Name	MICHAEL WAY
Position	Senior Group Leader
Year joined *(Crick or founder institute)*	2001

Career History

1982 – 1985 Cell and Molecular Biology BSc 1st Class (Hons) King's College, London, UK
1985 – 1988 Ph.D. Structural Studies, MRC Lab. of Molecular Biology, Cambridge, UK
1988 – 1991 MRC Postdoc Research Fellow, MRC Lab. of Molecular Biol, Cambridge, UK
1989 – 1991 Junior Research Fellow, Trinity Hall, Cambridge, UK
1992 – 1995 SERC/NATO Postdoctoral Fellow, Whitehead Institute, MIT, USA
1995 – 2001 Group leader in Cell Biology Prog., EMBL, Heidelberg, Germany
2001 – 2002 Junior Group Leader, ICRF, Lincoln's Inn Fields, London
2002 – 2004 Junior Group Leader, Cancer Research UK, London Research Institute,
2004 – 2015 Senior Group Leader, CRUK London Research Institute, London
2013 – now Professor of Virology, Dept. Infectious Disease, Imperial College, London
2015 – now Senior Group Leader, Cellular signalling and cytoskeletal function Lab., Francis Crick Institute, London

Major Awards, Honours and Prizes

1983 Sambrooke Exhibition in Natural Science (Undergrad)
1985 Jean Hanson Memorial Prize (Undergrad)
1989 Max Perutz Student Prize (PhD)
2006 Elected Member of EMBO
2015 Elected Fellow of the Academy of Medical Sciences

Membership of external committees, editorial boards, review panels, SABs etc

Editor in Chief
2012 – now Journal of Cell Science

Editor
2005 – now Journal of Cell Science

Editorial Board
2005 – now Cellular Microbiology
2007 – now Cell Host & Microbe
2009 – 2020 EMBO Journal
2009 – now EMBO Reports
2010 – now Small GTPases
2012 – now Developmental Cell
2019 – now Cell Structure and Function (Journal of Japanese Soc. Cell Biology).

Advisor
2017 Pathogens and Infection chapter, Molecular Biology of the Cell 7th Ed.

External Committees
2012 – now Ad Hoc member for Wellcome Trust Investigator award panel
2013 – 2016 Vice President European Cytoskeletal Forum (ECF)
2015 – 2018 Scientific advisory board "Towards outstanding research and training in tumour biology at IMM". EU funded project promoting interactions between Instituto de Medicina Molecular (Lisbon), Curie Institut (Paris) and DFKZ (Heidelberg).
2016 Search Panel for grp leaders in Cell Biology and Infection. Institut Pasteur, Paris.
2016 – now President European Cytoskeletal Forum
2016 – 2019 American Society for Cell Biology (ASCB) membership committee.
2017 Review panel for Cell Biology and Biophysics Unit, EMBL, Heidelberg, Germany.

Meetings organized
2016 Co-organizer of Cell Adhesion and Migration. 31st European Cytoskeletal Forum / Biochemical Society meeting. Cambridge, UK
2017 Co-organizer of Cellular Dynamics: Membrane-Cytoskeleton Interface. Journal of Cell Science, The Company of Biologists meeting. Southbridge, MA, USA.
2019 Co-organizer of Cellular Dynamics: Organelle-Cytoskeleton Interface. Journal of Cell Science, The Company of Biologists meeting. Lisbon, Portugal.
2021 Co-organizer of Cellular Dynamics: Host - Pathogen Interface. Journal of Cell Science, The Company of Biologists meeting. Lisbon, Portugal.

Teaching and Practical Courses
2015 1st Croucher Summer course in Advanced Imaging. University of Hong Kong
2015 Cell-to-cell communication course for PhD program in Molecular Medicine San Raffaele Scientific Institute, Milano. Italy
2016 Cell Biology course for PhD program at Gulbenkian Institute, Lisbon Portugal
2018 Summer School: Cell migration in health and disease Ecole Polytechnique, Paris
2019 2nd Cell Biology and Cancer course. Curie Institute, Paris, France
2020 Molecular Biology and Pathology of Viruses, MSc course, Imperial College

Lab Name	***Cellular Signalling and Cytoskeletal Function Laboratory***

Research programme and achievements

Intracellular pathogens have co-evolved with their hosts to develop multiple mechanisms to hijack the many cellular processes of their hosts to facilitate their entry, replication, survival and cell-to-cell spread. Understanding how pathogens take advantage of their host offers the promise of obtaining fundamental insights into basic cellular processes that are frequently deregulated during pathogenic situations. It also provides important insights into the underlying cause of disease and helps identify potential targets for therapeutic intervention. My lab's research uses a combination of quantitative imaging and biochemical approaches to study Vaccinia virus as a model system to interrogate the regulation and function of Src and Rho GTPase signalling, actin and microtubule-based transport as well as cell migration.

Main lab achievements since 2015

1. We have developed software designed for the automated quantification of cell migration and morphodynamics. Implemented as a plug-in for the open-source platform,

ImageJ, ADAPT is capable of rapid, automated analysis of migration and membrane protrusions, together with associated fluorescently labelled proteins, across multiple cells.

2. Using actin-based motility of Vaccinia as a model, we established that the human Arp2/3 complex actually comprises a family of eight complexes with different actin nucleating properties. This finding has far-reaching implications as Arp2/3-driven actin polymerisation is essential for multiple fundamental cellular processes. For example, a collaboration with Edgar Gomes in IMM Lisbon has subsequently demonstrated unique roles for Arp2/3 isoforms in T-tubule organization and nuclei positioning in skeletal muscle, while others have found mutations in one Arp2/3 isoform result in severe inflammation and immunodeficiency.

