TOWARDS A CURE

MARTINE WALMSLEY, HEAD OF RESEARCH STRATEGY

02 MAY 2025

www.pscsupport.org.uk

TOWARDS A CURE

- WHY IS RESEARCH SO IMPORTANT TO US?
- OPPORTUNITIES
- CHALLENGES
- PRIORITIES
- MEET THE RESEARCHERS
- GETTING TREATMENTS FASTER
- RESEARCH HIGHLIGHTS FROM LAST YEAR
- HOW YOU CAN HELP

PSC SUPPORT

Vision to see a world without PSC

Mission to improve the lives of people with primary sclerosing cholangitis through **research**, support and information, and improved patient care

WHY IS RESEARCH SO IMPORTANT TO US?

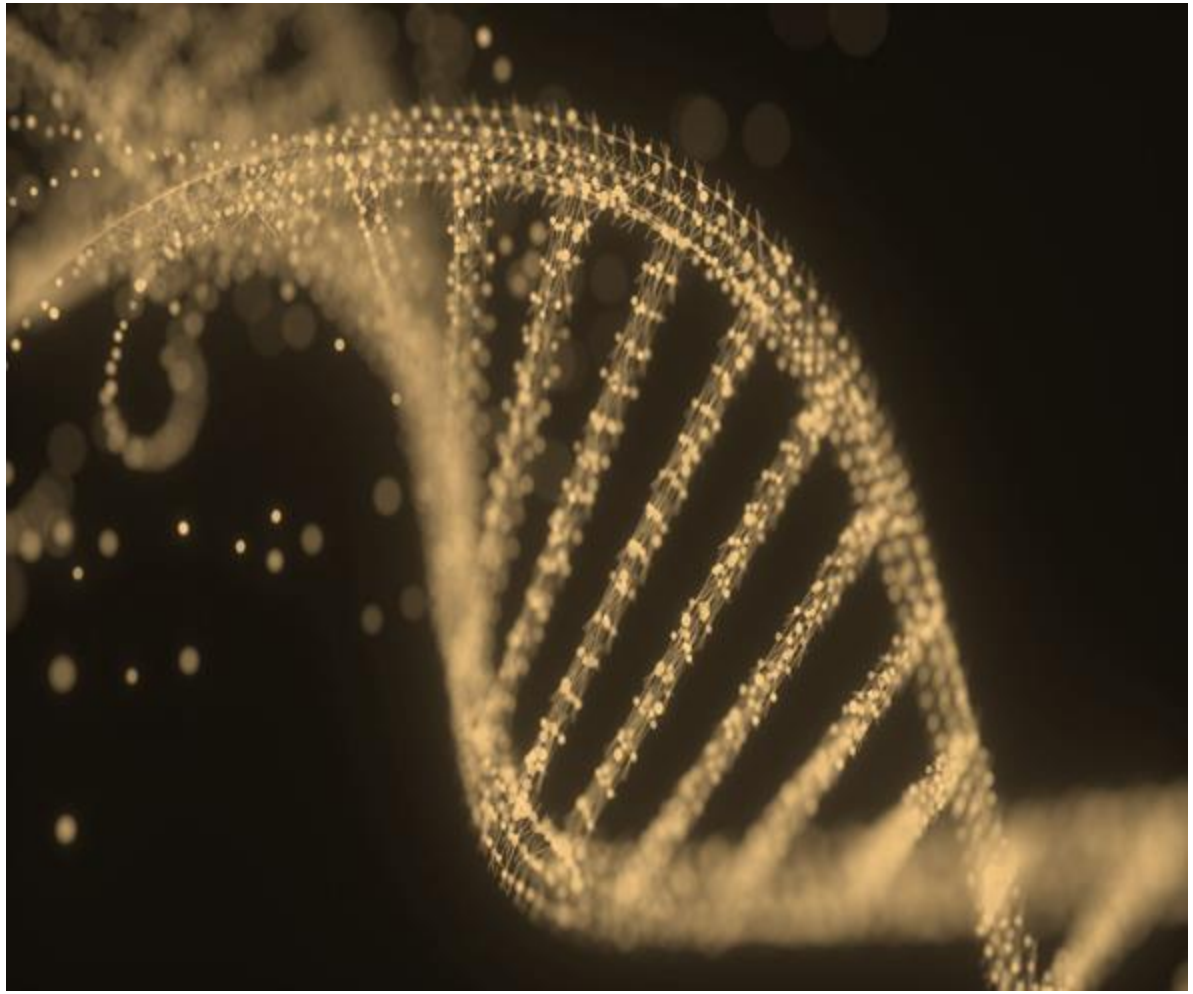
- Quick and definitive diagnosis
- Confidence in care (tailored and, personalised)
- Effective, curative treatment and no cancer risk
- No symptoms or complications
- Achieve full potential (work, education, family)

OPPORTUNITIES

- Clinical trials
- Tests to diagnose PSC, cancers and rPSC early (promising results)
- Biobanks
- An evolving research landscape and new technologies

SO, WHAT'S THE PROBLEM?

