £72,824:
Institute of Child Health, London, England

Year one of a two-year project to identify putative biomarkers in MPS disorders and investigate at a molecular level the secondary effects of GAG storage, recognising that biomarkers could be a useful tool to monitor the effectiveness of treatments.

Dr Rob Wynn, Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Final year of a three-year project to study the sue of Mesenchymal stem cells (MSCs) to target cells to correct the enzyme defect in MPS II, Hunter, and MPSIII, Sanfilippo, patients. The study included the testing of the hypothesis that MSCs from MPS II patients can be transduced with the retroviral vector containing the IDSG.

2002

Dr Rob Wynn £35,786:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year two of a three-year project to study the sue of Mesenchymal stem cells (MSCs) to target cells to correct the enzyme defect in MPS II, Hunter, and MPS III, Sanfilippo, patients. The study included the testing of the hypothesis that MSCs from MPSII patients can be transduced with the retroviral vector containing the IDSG.

Dr James Edmond Wraith £190,787:

Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England Dr Rob Wynn, Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England, Dr Bryan Winchester Institute of Child Health, London, England

Final year of a three-year two-centre programme grant:

- To establish the molecular basis of novel mutations found in patients with MPSI, Hurler disease, and MPSIII, Sanfilippo disease
- To develop gene therapy for MPS diseases using herpes virus vectors
- To develop gene therapy using bone marrow cells and to investigate how the patient tolerates these new cells
- To produce antibodies for use in gene therapy

Dr Rob Wynn £35,786:

Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year two of a three-year project to study the sue of Mesenchymal stem cells (MSCs) to target cells to correct the enzyme defect in MPS II, Hunter, and MPS III, Sanfilippo, patients. The study included the testing of the hypothesis that MSCs from MPSII patients can be transduced with the retroviral vector containing the IDSG.

2001

Dr Rob Wynn £24,869:

Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year one of a three-year project to study the sue of Mesenchymal stem cells (MSCs) to target cells to correct the enzyme defect in MPS II, Hunter, and MPS III, Sanfilippo, patients. The study included the testing of the hypothesis that MSCs from MPS II patients can be transduced with the retroviral vector containing the IDSG.

Dr James Edmond Wraith £203,079:

Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England Dr Rob Wynn Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England, Dr Bryan Winchester, Institute of Child Health, London, England

Year two of a three-year two-centre programme grant:

- To establish the molecular basis of novel mutations found in patients with MPSI, Hurler disease, and MPSIII, Sanfilippo disease
- To develop gene therapy for MPS diseases using herpes virus vectors
- To develop gene therapy using bone marrow cells and to investigate how the patient tolerates these new cells
- To produce antibodies for use in gene therapy

2000

Dr James Edmond Wraith £186,000:

Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England Dr Rob Wynn, Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England, Dr Bryan Winchester Institute of Child Health, London, England

Year one of a three-year two-centre programme grant:

a) To establish the molecular basis of novel mutations found in patients with MPS I, Hurler disease, and MPS III, Sanfilippo disease
b) To develop gene therapy for MPS diseases using herpes virus vectors
c) To develop gene therapy using bone marrow cells and to investigate how the patient tolerates these new cells
d) To produce antibodies for use in gene therapy

The Mucopolysaccharidoses (MPS) result from genetic defects in enzymes involved in the turnover of large molecules call glycosaminoglycans (GAGs) which are important in maintaining the body's skeleton and brain function. Research indicated that it might be possible to replace the defective enzyme in MPS by putting a good copy of the gene that is responsible for the synthesis of the defective enzyme into the patient's cells – gene therapy. The major problems with gene therapy are rejection of the replacement protein by the immune system of the body, getting the enzyme into all tissues, particularly the brain, and the short life of the replacement gene or enzyme. These projects sought to solve these problems.

Dr James Edmond Wraith £31,000:

Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

To fund 50% of the final year of a three-year appointment for a second Consultant Paediatrician to specialise in the diagnosis and clinical

management of MPS children and their families throughout the United Kingdom.

