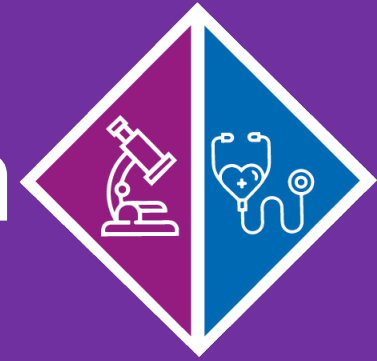


# Translational Research

## Manchester 2023



## Closing Session

Closing Keynote, final remarks and prizegiving

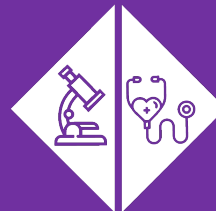
**Chair:**  
Prof Luke Georghiou



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programme



@Translation\_Mcr



#TranslationMCR23

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wellcome

# Translational Research

► Manchester 2023



## CLOSING KEYNOTE, FINAL REMARKS AND PRIZE GIVING

**Chair:** Professor Luke Georghiou, Deputy President and Deputy Vice-Chancellor at the University of Manchester

### CLOSING KEYNOTE ADDRESS

#### ***Towards matrix therapies in the Alport Research Hub***

**Professor Rachel Lennon**, Professor of Nephrology and Consultant Paediatric Nephrologist

**14:20 – 14:45**

### Questions and Answers

**14:45 - 14:50**

### CLOSING REMARKS AND PRIZE GIVING

**Professor Luke Georghiou**, Deputy President and Deputy Vice-Chancellor at the University of Manchester

**14:50 – 15:00**

# Towards matrix therapies in the Alport Research Hub

**Rachel Lennon**

*Paediatric Nephrologist*

*Director of the Wellcome Centre for Cell-Matrix Research*

*Director of the Stoneygate and Kidney Research UK Alport Research Hub*

Translational Research at Manchester: 11<sup>th</sup> September 2023



The University of  
**Nottingham**

UNITED KINGDOM • CHINA • MALAYSIA



University of  
**BRISTOL**

**MANCHESTER**  
1824

The University of Manchester

1989-1994

BMedSci

BMBS

I want to be a paediatrician...

A paediatric nephrologist...

A clinical academic...

2004-2008

Wellcome PhD fellowship

NIHR clinical lecturer

Family move to Manchester



Alina



Adam

2008-

NIHR clinical lecturer

Paediatric nephrologist

Wellcome Intermediate Fellow

Wellcome Senior Fellow

Lead for NIHR IAT

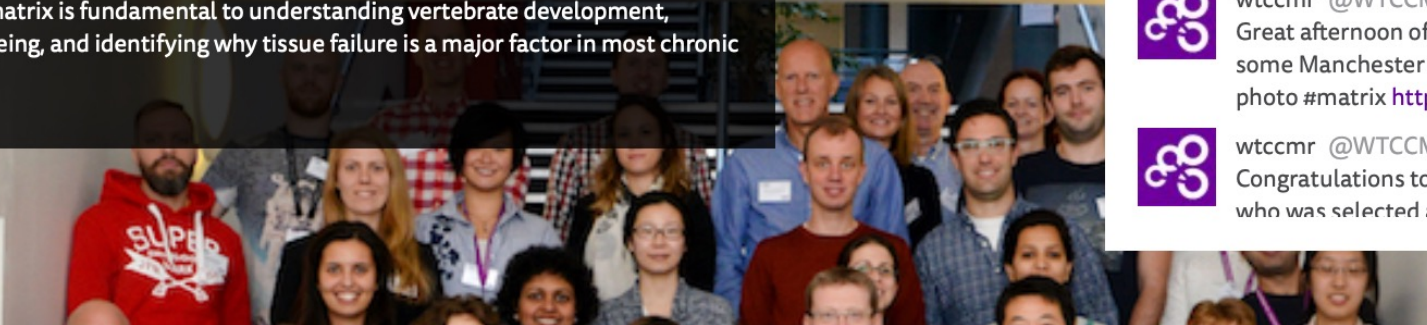
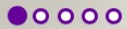
Centre Director

