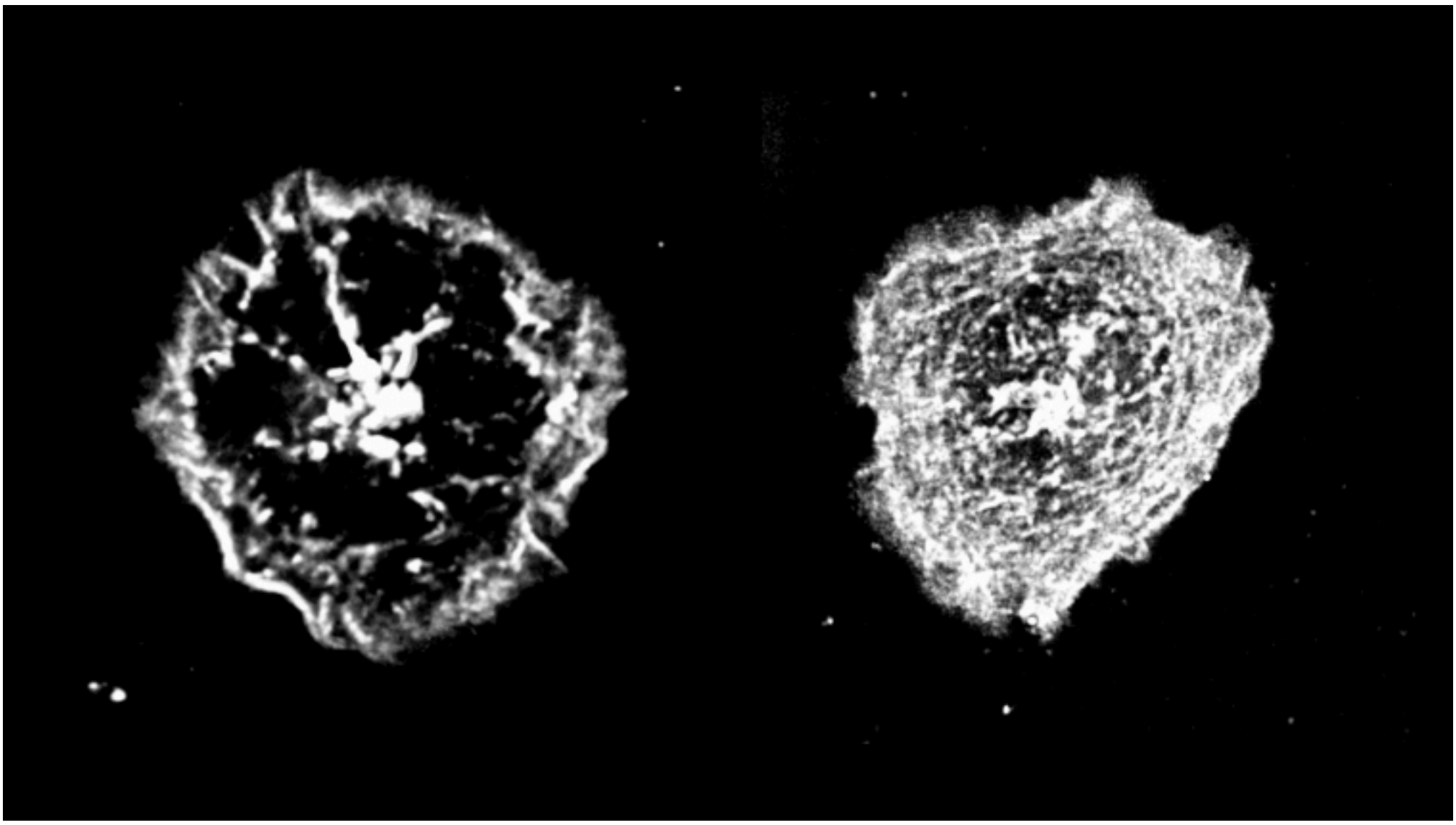
Sabrina Simoncelli #13



Sabrina Simoncelli. 'Wild and Knock-Out T Cells'. 2023

About the Research

Breakthroughs in biological sciences are often accompanied with advances in imaging. Over the past two decades, several innovations in instrumentation, data analysis and dye design powered the resolution revolution in fluorescence microscopy, allowing to see beyond the diffraction limit of light.