WHY? PSC RESEARCH IS HARD!



- No single pathway to a treatment - no silver bullet
- Rare and varied population
- Lack of fit for purpose tests
- Inadequate cancer and rPSC detection
- Biological test results don’t relate to how we feel and function

OUR PRIORITIES

Unlock understanding

- Generate fundamental scientific knowledge about PSC

Uncover biological processes underlying PSC

Establish biological markers

Monitor and predict disease progression

Detect cancer

Accelerate treatment development

- Fast-track the development of effective treatments

New trial designs

Repurposing existing drugs

stop worsening disease

manage symptoms

reduce cancer risk

improve quality of life

Promote personalised care

- Make healthcare work for people with PSC

Better evidence for treating PSC

Tools to assess symptoms

Timely and compassionate care

Access to psychological support

MEET THE RESEARCHERS

Dr James Sun

Alice Freer

Dr Rodrigo Motta

Characterising genetic changes in the bile ducts in PSC

Dr James Sun

Pre-doctoral Clinical Research Excellence Fellow

King's Health Partners Centre for Translational Medicine and The Francis Crick Institute

PSC Support Information Day – The Celtic Manor Resort

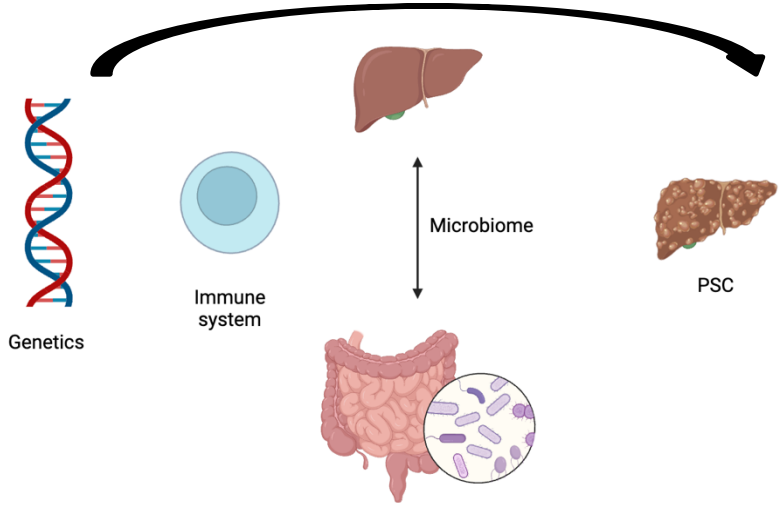
3 May 2025

Background

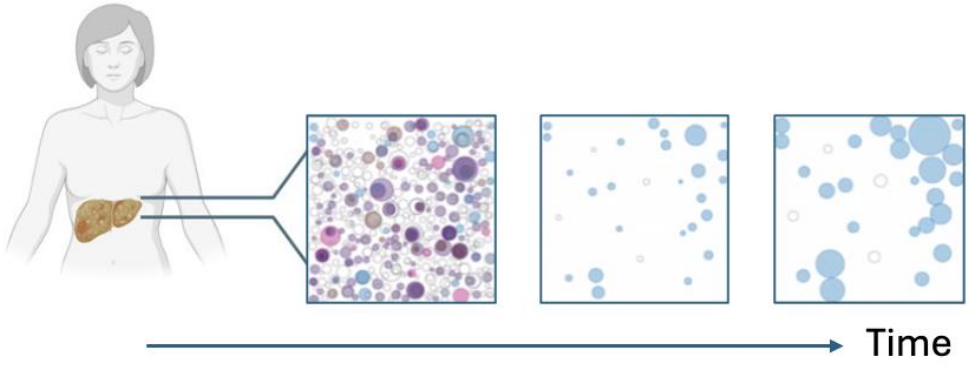
The cause of PSC is still unknown

We have no medical treatments

Liver transplantation is limited

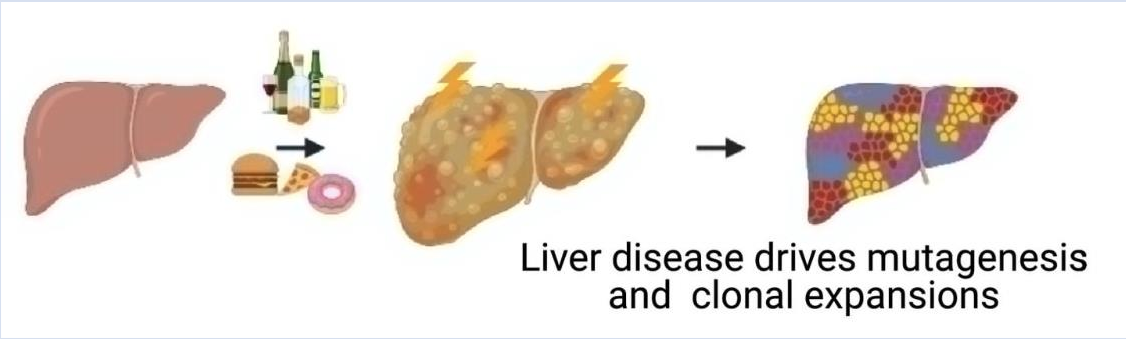


Somatic mutations occur during our life



Identify the driver mutations

Somatic mutations in liver disease

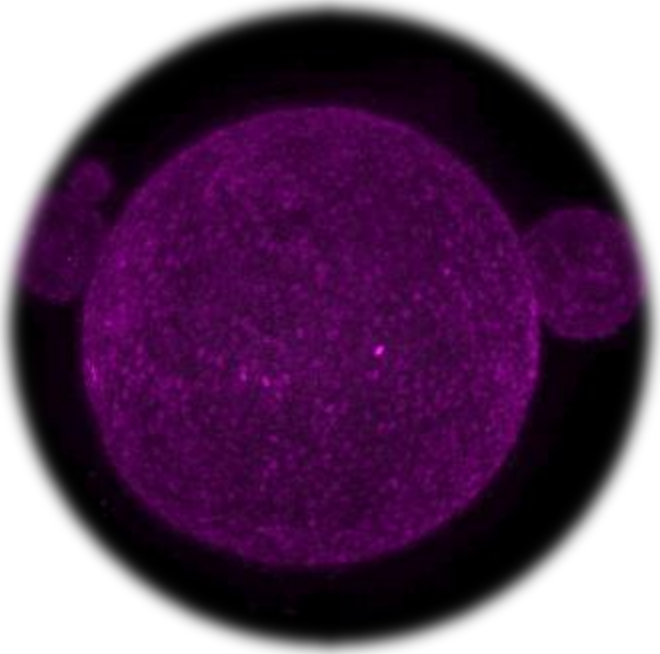


Olafsson, Sigurgeir et al.
Trends in Genetics, Volume 37, Issue 10, 872 - 881