Alport Hub Director

MATRIX IS ESSENTIAL FOR MULTICELLULAR LIFE

## About us

It surrounds and supports cells and accounts for one third of our body mass. We believe that defining the principles that govern the two-way interaction between cells and matrix is fundamental to understanding vertebrate development, healthy ageing, and identifying why tissue failure is a major factor in most chronic diseases.



### LATEST TWEETS

 Follow @wtccmr



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Basement membrane discovery pipeline uncovers network complexity, key regulatory proteins, and more connections bet...  
<https://t.co/EhrN8hwwq>

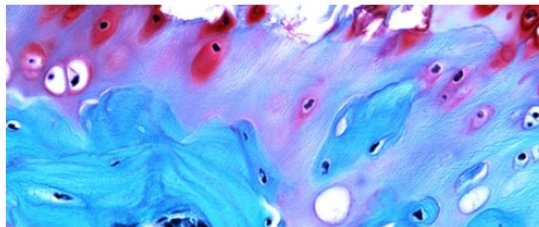


wtccmr @WTCCMR  
Great afternoon of talks yesterday, even some Manchester sunshine for a group photo #matrix <https://t.co/U6apa9kpqb>



wtccmr @WTCCMR  
Congratulations to @JHerrera\_IPFecm who was selected as the winner of the

### Chrono-Matrix



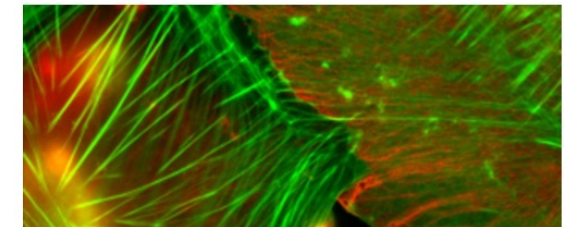
We have shown that many tissues have prominent peripheral circadian mechanisms that regulate matrix.

### Immuno-Matrix



The extracellular matrix has long been known to have an important role in leukocyte adhesion and migration.