3. During its egress Vaccinia recruits a signalling network to induce actin polymerisation to enhance its cell-to-cell spread. In our efforts to understand how this complex signalling network is organised and operates we have uncovered the basis for the recruitment of intersectin-1, a RhoGEF that locally activates Cdc42. This activation promotes N-WASP-Arp2/3 driven actin polymerisation and viral spread.

4. In contrast to most DNA viruses, Vaccinia replicates its genome in the cell cytoplasm. For over 30 years, it has been thought that genome replication was mediated by viral proteins and independent of host involvement. We have shown, in contrast to these long-held beliefs, that Vaccinia recruits components of the eukaryote DNA replication and repair machinery to amplify its genome in the host cytoplasm.

5. The actin cortex regulates the shape and mechanical integrity of cells. It also plays an important role in controlling what gets in and out of a cell. By analysing the basis of Vaccinia-induced cell blebbing early during infection we uncovered a new RhoGTPase signalling pathway involving RhoD, Pak6 and RhoC that regulates myosin driven cell contraction.

6. We showed that septins, conserved components of the cytoskeleton, suppress the release of Vaccinia from infected cells by acting as “restriction factors” to entrap virions at the plasma membrane. Nck-mediated recruitment of dynamin by the virus as well as formin-driven actin polymerisation displaces septins to overcome their antiviral effect. This is the first demonstration that septins can inhibit the spread of viral infection.

Ongoing and Future work

1. We continue to examine how different subunit isoforms impact on the properties, interactions and cellular function of Arp2/3 complex family members. We have also generated conditional mice to examine the role of Arp2/3 isoforms in development and tissue homeostasis.

2. We are re-wiring the Vaccinia signalling cascade and building synthetic networks to understand the principals of how signalling networks regulate actin polymerisation.

3. We are analysing microtubule-based motility of Vaccinia including establishing *in vitro* motility assays to understand the mechanistic basis of motor recruitment and regulation.

4. We are performing cryo-electron tomography of infected cells to uncover the ultrastructural organisation of septins and clathrin on Vaccinia.

5. We are analysing how Vaccinia manipulates RhoGTPases and their signalling.

6. We are using Vaccinia to develop novel oncolytic strategies for ovarian cancer.

Research outputs

Jasmine V. G. Abella, Chiara Galloni, Julien Pernier, David J Barry, Svend Kjær, Marie-France Carlier and Michael Way. (2016) *Isoform diversity in the Arp2/3 complex determines actin filament dynamics*. Nature Cell Biology 18: 76-86. DOI: 10.1038/ncb3286
The Arp2/3 complex, consisting of seven evolutionarily conserved subunits, generates branched actin networks during many fundamental cellular processes. Taking advantage of actin-based motility of Vaccinia virus as a model system, we demonstrate for the first time that in humans the Arp2/3 complex is actually a family of different complexes with distinct actin-nucleating properties.

Xenia Snetkov, Ina Weisswange, Julia Pfanzelter, Ashley C. Humphries and Michael Way. (2016) *NPF motifs in the vaccinia virus protein A36 recruit intersectin-1 to promote Cdc42:N-WASP-mediated viral release from infected cells*. Nature Microbiology 1:16141. DOI: 10.1038/nmicrobiol.2016.141
Vaccinia virus recruits a signalling network to induce actin polymerisation to enhance its cell-to-cell spread. This study, which described the first viral protein containing NPF motifs, uncovered the molecular basis for the recruitment of intersectin-1, a RhoGEF that activates Cdc42 to increase exit of Vaccinia from infected cells using its actin-based motility.

Charlotte H. Durkin, Flavia Leite, João V. Cordeiro, Yutaka Handa, Yoshiki Arakawa, Ferran Valderrama and Michael Way. (2017) *RhoD inhibits RhoC-ROCK dependent cell contraction via PAK6*. Developmental Cell 41:315-329. DOI: 10.1016/j.devcel.2017.04.010
RhoA-mediated regulation of myosin-II activity in the actin cortex controls the ability of cells to contract and bleb during a variety of cellular processes. Cell contraction and blebbing are also frequently observed as part of the cytopathic effects induced by many different viruses during their replication cycles. By analysing the molecular basis of Vaccinia-induced cell blebbing early during infection we uncovered a new RhoGTPase signalling pathway regulating myosin driven cell contraction.

Julia Pfanzelter, Serge Mostowy and Michael Way. (2018) *Septins suppress the release of Vaccinia virus from infected cells*. Journal of Cell Biology 217:2911-2929. DOI: 10.1083/jcb.201708091
Septins are conserved components of the cytoskeleton that play important roles in many cellular processes including division and migration. They can also suppress bacterial infection by forming cage-like structures around intracellular pathogens such as Shigella. Using a combination of approaches, we demonstrated that septins act as “restriction factors” to entrap virions at the plasma membrane and inhibit the release of Vaccinia virus from infected cells. This study represented the first demonstration that septins can inhibit the spread of viral infection.

Ottilie von Loeffelholz, Andrew Purkiss, Luyan Cao, Svend Kjaer, Naoko Kogata, Guillaume Romet-Lemonne, Michael Way* and Carolyn A. Moores*. (2020) *Cryo-EM of human Arp2/3 complexes provides structural insights into actin nucleation modulation by ARPC5 isoforms*. Biology Open 9: bio.054304. DOI: 10.1242/bio.054304

In 2016 my lab was the first to demonstrate that the Arp2/3 complex in humans and other mammals is actually a family of complexes with different properties (1). However, it is still unclear why these eight complexes are so different and whether they have distinct cellular functions. This study, which was the first cryo-EM analysis of the Arp23 complex when it appeared on BIoRxiv provided structural insights into differences between the Arp2/3 family members.