Somatic mutations in bile duct cells in PSC have not been studied before

What do I aim to achieve?

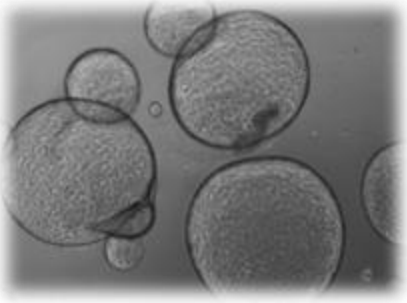
1. Analyse genetic makeup of bile ducts in PSC
2. Use bile duct organoids to model the effect of genetic changes



What am I doing?

Tissue collection

DNA sequencing



Organoid model

How could this help people with PSC?

THE FRANCIS CRICK INSTITUTE

Identify high/lower risk subgroups

Find potential drug targets

Who are the study team?

THE FRANCIS CRICK INSTITUTE

Supervisors

Foad Rouhani
Somatic mutation expert
Group leader at Francis Crick Institute
KCH Liver Transplant Surgeon

Alberto Sanchez-Fueyo
Translational research expert
Professor of Hepatology
Deputy Director RW-ILS

Collaborator

Deepak Joshi
Consultant Hepatologist
KCH Endoscopy lead

Thank you to patients, their families and my funders

THE FRANCIS CRICK INSTITUTE

Please feel free to contact me if you have any specific questions

james.sun@nhs.net

UKRI Medical Research Council

UCL

Imperial College London

King's College London

wellcome

CANCER RESEARCH UK

How central and peripheral mechanistic factors link to the variability and severity of **fatigue** in PSC- **SOLVE Fatigue**

Alice Freer

BSc Physiotherapy

MRes Health Research

HEE Masters to PhD Internship

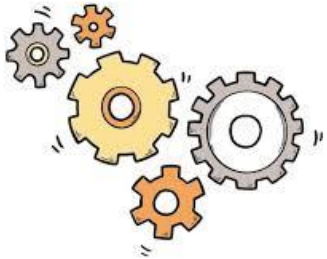
Research Fellow at University of Birmingham

Problem

Fatigue affects 7/10

Defined as central or peripheral

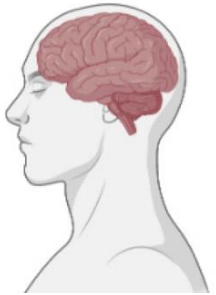
Mechanisms



Treatments

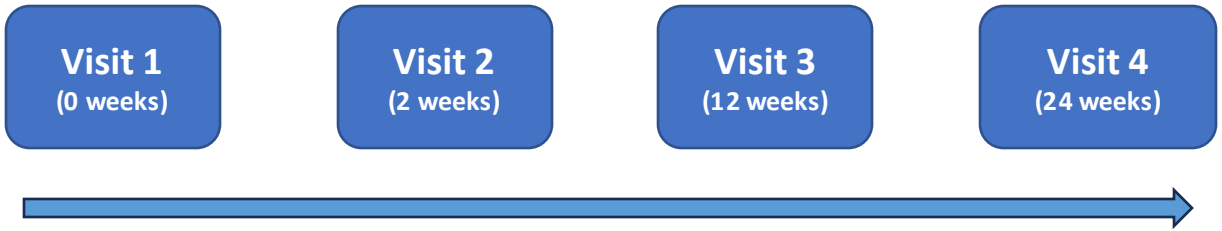
Aim

- Assess the extent of peripheral and central fatigue in PSC



- Determine the relationship between peripheral and central mechanisms of fatigue and their contributions to disease severity