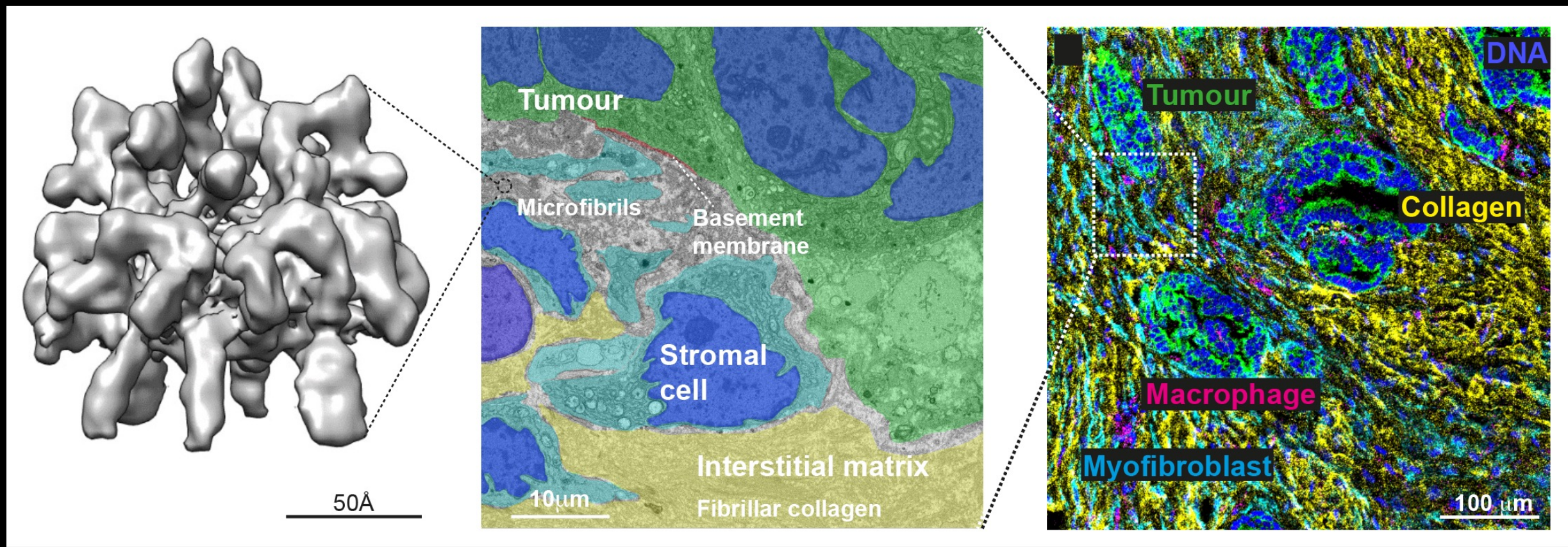
### Mechano-Matrix



Mechanical forces contribute to all levels of vertebrate development, morphology, and tissue function.



*Recruiting to multiple positions across technical, academic and data science roles*



*Matrix across scales and in time and space*

5-year programme award  
2022-2027



## Vision

To transform the understanding and treatment of Alport Syndrome through robust, reproducible clinical and laboratory research

## Outcomes

1. Improved understanding of disease mechanisms in Alport syndrome
2. Identification of genetic and clinical risk factors for more severe disease
3. Robust preclinical testing of new treatments for Alport syndrome





Rachel Lennon



Mychel Morais

Stoneygate and  
Kidney Research UK  
**Alport Research Hub.**



Angela Branson



Neil Turner



Bernard Davenport



Maryline Fresquet



Danny Gale



Royal Manchester Children's Hospital

STONEGATE  
TRUST

Kidney Research UK

**Alport  
Research  
Hub.**

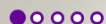
# The Physical Hub: Manchester



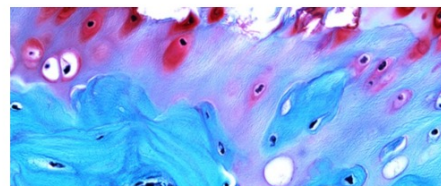
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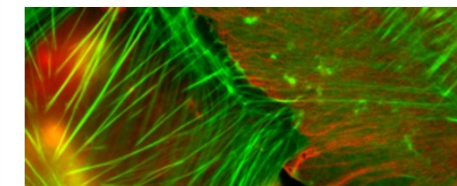
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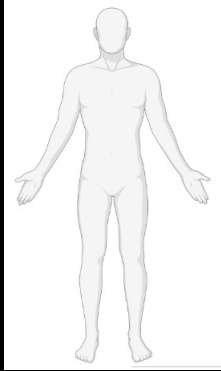


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[www.wellcome-matrix.org](http://www.wellcome-matrix.org)

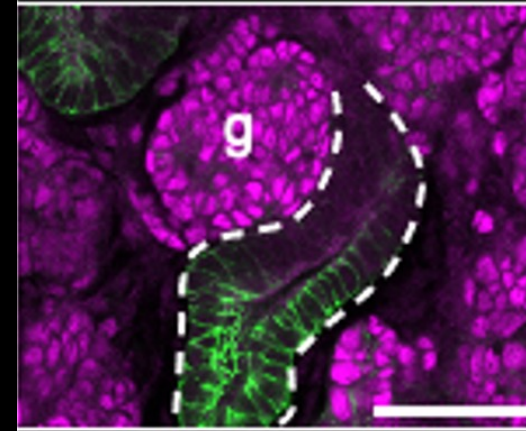
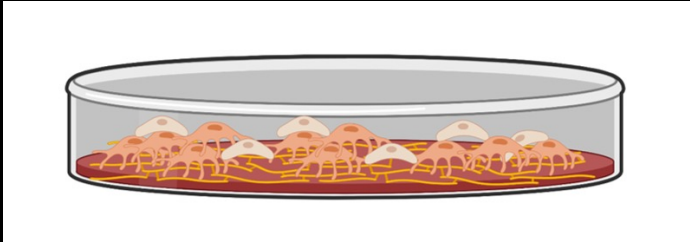