Dr Guy Besley £39,016: Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Final year of a three-year grant to extend the range of mutation analyses offered to MPS families by employing a dedicated member of staff to undertake these investigations.

1999

Dr James Edmond Wraith £28,000;
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
To fund 50% of year two of a three-year appointment for a second Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom.

Dr Guy Besley £37,918:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year two of a three-year grant to extend the range of mutation analyses offered to MPS families by employing a dedicated member of staff to undertake these investigations.

Dr Robin Coffin £42,012:
University College London Medical School, London, England
Final year of a two-year grant to research gene therapy for Mucopolysaccharide diseases using herpes simplex virus vectors.

Dr Bryan Winchester £44,000:
Institute of Child Health, London, England
Final year of a four-year grant to establish mutational analysis in patients with Mucopolysaccharidoses types MPS I, MPS IIIA and MPS IIIB as a prerequisite for gene therapy and enzyme replacement therapy.

1998

Dr James Edmond Wraith £26,000:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
To fund 50% of year one of a three-year appointment for a second Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom.

Dr Guy Besley £44,268:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year one of a three-year grant to extend the range of mutation analyses offered to MPS families by employing a dedicated member of staff to undertake these investigations.

Dr Robin Coffin £37,910:
University College London Medical School, London, England
Year one of a two-year grant to research gene therapy for Mucopolysaccharide diseases using herpes simplex virus vectors.

Prof John Hopwood £15,000:
Adelaide Women and Children's Hospital, Adelaide, Australia
Final six months of an 18-month grant to develop high yielding expression systems to enable enzyme replacement therapy for MPS IVA, Morquio disease.

Dr Bryan Winchester £43,725:
Institute of Child Health, London, England
Year three of a four-year grant to establish mutational analysis in patients with Mucopolysaccharidoses types MPS I, MPS IIIA and MPS IIIB as a prerequisite for gene therapy and enzyme replacement therapy.

1997

Dr Bryan Winchester £43,725:
Institute of Child Health, London, England
Year two of a four-year grant to establish mutational analysis in patients with Mucopolysaccharidoses types MPS I, MPS IIIA and MPS IIIB as a prerequisite for gene therapy and enzyme replacement therapy.

Dr Linda Lashford £15,000:
Patterson Institute, Christie Hospital, Manchester, England
50% of the final year of a two-year grant to optimise retro-viral vectors for gene delivery to the haemopoietic system in MPS I, Hurler disease.

Dr Bryan Winchester £1,200:
Institute of Child Health, London, England
To look for mutations in Alpha Mannosidosis patients in collaboration with the Norwegian group at the University of Tromso who isolated the gene.

Dr James Edmond Wraith £41,880:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Final year of a two-year grant working collaboratively with Dr Linda Lashford to support the clinical development of gene therapy by studying the efficacy of transplanted autologous retroviral transduced bone marrow in patients with MPSI, Hurler disease, and the development of gene transfer as a treatment strategy for patients with MPS II, Hunter disease.

Prof John Hopwood £30,000:
Adelaide Women and Children's Hospital, Adelaide, Australia
Year one of an 18-month grant to develop high yielding expression systems to enable enzyme replacement therapy for MPS IVA, Morquio disease

1996

Dr Charles Pennock £2,500:
South Mead Health Services, Bristol, England
A grant to cover costs of reagents and consumables in identifying mutations of the iduronidase gene for MPS I.

Dr Bryan Winchester £5,000:
Institute of Child Health, London, England
A grant to cover 5/8 for consumables for experimental gene therapy for Fucosidosis.

Dr Linda Lashford £16,295:
Patterson Institute, Christie Hospital, Manchester, England
50% of the first year of a two-year grant to optimise retro-viral vectors for gene delivery to the haemopoietic system in MPS I, Hurler disease.