Methods

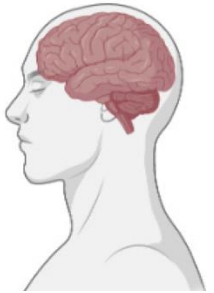


- Self reported questionnaires
- General observations
- Exercise test (walking and breathing tests)
- Muscle testing (muscle ultrasound)
- Central nervous system test (non-invasive electrical testing)
- Strength (hand grip)
- Blood tests and stool samples
- Accelerometers provision/collection

- N=80 participants (20 PSC +/-IBD with fatigue, 15 PSC without fatigue, 15 IBD, 15 MASLD and 15 healthy controls)
- Single site (UHB)
- 4 visits over 24 weeks
- Observational study

Outcome	Screening Visit	Visit 1 Reliability 4 weeks after screening (Week 0)	Visit 2 (Week 2)	Visit 3 (Week 12)	Visit 4 (Week 24)
Patient Reported Outcome					
FIS (fatigue)	X	X	X	X	X
Peak Pruritis (NRS) (itch)	X		X	X	X
FSS (fatigue)			X	X	X
ESS (Sleep)			X	X	X
HADS (Mood)			X	X	X
SF-36 (QoL)			X	X	X
Liver Disease specific					
CLDQ (MASLD and PSC)			X	X	X
IBDQ (IBD only)			X	X	X
Physical Outcomes					
Muscle fatigability					
Time to task failure		X	X	X	X
ISWT with breath-by-breath analysis		X	X	X	X
Twitch interpolisation with EMG + TMC		X	X	X	X
Muscle Ultrasound		X	X	X	X
Central fatigability					
Twitch interpolisation with EMG + TMC		X	X	X	X

PSC Support



Outcome	Screening Visit	Visit 1 Reliability 4 weeks after screening (Week 0)	Visit 2 (Week 2)	Visit 3 (Week 12)	Visit 4 (Week 24)
Sleep					
Accelerometry		X		X	
Physical activity					
Accelerometry		X		X	
Biomarkers					
Blood test			X	X	X
Stool sample			X	X	X

PSC Support

PPIE

Inclusion Criteria

Inclusion criteria for study participants (PSC/MASLD/IBD)

- A formal confirmed diagnosis of their underlying chronic condition:

IBD cohort patients will have endoscopic or radiological evidence.
Some of the CLD cohorts will have had a liver biopsy, serological and radiological confirmation will be sufficient.

- Adults aged ≥ 16 years
- Able to confirm written consent to the study
- Meeting criteria of PSC/MASLD (as per British Association of the Study of Liver Guidance)
- Meeting criteria for IBD as per the British Society of Gastroenterology guidance.

PSC Support

"With the grant from PSC support I am aiming to gain a greater understanding into the mechanisms or patterns of fatigue in PSC. This will provide a stepping stone into the development of potential treatment options (that include exercise, health psychology, sleep support) on an individual basis."

"This is important because currently fatigue is not well understood and therefore poorly managed and rarely asked about. Fatigue is described as an invisible symptom of PSC that is misunderstood and causes significant impact on quality of life."

What does this mean for the future?

PSC Support

Exercise referral

Health and wellbeing

Holistic care

Energy expenditure

Fatigue

Sleep

PSC Support

Understanding changes in the DNA to detect early signs of bile duct cancer in PSC