While there currently are many nanoscopy methods that circumvent this limitation, they all have trade-offs between resolution, speed, field of view, biocompatibility, sensitivity, and experimental complexity. To push the technology further, the lab explores new approaches ranging from image analysis routines (to extract richer structural and mechanistic information of protein complexes, interactions and assemblies); to the synergistic integration of photonic nano-structures.

We use a combination of experimental and computational techniques, including microscopy, optics, spatial statistics, nano-fabrication and image processing. We are particularly interested in super-resolution microscopy (also known as nanoscopy), which are fluorescence microscopy techniques that allow us to visualise the spatial organisation of single molecules and molecular assemblies, with the highest level of resolution and specificity. Our main biological application is in T cells, which are white blood cells that are essential for human immunity.

The exhibition features some super-resolved microscopy videos from Megan Joseph's PhD to understand the role of a particular protein, known as PTPN22, in T cell activation. This protein can harbour a mutation that is associated with over 15 different autoimmune diseases such as type 1 diabetes, systemic lupus erythematosus, and rheumatoid arthritis. Her work could help to elucidate the mutated protein's role within autoimmune disease. .

More specifics about the images:

In general, one technique Biologists will use to try to understand more about the function of a protein is to get rid of that protein and see what happens to the system. Megan has T cells, created by a previous PhD researcher, which do not have any PTPN22 protein within them as the gene that codes for the PTPN22 protein has been removed from their genome. These cells are known as PTPN22 knock out or KO cells. These cells were created using CRISPR technology. Megan compares the behaviour of these cells to T cells that have the predominating natural form of PTPN22 which are known as wild type T cells.

The videos you are seeing are comparing the PTPN22 knock out (KO) cells (left) to wild type (WT) T cells (right). In these videos T cells are settling and activating on a glass microscope slide coated with biological molecules that encourage them to activate. The T cells are forming a T cell synapse on the glass slide. It takes T cells around 8 minutes to form a stable synapse, to ensure the whole event was captured images were taken every 10 seconds for 20 minutes.

The reason a high-resolution microscope is needed to see these activating events is because T cells have a diameter of around 5-7 μm (0.005-0.007 mm) which is less than half the diameter of the thinnest human hair. The actin filaments you can see within the T cells have a diameter of around 7 nm (0.000007 mm) this is around 2500 times smaller than the width of a human hair! You can see the actin ring appearing in the wild type (WT) T cells over time within these images. However, the PTPN22 knock out (KO) cells appear to have a different structure of actin within their T cell synapse. What do you see?

About the Researchers

Dr. Sabrina Simoncelli, born in Buenos Aires, Argentina, is a Royal Society Dorothy Hodgkin Fellow and Associate Professor in Nanoscale Characterization, joint between the London Centre for Nanotechnology and the Department of Chemistry at University College London, UK (2020-to present).

