Name	JEREMY CARLTON
Position	Seconded Group Leader (King's)
Year joined *(Crick or founder institute)*	2017

Career History

2001-2005: PhD, Department of Biochemistry, University of Bristol, Cullen Lab
2006-2012: Postdoc, Department of Infectious Diseases, KCL, Martin-Serrano Lab
2012-2017: Wellcome Trust Research Career Development Fellow, KCL
2017-Present: Wellcome Trust Senior Research Fellow, KCL/Crick

Major Awards, Honours and Prizes

2006-2009: Beit Memorial Research Fellowship for Medical Research
2010: Biochemical Society Early Career Research Medal
2012-2017: Wellcome Trust Research Career Development Fellow, KCL
2017-onwards: Wellcome Trust Senior Research Fellow, KCL/Crick
2017-2020: EMBO Young Investigator Programme
2020: Journal of Cell Science Cell Scientist to Watch

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

Editorial Advisory Board, Review Commons (2020-onwards)
Chair Biochemical Society Cell Biology Theme Panel (2016-2018)
Member Biochemical Society Cell Biology Theme Panel (2012-2016)

Lab Name	***Organelle Dynamics Laboratory***

Research programme and achievements

Achievements from previous role
My lab focus on understanding membrane trafficking and organelle remodelling during dynamic processes such as cell division. As a newly independent group leader, my lab discovered how membranes were sealed around the reforming nuclear envelope during mitotic exit through the employment of a membrane remodelling complex called ESCRT-III. We described roles for this machinery in sealing the nuclear envelope (Olmos et al., Nature, 2015) and discovered a membrane-interacting region of a nuclear envelope-specific ESCRT-III component that was essential for assembling ESCRT-III at the reforming nuclear envelope (Olmos et al., Current Biology 2016).

Current Research Programme
We have used secondment to Crick to expand our research programme, both by developing our analysis of ESCRT-III assembly at the nuclear envelope and initiating new work in a number of areas. For the development of the role of ESCRT-III in nuclear

envelope regeneration, we have discovered how the biology of this process is regulated by classical cell cycle control mechanisms, namely direct phosphorylation of CHMP7 by CDK1. This work is currently under revision in eLife. We have also examined the membrane binding element of CHMP7 in a biophysical study where we have benefited from the Crick NMR platform, the protein production STP and lipidomic collaborators at King's. This work is ongoing.

To expand my research programme, I am developing a broader interest in membrane and organellar integrity. Through a Crick/King's PhD student, we are examining the links between nuclear envelope stability and blebbing and the migratory advantage this gives metastatic melanoma cells. This work is nearing completion and has involved collaboration with the Making Lab and the EM core facility and academics at QMUL. Following this membrane integrity theme, I am also branching out into examining the contribution of membrane damage and repair to neurodegenerative diseases through a recently awarded Chan Zuckerburg Initiative grant, and I share supervision of a PhD student examining the role of ESCRT proteins in membrane repair. The major focus of my lab's expansion at Crick has been to analyse the mitotic inheritance of other organelles (notably the ER). This is a largely unresolved question in biology, and we are leveraging support of the EM core to use volume electron microscopical approaches to document how the ER is separated during division. These EM analyses are paired with biochemical and light microscopical examination of the inheritance process in living cells. This is a major project, and I am grateful to Lucy for introducing us to the Zooniverse Citizen Science platform which will be essential for analysing and reconstructing the large volumes of FIB-SEM data generated.

During the Covid period, we turned to analysing the membrane trafficking pathways exploited by SARS-CoV-2 structural proteins and have discovered an important intracellular trafficking mechanism that we believe will help SARS-CoV-2 assemble.

Future Plans

Future Plans for return to King's involve developing more our analysis of organelle inheritance during division. I would like to look next at the interplay between different organelles, how organelle contacts are remodelled during division and how these contacts (largely with the ER) govern organellar inheritance during this process. We have some interesting data that has come from our FIBSEM analysis which suggests that the ER is remodelled during division by sliding around mitochondria and analysis of the co-regulation of these organelles during division will be an important next step. This will be work that has been initiated and directly stimulated by my interactions with Crick scientists in the EM core. Building upon our discovery of mitotic regulation of ESCRT-III function during nuclear envelope regeneration, I will next look to see how cell signalling programmes can influence organelle inheritance. Lastly, I would like to continue looking at ESCRT-III dependent nuclear envelope regeneration, but in terms of how inner nuclear membrane proteins that are necessary for ESCRT recruitment are released to allow proper structuring of chromatin in the daughter cells. I hope to work these aims into a renewal of my Wellcome Senior Research Fellowship.

Research outputs

Olmos Y, Hodgson L, Mantell J, Verkade P and Carlton JG. (2015) ***ESCRT-III controls nuclear envelope reformation*****. Nature 522:236-9. DOI: 10.1038/nature14503**
This paper showed for the 1st time that the ESCRT-III complex localised to the nuclear envelope and controlled nuclear envelope reformation, opening a new field in ESCRT-biology.

Olmos, Y, Perdrix-Rosell A and Carlton JG. (2016) ***Membrane binding CHMP7 directs ESCRT-III-dependent nuclear envelope reformation*****. Curr. Biol. 26:2635-41. DOI: 10.1016/j.cub.2016.07.039**
This paper showed that CHMP7 is an ER-localised membrane-binding protein. We showed that the ability of CHMP7 to bind ER membranes was essential for assembling ESCRT-III at the reforming NE and for post-mitotic nuclear regeneration.

Monypenny J, Milewicz H, Flores-Borja F, Weitsman G, Cheung A, Chowdhury R, Burgoyne T, Arulappu A, Lawler K, Barber PR, [et al.,] Carlton JG and Ng T. (2018) ***ALIX regulates tumour-mediated immunosuppression by controlling EGFR activity and PD-L1 presentation*****. Cell Rep. 24:630-41. DOI: 10.1016/j.celrep.2018.06.066**
This paper showed that the key immunosuppressive molecule, PD-L1, was secreted from cells on exosomes and that the ESCRT-associated protein, ALIX, was essential for incorporating PD-L1 onto these structures.

Ventimiglia, LN, Cuesta-Geijo MA, Martinelli N, Caballe A, Macheboeuf P, Miguet N, Parnham IM, Olmos Y, Carlton JG, Weissenhorn et al. (2018) ***CC2D1B coordinates ESCRT-III activity during the mitotic reformation of the nuclear envelope*****. Dev. Cell 47:547-63. DOI: 10.1016/j.devcel.2018.11.012**
This paper demonstrated that ESCRT-interacting proteins could control the dynamics of ESCRT-III assembly at the reforming nuclear envelope.

Terry SJ, Dona F, Osenberg P, Carlton JG and Eggert US. (2018) ***Capping protein regulates actin dynamics during cytokinetic midbody maturation*****. Proc. Natl. Acad. Sci. U.S.A. 115:2138-43. DOI: 10.1073/pnas.1722281115**
This paper showed that retarding actin polymerisation in the midbody was necessary for proper recruitment of ESCRT-III and completion of cytokinesis.