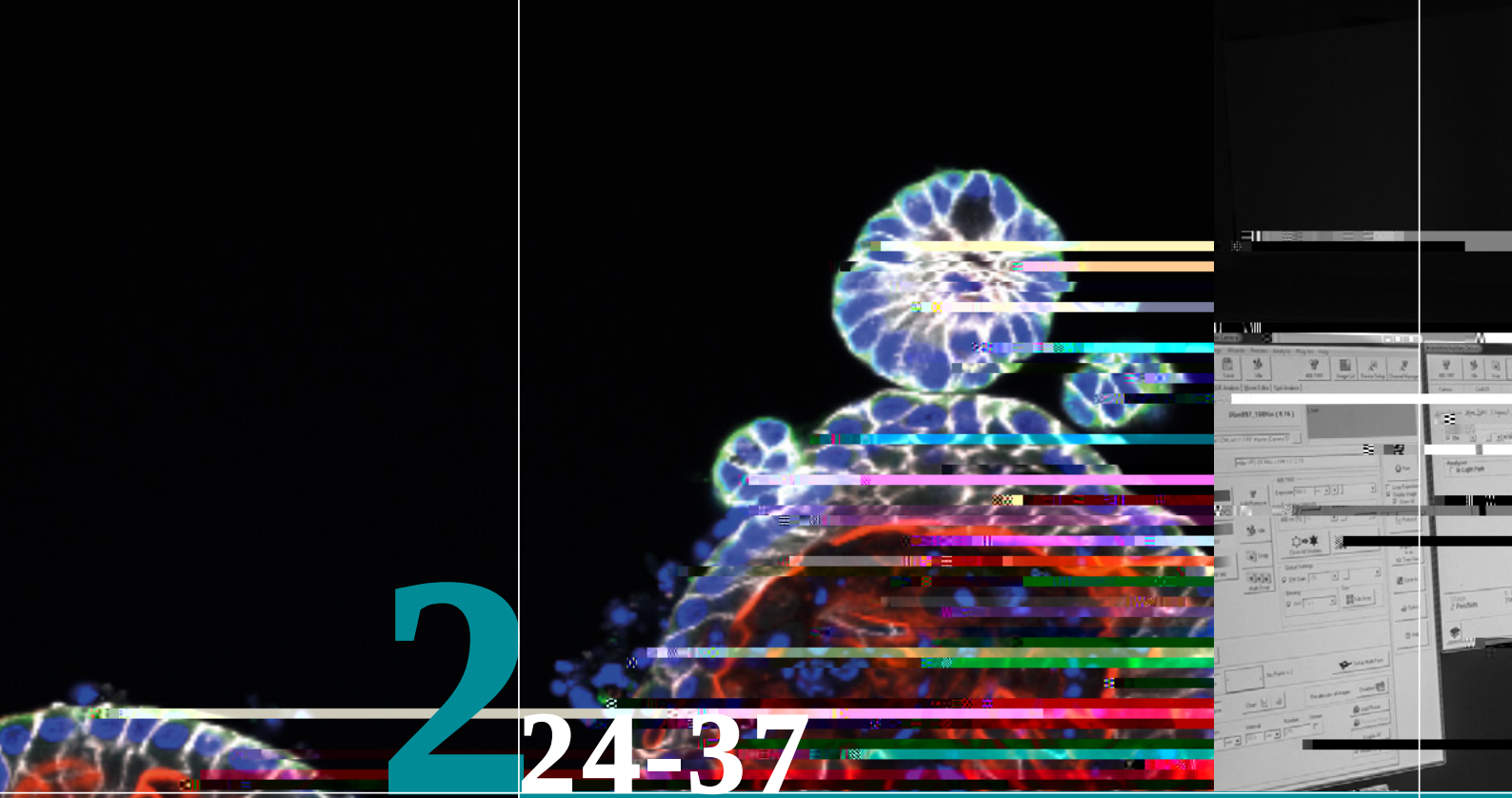
Babraham Institute

Annual Research Report

Signalling



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Signalling

The process of cell signalling consists of several interconnected mechanisms that allow cells to communicate, co-ordinate and respond rapidly to change. By examining these signalling mechanisms and their interactions we seek to understand the effects of signalling on cell growth, survival and behaviour.