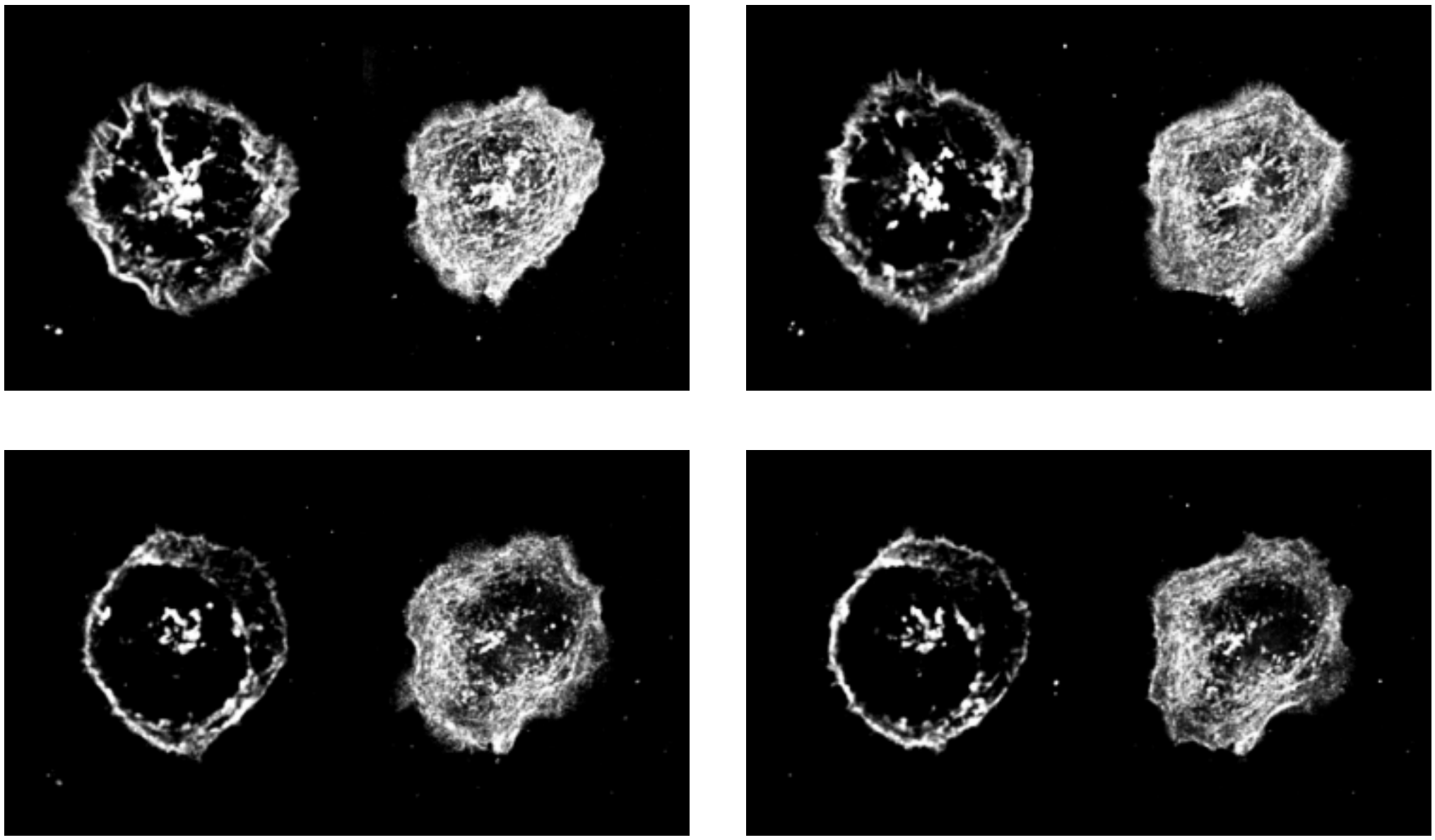
Since her PhD (2010-2014) at University of Buenos Aires (Argentina), Sabrina developed single-molecule localization microscopy techniques to enable quantitative measurements of processes in the field of nanotechnology, material sciences and biology. She deepened and broader her expertise during her post-doctoral positions at Ludwig-Maximilian-University, Germany (2014–2016), Imperial College London, UK (2016–2018) and King’s College London, UK (2018-2020).

Since 2020, her group’s research focuses on the application and development of physical and chemical approaches to study biological phenomena at the nano-scale, particularly in the field of T cell immunology.

Megan Joseph was born in East London and received her degree in Biological Sciences and Masters in Immunology from Imperial College London. She then started work on her PhD with the London Interdisciplinary Doctoral Program. Working in the Simoncelli Lab, alongside Sabrina, her PhD focuses on using super resolution microscopy techniques to study T cell biology with a focus on understanding auto-immune disease mechan

https://simoncelli-lab.com

More images from the movie



Sabrina Simoncelli. ‘Wild and Knock-Out T Cells’. Stills from the movie. 2023

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