## A: Investigate basement membrane assembly



### Cells in culture

*How do cells make basement membranes?*



PMID: 35076391

### Organoids

*How do complex structures form?*



Rachel

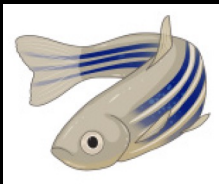


Maryline

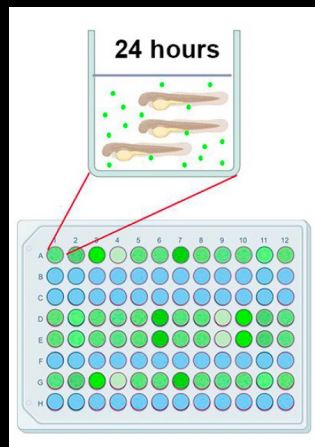
## B: Test new therapies

### Zebrafish

*What happens to function?*



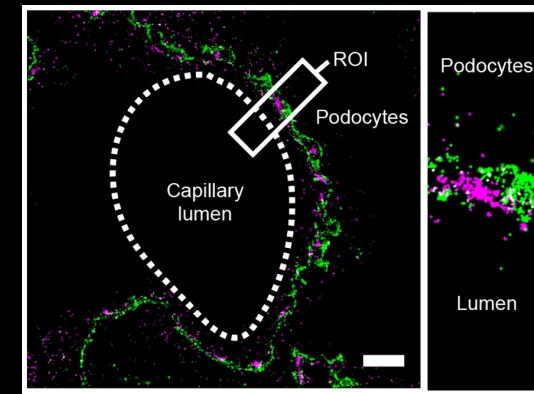
High  
throughput



PMID: 35716957

### Alport mouse

*What happens to function?*



PMID: 34049963



Bernard



Mychel

# Progress in the physical hub

Stoneygate and  
Kidney Research UK  
**Alport Research Hub.**

**A**



Matrix  
biomarkers in  
Alport syndrome

**C**

Externally funded studies with  
commercial partners—

- One completed and progressing to a clinical trial
- Gene therapy programme
- Zebrafish screening programme
- Four in negotiation

**B**



Repairing basement  
membranes in  
Alport syndrome



Pinyuan Tian

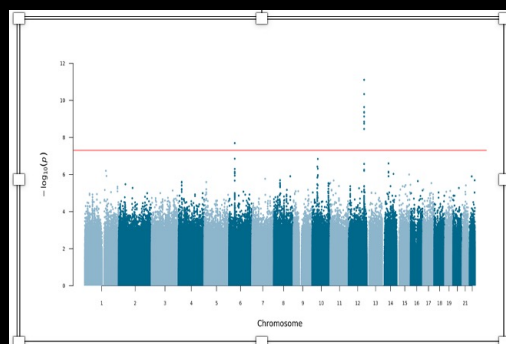
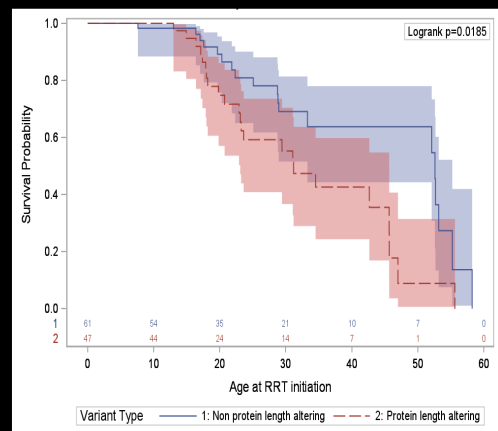
Collaboration with Jeff Miner (WashU),  
Antony Adamson Manchester