Our current focus is to discover the role that signalling has in helping cells to respond and adapt to damage, illness, dietary changes and ageing by investigating:

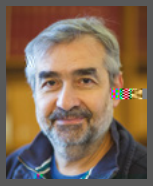
- How cells called neutrophils detect and respond to infections
- How changes in diet affect metabolism and growth
- The effect of signalling mechanisms on the rate of ageing
- The role of autophagy in recycling cell components following damage or starvation

Group Leaders

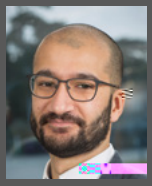
Simon Cook

Oliver Florey

Phill Hawkins



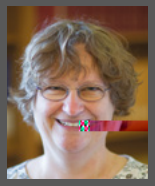
Nicholas Ktistakis



Rahul Samant

Hayley Sharpe

Len Stephens



Heidi Welch

Group members

Senior research associates:
Karen Anderson
Sabine Suire

Senior research scientist:
Simon Rudge

Senior postdoctoral researcher:
Tamara Chessa

Research felloel5

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Nicholas Ktistakis

Group members

Senior postdoctoral researcher:
Maria Manifava

Research assistants:
Bonnie Man
Peri Tate (Left 2019)

Visiting students:
Qashif Ahmed
Angela Braho
Emilia Hubbard (Left in 2019)
Katerinai Kafka (Left in 2019)
Nikolaos Kontopoulos (Left in 2020)
Theodora Maniati (Left in 2020)
Felipe Renna
Milene Ortiz Silva
Filianna Tanti (Left in 2019)
Charalampos Toramanidis

Visiting scientists:
Luisa Giudici (Left in 2019)
Varvara Kandia

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Current Aims

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on iPSC-derived neuro
understand how autopha
neurodegeneration.

Progress in 2019 and 202

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autophagy and mitophagy u
extensive collection of live im
and discovered a possible exp
for why the process of mitopha
involves the sequential transloc
of autophagy components to the

Rahul Samant

Group members

Postdoc research scientist:
Harvey Johnston

PhD student:
Yasmeen Al-Mufti

Research assistant:
Estelle Wu

Why misfolded proteins accumulate with age

Cellular accumulation of misfolded proteins is a hallmark of ageing. In young cells, the proteostasis network limits toxicity by activating one or more systems for misfolded protein clearance. We focus on how these clearance systems are integrated within the network to maintain proteome health during youth, and how loss of this integration contributes to cellular senescence, another ageing hallmark with strong links to chronic in ammation and organismal frailty.

Current Aims

We use two evolutionarily distant cell types, budding yeast and primary human broblasts, to identify common, conserved lines of communication between di erent clearance systems of the proteostasis network, and investigate how these are re-wired during replicative ageing (yeast) and senescence (mammals). Our lab employs multi-disciplinary approaches such as super-resolution imaging, ow cytometry, and mass spectrometry-based proteomics to measure proteostasis capacity and

Hayley Sharpe

Group members

Postdoc research scientists:
Gareth Fearnley (Left in 2020)
Katie Mulholland
Kasia Wojdyla

PhD students:
Roksana Dutkiewicz
Ian Hay
Ti any Lai
Lauren Maggs

Research assistant:
Oisharja Rahman

Visiting students:
Oliver Cottrell (Left in 2019)
Iain Hay
Katherine Young

Cell signalling through tyrosine phosphatases

The reversible phosphorylation of protein tyrosine residues enables cells to dynamically respond to changes in their environment and is regulated by the antagonistic actions of kinases and phosphatases. We focus on the understudied phosphatases to understand how they signal, their roles in health and disease and how they are regulated, particularly by reactive oxygen species, which are implicated in the ageing process.