Dr Bryan Winchester £36,797:
Institute of Child Health, London, England
Year one of a four-year grant to establish mutational analysis in patients with Mucopolysaccharidoses types MPS I, MPS IIIA and MPS IIIB as a prerequisite for gene therapy and enzyme replacement therapy.

Dr James Edmond Wraith £41,100:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year one of a two-year grant working collaboratively with Dr Linda Lashford, to support the clinical development of gene therapy by studying the efficacy of transplanted autologous retroviral transduced bone marrow in patients with MPS I, Hurler disease, and the development of gene transfer as a treatment strategy for patients with MPS II, Hunter disease.

1995

Dr Linda Lashford £16,000:
Patterson Institute, Christie Hospital, Manchester, England
The cost of meeting quality control procedures necessary to manufacture clinical trial grade material for gene therapy for MPS I, Hurler disease.

Dr Gail Lebens £18,000:
Patterson Institute, Christie Hospital, Manchester, England
Final year of a three-year grant to develop "Gene Therapy for MPS I, Hurler disease".

1994

Dr Bryan Winchester £15,635:
Institute of Child Health, London, England
One year grant to carry out mutation analysis of MPS in a research setting.

Dr Gail Lebens £16,000:
Patterson Institute, Christie Hospital, Manchester, England
Year two of a three-year grant to develop "Gene Therapy for MPS I, Hurler disease".

1993

Miss Lesley Heptinstall £9,000:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Final year of a three-year grant (60% of annual salary) to fund the post of senior biochemist applying DNA technology to the diagnosis and carrier testing for MPS diseases.

Dr Ruth McDermott £15,000:
Patterson Institute, Christie Hospital, Manchester, England
Year one of a three-year grant to develop "Gene Therapy for MPS I, Hurler disease".

1992

Miss Lesley Heptinstall £11,000:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year two of a three-year grant (60% of annual salary) to fund the post of senior biochemist applying DNA technology to the diagnosis and carrier testing for MPS diseases.

Dr James Edmond Wraith £18,000:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Six-month extension to final year grant of a four-year appointment as Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom. At this point Salford Health Authority took over the responsibility for funding Dr Wraith's post of Consultant Paediatrician

1991

Dr Bryan Winchester £1,000:
Institute of Child Health, London, England
Consumables to facilitate the biochemical screening in the diagnosis of children with MPS III, Sanfilippo disease.

Miss Lesley Heptinstall £10,000:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year one of a three-year grant (60% of annual salary) to fund the post of senior biochemist applying DNA technology to the diagnosis and carrier testing for MPS diseases.

Dr John Walters £36,000:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year one of a two-year appointment for a second Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom. This grant was discontinued after one year and Salford Health Authority took over the funding of this post.

Dr James Edmond Wraith £27,700:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Final year of a four-year appointment as Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom.

1990

Dr Steven Alani £200:
Hope Hospital, Manchester, England
To attend the fifth European congress of neurophysiology.

Dr James Edmond Wraith £25,300:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year three of a four-year appointment as Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom.

1989

Dr Martin Bax £15,000:
Westminster Children's Hospital, London, England
A study over 1 year to describe the feeding difficulties of children with MPS diseases.

Dr James Edmond Wraith £31,254:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England
Year two of a four-year appointment as Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom.

1988

Prof John Hopwood In Kind:
Adelaide Women and Children's Hospital, Adelaide, Australia
Organised the collection and despatch of over 100 blood samples from MPS II, Hunter children, and MPS I, Hurler children, which in 1990 and 1991 respectively resulted in the isolation of the genes for these diseases.

Dr Charles Pennock £300:
Bristol Maternity Hospital, Bristol, England
Cost of couriering blood samples from parents of children with MPS III, Sanfilippo disease, in order that carrier detection using a method described by Dr Ruben Matelon in the USA, could be undertaken.

Dr James Edmond Wraith £34,272:
Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, England

Year one of a four-year appointment as Consultant Paediatrician to specialise in the diagnosis and clinical management of MPS children and their families throughout the United Kingdom. At the end of this four-year grant, Salford Health Authority agreed to take over the responsibility for Dr Wraith's continuing funding in this field.