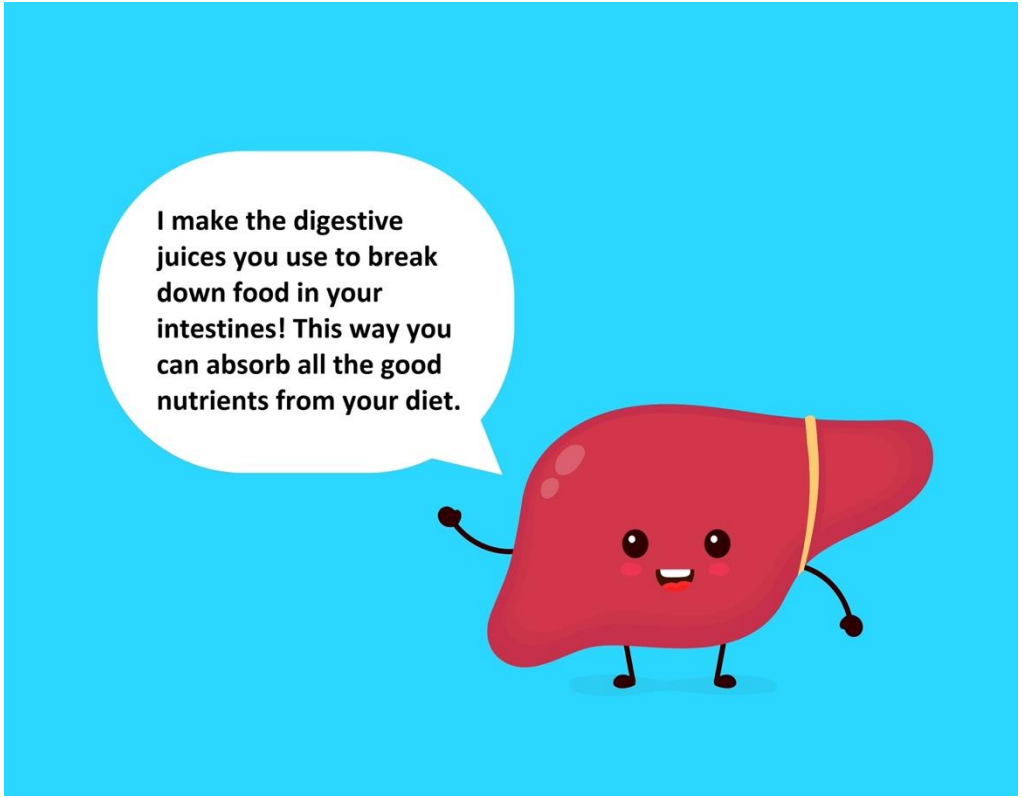
Rodrigo Motta

Translational Gastroenterology and Liver Unit

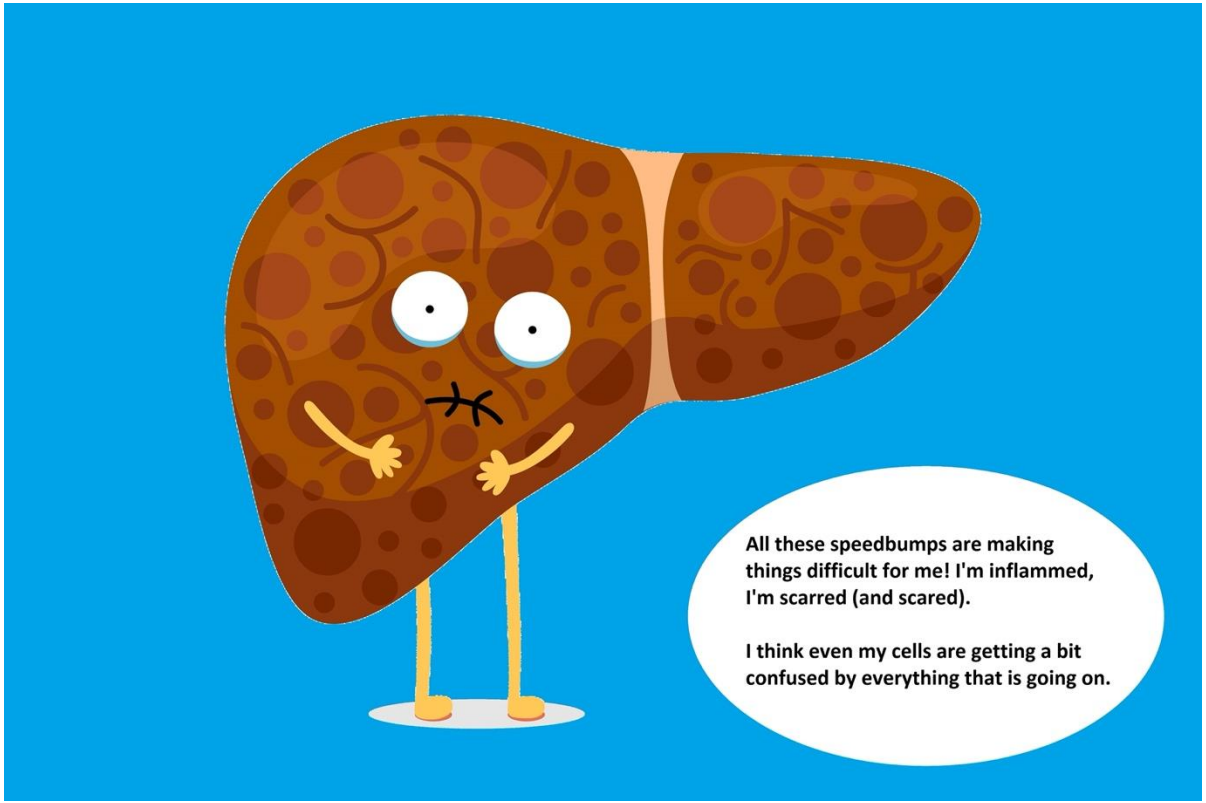
Nuffield Department of Medicine

University of Oxford

The normal liver



The damaged liver



DNA and its interaction with the environment

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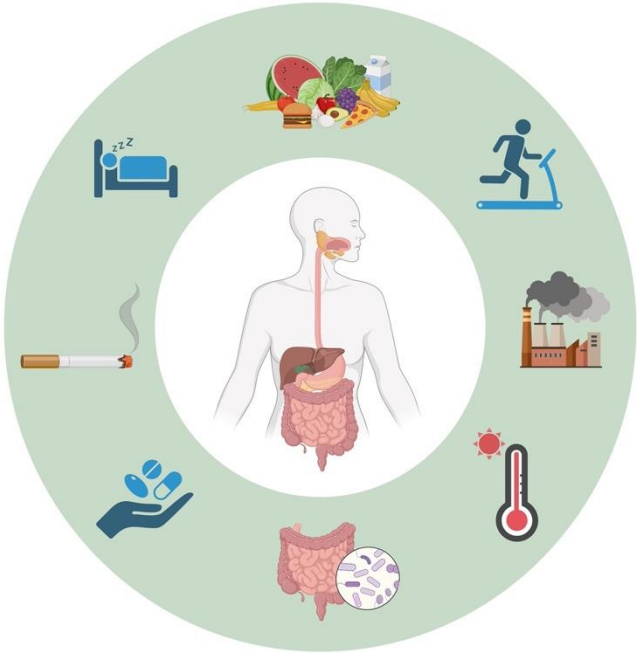

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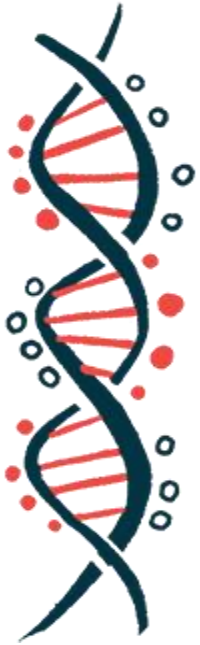
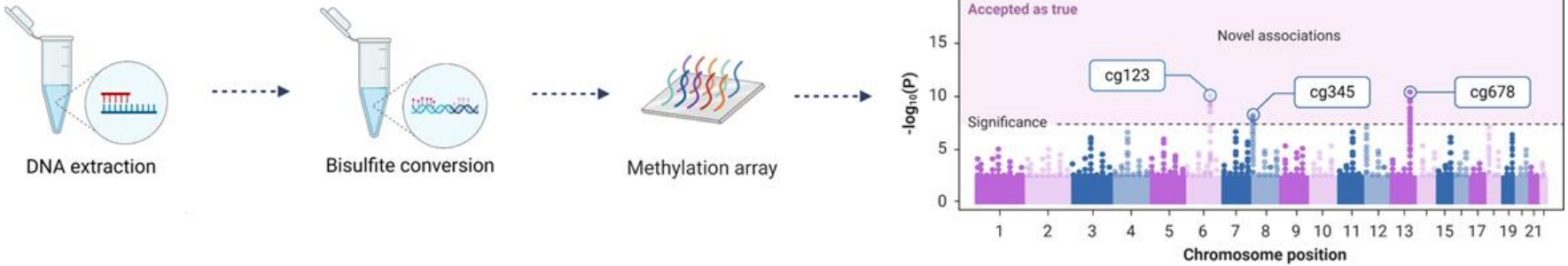


DNA methylation

Objectives of our study

- Explore DNA methylation changes in blood and digestive juices from patients with PSC compared to those with PSC and high risk for cancer and those with bile duct cancer.



Expected outcomes of our study

1) Develop a marker to help with early detection of bile duct cancer

   - Investigations and care tailored to each patient and their risk and needs.

2) Understand better the process that leads to cancer in patients with PSC

   - Potentially identify targets for medical treatment.