Current Aims

Our overarching aim is to understand mechanisms of tyrosine phosphatase signalling in order to understand their fundamental functions but also to reveal new approaches to targeting them in disease, to overcome their undruggable reputation. Our current work is focused on a family of receptor tyrosine phosphatases that are present on the cell surface and form homophilic interactions at points of cell–cell contact. The receptor PTPRK is a tumour suppressor and had been suggested to regulate cell adhesion. To as dec
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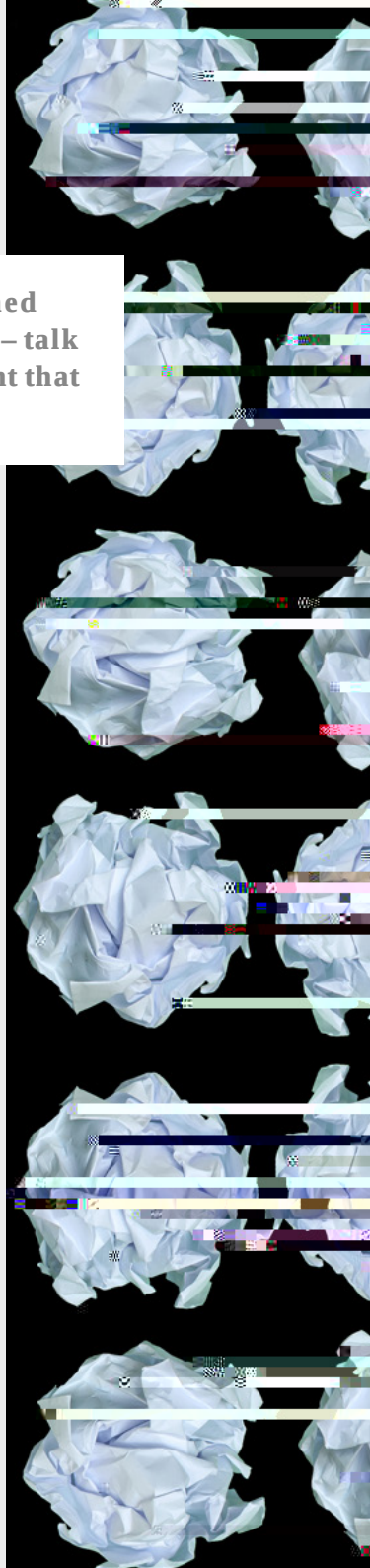
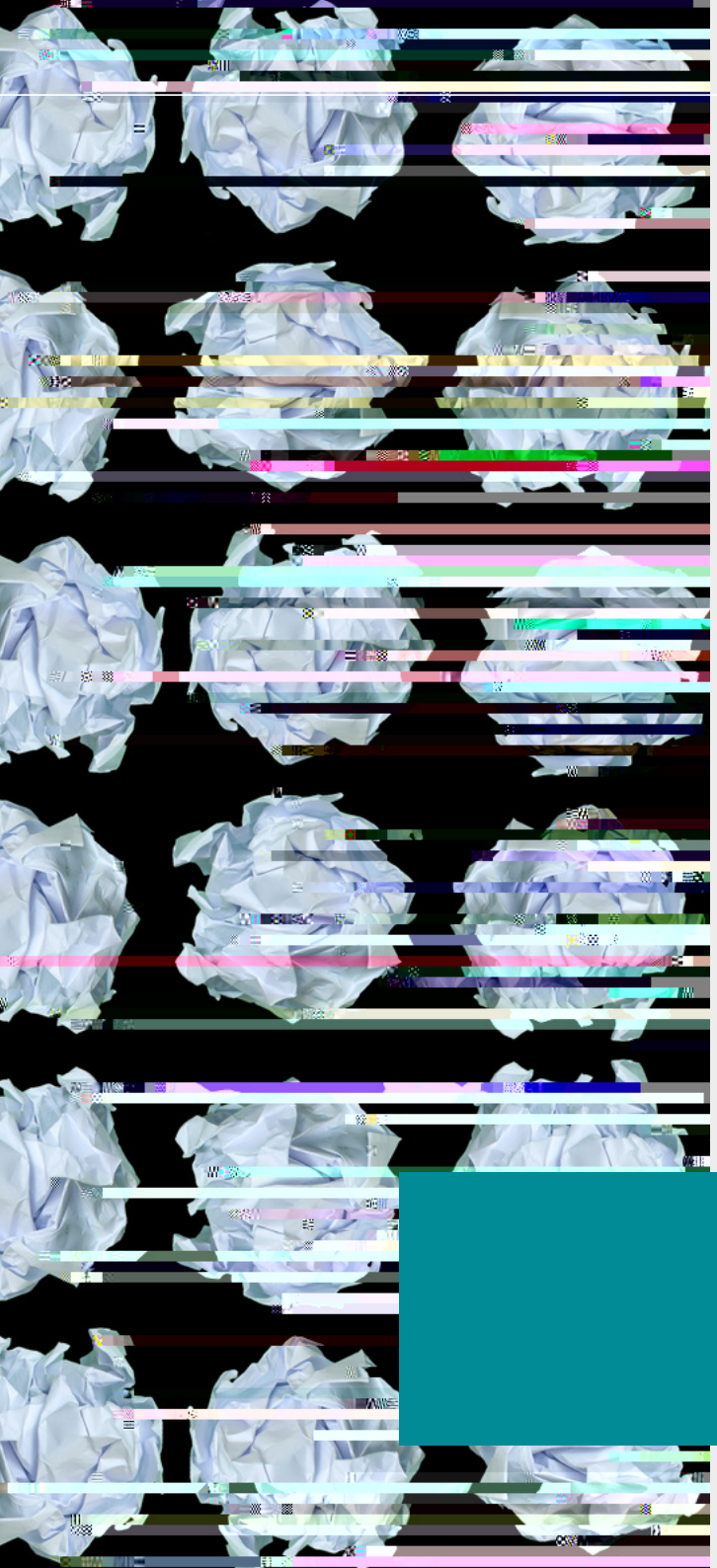
The adhesive receptor protein tyrosine phosphatase PTPRK is expressed in epithelial cells at sites of cell–cell contact. We have identi ed key substrates linked to cell adhesion (left). Transmission electron microscopy images reveal that deleting PTPRK from mammary epithelial cells leads to disrupted cell junctions and adhesions, as well as decreased cell height, reminiscent of an epithelial to mesenchymal transition (right).

Publications

www.babraham.ac.uk/our-research/signalling/heidi-welch

Setting up a new group is exciting and daunting. Two group leaders who joined the Signalling programme in 2019 – Dr Hayley Sharpe and Dr Rahul Samant – talk about their research and the supportive, collaborative and open environment that they say marks out the Institute.





This quality control machinery declines as we age. As a result, most age-related diseases, including Alzheimer's disease, Parkinson's

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