Dr Irwin Olsen £5,000:
Mathilda and Terrence Kennedy Institute, London, England

Final year of a two-year grant to fund PhD student, Mr George Bou-Gharios, to study the use of the electron-microscope for cell to cell transfer of lysosomal enzymes from lymphocytes.

Dr Diana Chase £6,000:
Unilever Research Laboratories, London, England

A six-month extension to continue to attempt to isolate the Hunter enzyme.
Athough Dr Chase's attempt was not successful, her work did result in some biochemical developments for another metabolic condition, Wilson's disease.

Dr Martin Bax & Dr John Watters £10,500:
Westminster Children's Hospital, London, England

A project to continue to study the sleep disturbance of children with MPSIII, Sanfilippo disease, involving detailed observations of children's sleep patterns in their homes.

1987

Dr Irwin Olsen £5,000:
Mathilda and Terrence Kennedy Institute, London, England

First year of a two-year grant to fund PhD student, Mr George Bou-Gharios, to study the use of the electron-microscope for cell to cell transfer of lysosomal enzymes from lymphocytes.

Dr Diana Chase £12,000:
Unilever Research Laboratories, London, England

An attempt to isolate the MPSII deficient enzyme from other proteins and to study its structure.

Dr Martin Bax and Mrs Gillian Colville £10,000:
Westminster Children's Hospital, London, England

A psychosocial research project to look specifically at three major problems identified in the earlier natural history study of MPS diseases.

- Developmental assessments for children with MPS I Hurler, Hurler Scheie and Scheie disease
- To establish the distinction between boys with progressive neuro-degeneration of MPS II, Hunter disease and those with a more attenuated form
- Behavioural and sleep problems in children with MPS III, Sanfilippo disease.

1986

Mr Ben Taylor £1,335:
University College Hospital, London, England

To attend a conference on spinal cord monitoring and to work alongside Dr Steven Kopits in his MPSIVA, Morquio clinic in Baltimore, USA.

Prof Matteo Adinolfi & Dr Diana Chase In Kind:
Guy's Hospital, London, England

Over 50 families of children with MPS II, Hunter disease, provided hair root samples and donated 10ml of blood for research to establish a simple screening test method for Hunter carrier status.

Dr Steven Kopits £4,200:
Saint Joseph's Hospital, Baltimore, USA

Introduction of a specialist technique to fuse the cervical spines of children with MPS IVA, Morquio disease. This resulted in the first successful surgery of its kind in England performed jointly by Dr Kopits and Mr Andrew Ransford and his team at University College Hospital, London, England. Children and adults with Morquio disease now receive this treatment which has been developed and refined over the last 20 years in London, Birmingham and Manchester. Without this surgery, children with underdeveloped or missing occipital pegs at C1 and C2 of the cervical spine, or developing compression of the cervical spine, usually develop paraplegia or quadriplegia and die at a much earlier age.

Dr Irwin Olsen £3,000:
Mathilda and Terrence Kennedy Institute, London, England
The purchase of a fluorimeter to rapidly and accurately measure minute quantities of the deficient enzyme in cells and tissues from MPS children.

Dr Martin Bax £10,000:
Westminster Children's Hospital, London, England
Year 2 of a systematic study of the natural history of MPS disease involving over 200 MPS families.

1985

Dr Martin Bax £10,000:
St Mary's Hospital, London, England
A systematic study of the natural history of the Mucopolysaccharidoses in affected children. Year 1 of the grant to study over 80 affected families through questionnaires and home visits.

1984

Dr Irwin Olsen £3,700:
Mathilda and Terrence Kennedy Institute, London, England
Automated sampling and recording equipment to facilitate the measurement of changes in enzyme activity in cells from MPS children.

Dr Lubec In Kind:
Vienna Children's Hospital, Vienna, Austria
Samples of hair from MPS children, their siblings and parents provided in order to carry out further research into the early detection and screening for MPS.

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