1. Drive for complete registration of UK patients
2. Enrich data in RaDaR records
3. Detailed analysis of genetic and other influences

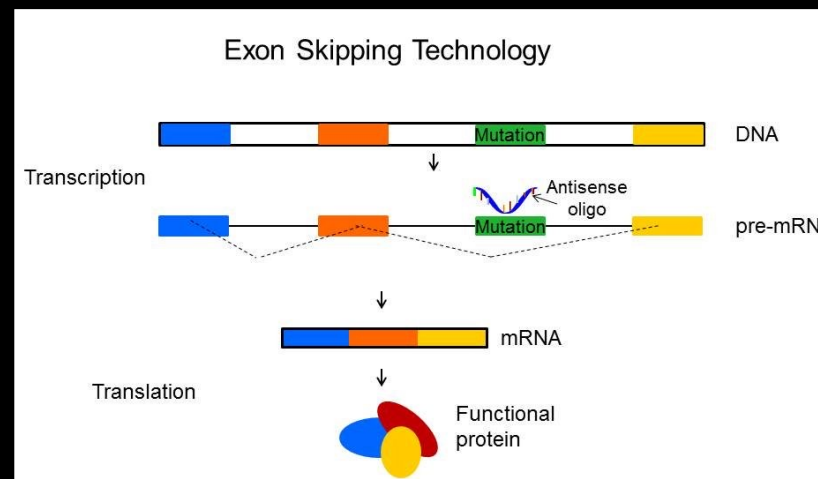
## A: What factors influence outcomes?

Well-controlled association analyses incorporating  
UK BioBank and 100,000 Genomes Data—



## B: Which clinical trial?

Gene therapy, Exon skipping, ER stress  
Stop codon read-through



Danny



Neil



Angela



Rachel

- New projects funded by an annual application round
- Peer review through Kidney Research UK
- Timelines: 2023✓, 2024, 2025

## A short film about the Alport Hub...



Sam Clarke-  
Film maker  
and patient



# Thank you to the team...

Maryline Fresquet,  
Bernard Davenport, Richard Naylor,  
Pinyuan Tian, Mychel Morais,  
Becky Preston, Anna Li,  
Emily Williams, Shaun Wright,  
Tomohiko Yamamura,  
Megan Priestley, Daisy Flatman,  
Holly Sedgwick,  
Miriam Hernandez-Meadows



@LennonLab @wtccmr



# Collaborations and funding

Patient  
organisations



**University College London**  
Danny Gale

**University of Edinburgh**  
Neil Turner

## Manchester

Craig Lawless  
Jamie Ellingford  
Martin Humphries  
Christoph Ballestrem  
Qing Jun Meng

## Core Facilities

David Knight  
Antony Adamson  
Aleksandr Mironov

**Washington University, St Louis, USA**  
Hani Suleiman, Jeff Miner

**Duke University, USA**  
David Sherwood

**Vanderbilt Medical Centre, USA**  
Roy Zent



Stoneygate and  
Kidney Research UK  
**Alport Research Hub.**



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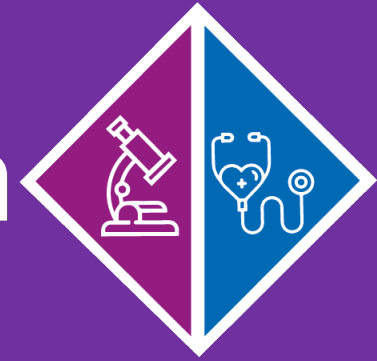
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## Manchester 2023



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