Acknowledgements

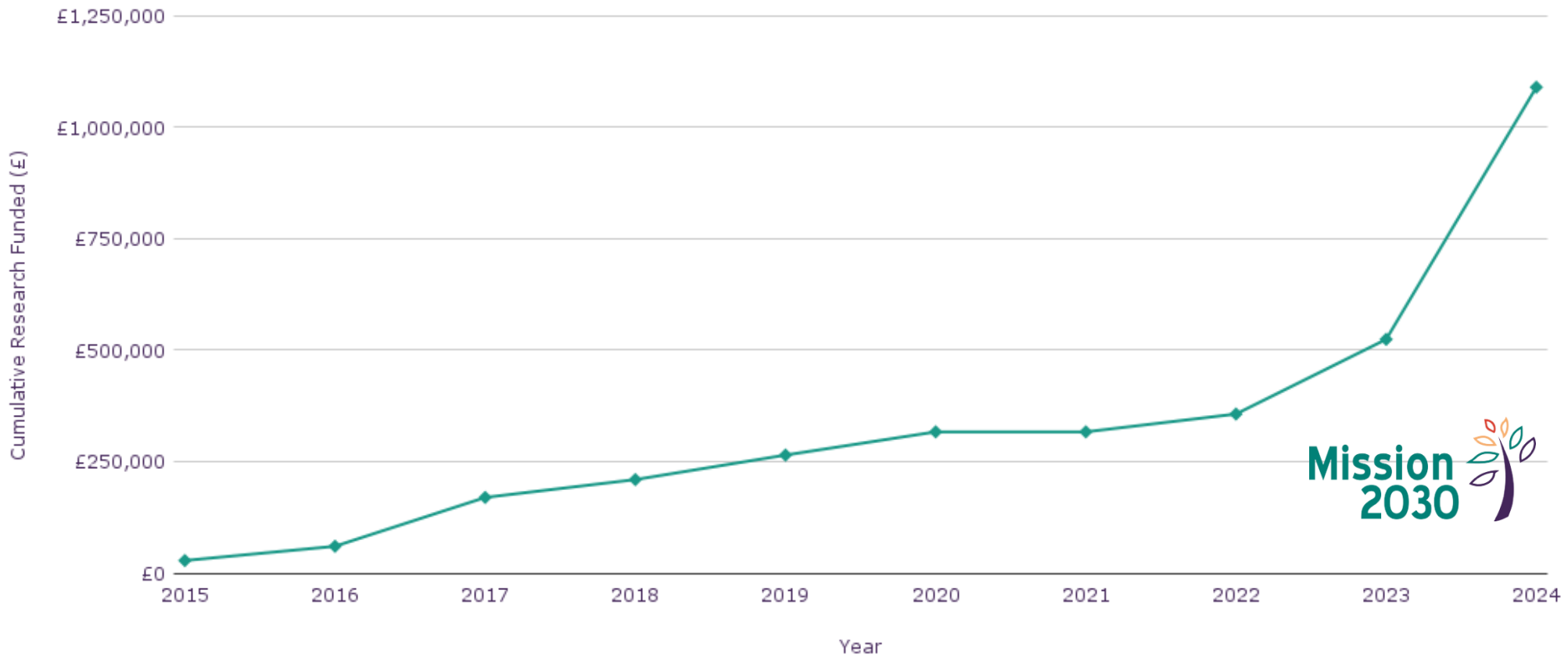
30 PSC Support years together

Martine Walmsley
Mark Chatterley
Patients and their families

TRANSLATIONAL GASTROENTEROLOGY and LIVER UNIT

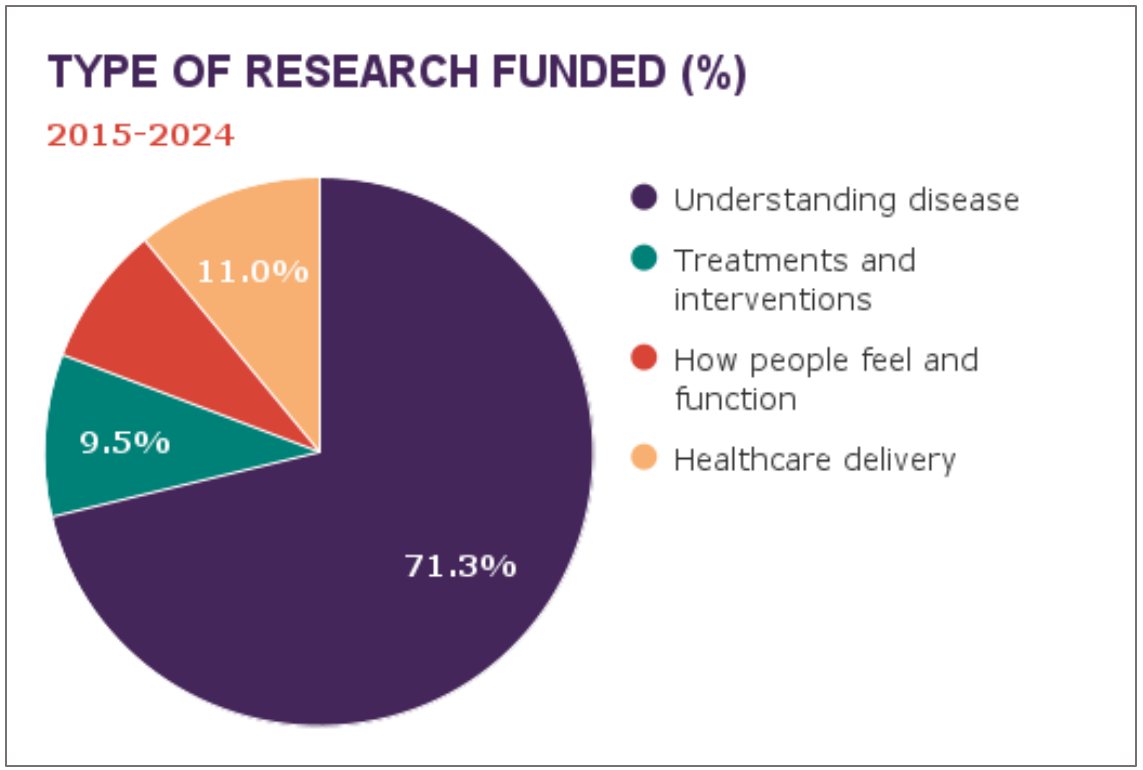
Dr Emma Culver
Dr Alexandra Noble
Prof Jack Satsangi
Research nurses
Clinical research practitioners

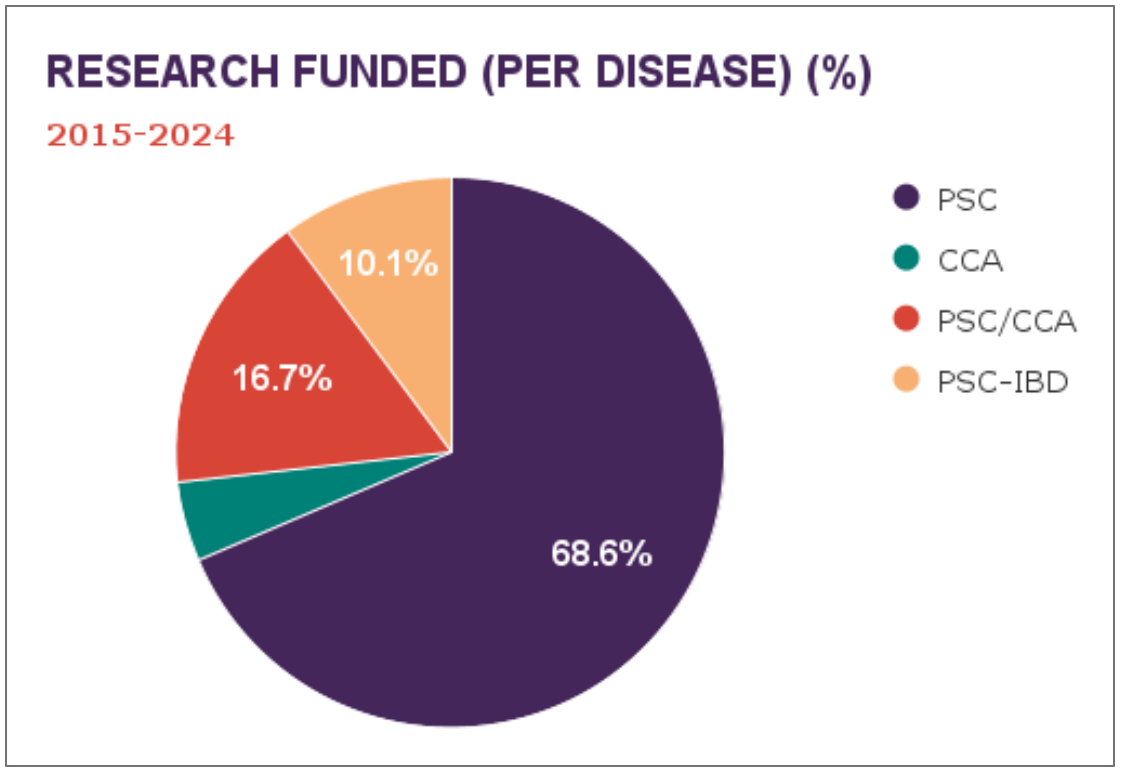
A DECADE OF RESEARCH FUNDING



ASSOCIATION OF MEDICAL RESEARCH CHARITIES

HOW OUR RESEARCH IS SPLIT





CCA = bile duct cancer
IBD = inflammatory bowel disease

HOW WE DECIDE WHAT TO FUND

Experts send detailed reviews on applications to the Scientific Review Committee (SRC)

The SRC reads all applications and reviews and sends a report to the Trustees

The Trustees make the final decision

EXPERT REVIEW OF EVERY FUNDING APPLICATION

SPEEDING UP TREATMENTS

PSC Support

Fund research

Direct research

Support research

amrc
ASSOCIATION OF MEDICAL RESEARCH CHARITIES

ADVOCACY

PPIE

OUR RESEARCH FOCUS – TIME AND MONEY 2024/25

PSC Support

We received **18** funding applications totalling **£1,766,429** from **Australia, Italy, Germany, Sweden. UK, USA and Denmark.**

We supported **11 research funding applications** and **3 studies**, helping secure at least **£14million for research**.

We agreed to fund **8** new projects totalling **£565,160** bring our portfolio of **17 active grants** to **£914,660**

Members of our **Patient Panels** contributed **92 hours** of their time to ensure the **research we support** reflects PSC patient needs and priorities

We contributed to 11 scientific publications about PSC, PSC-IBD and CCA.

We delivered 9 presentations on PSC to clinicians and scientists, and joined fellow experts in 1 Panel Discussion.

We attended **8 scientific conferences** to learn, influence and network - flying the PSC flag.

And supported **7 clinical trials**

HOW CAN YOU GET INVOLVED?

Join our Patient Panel

- Give your opinion on research plans
- Help write things in a clear way
- Advise researchers on the direction of their research
- Help researchers develop funding applications
- Help govern clinical trials and research studies

Volunteer!

- Position available now

Fundraise

- Help us fund more research

Take a survey

- Your experiences and views are important

Speed up research

Influence research

Improve the quality of research

Improve outcomes for us all

martine@pscsupport.org.uk

SUMMARY

- Research is hard, but we're making progress
- More clinical trials and studies than ever
- Treatments ARE coming
- We CAN make a difference