

ALBAN ORDUREAU, PH.D.

Memorial Sloan-Kettering Cancer Center
1275 York Avenue, RRL 5XX
New York, NY 10021, U.S.A

Phone:
Email: alban_ordureau@hms.harvard.edu

RESEARCH EXPERIENCE

POST-DOCTORAL RESEARCH SCIENTIST

November 2012 – December 2020

DEPARTMENT OF CELL BIOLOGY – HARVARD MEDICAL SCHOOL

Boston, U.S.A

Supervisor: Professor J. Wade Harper

- *Project:* I studied and determined how the Ubiquitin E3 ligase, mutated in Parkinson's disease, called Parkin is activated and specifically retained with the help of phosphorylated-ubiquitin chains onto damaged mitochondria. This work establishes new biochemical details for the PINK1/Parkin pathway and mechanistically links genes mutated in Parkinson's disease and amyotrophic lateral sclerosis in a common selective autophagy pathway.

POST-DOCTORAL RESEARCH SCIENTIST

October 2011 – October 2012

MEDICAL RESEARCH COUNCIL PROTEIN PHOSPHORYLATION UNIT - UNIVERSITY OF DUNDEE

Dundee, U.K.

Supervisor: Professor Sir Philip Cohen, FRS, FRSE, FMedSci, FAA

- *Project:* I studied and characterised a transcription factor called DEAF1 that I previously identified as a Pellino1-interacting protein during my PhD. I was able to demonstrate that similar to the E3 ligase Pellino1 it stimulates the IFN β gene transcription by enhancing the interaction of IRF3 with the IFN β promoter. This work established DEAF1 as a novel signaling component required for IFN β production by viral double-stranded RNA.

PH.D. STUDENT

January 2007 – September 2011

MEDICAL RESEARCH COUNCIL PROTEIN PHOSPHORYLATION UNIT - UNIVERSITY OF DUNDEE

Dundee, U.K.

Supervisor: Professor Sir Philip Cohen, FRS, FRSE, FMedSci, FAA

- *Project:* The interplay between protein phosphorylation and protein ubiquitination in regulating innate immunity.
- My doctoral studies focused on investigating the regulation and function of post-translational modifications such as phosphorylation and ubiquitination in innate immune signalling. I developed a robust and specific method to purify and study the ligand-induced formation of endogenous poly-ubiquitylated-proteins. I used these methods to study many proteins, including the IRAK1 protein for which I developed a keen interest and focused on during my Ph.D. This led me to show that Pellino E3 ligases can be activated upon phosphorylation by kinases such as IRAK1, resulting in the poly-ubiquitination of substrates.

EDUCATION AND AWARDS

Ph.D., Biochemistry and Biomedical Sciences

January 2007 – October 2011

UNIVERSITY OF DUNDEE – MRC-PPU

Dundee, United Kingdom

Thesis: An investigation of the role of E3 ubiquitin ligases in regulating innate immunity.

Master of Biology Biotechnology and Therapeutic Research

September 2002 – May 2006

FACULTY OF SCIENCES AND TECHNOLOGIES – UNIVERSITY OF NANTES

Nantes, France

Fellowship: - Medical Research Council Four-Year Ph.D. Studentship (2007 - 2010).

- Edward R. and Anne G. Lefler Center Postdoctoral Fellowship (2015 - 2017).

COMPLETE PUBLICATION LIST (35)

- McKenna, M.J.*, Sim, S.I.*, **Ordureau, A.**, Wei, L., Harper, J.W., Shao, S., Park E. (2020) The endoplasmic reticulum P5A-ATPase is a transmembrane helix dislocase. *Science* 369(6511)
- Sinha, N.K.*, **Ordureau, A.***, Best, K.M.*, Saba, J.A., Zinshteyn, B., Sundaramoorthy, E., Fulzele, A., Garshott, D.M., Denk, T., Thoms, M., Paulo, J.A., Harper, J.W., Bennett, E.J., Beckmann, R., Green, R. (2020) EDF1 coordinates cellular responses to ribosome collisions. *eLife* 9, e58828
- An, H.*, **Ordureau, A.***, Korner, M., Paulo, J.A., Harper, J.W. (2020) Systematic Quantitative Analysis of Ribosome Inventory During Nutrient Stress. *Nature* 583(7815), 303-309
- Martinez-Chacin, R.C., Bodrug, T., Bolhuis, D.L., Kedziora, K.M., Bonacci, T., **Ordureau, A.**, Gibbs, M.E., Weissmann, F., Qiao, R., Grant, G.D., Cook, J.G., Peters, J-M., Harper, J.W., Emanuele, M.J., Brown, N.G. (2020) Ubiquitin chain elongating E2 UBE2S activates the RING E3 APC/C for substrate priming with UBE2C. *Nature Structural & Molecular Biology* 27(6):550-560.
- **Ordureau, A.**, Paulo, J.A., Zhang, J., An, H., Swatek, K.N., Cannon, J.R., Wan, Q., Komander, D., Harper J.W. (2020) Global landscape and dynamics of Parkin and USP30-dependent ubiquitylomes in iNeurons during mitophagic signaling. *Molecular Cell*. 77(5):1124-1142.
- Ahfeldt, T., **Ordureau, A.**, Bell, C., Sarrafha, L., Sun, C., Piccinotti, S., Grass, T., Parfitt, G.M., Paulo, J.A., Yanagawa, F., Uozumi, T., Kiyota, Y., Harper, J.W., Rubin, L.L. (2020) Pathogenic pathways in early onset autosomal recessive Parkinson's disease discovered using isogenic human dopaminergic neurons. *Stem Cell Reports*. 14 (1), 75-90.
- Jacoupy, M., Hamon-Keromen, E., **Ordureau, A.**, Erpapazoglou, Z., Coge, F., Corvol, J-C., Nosjean, O., Mannoury La Cour, C., Millan, M. J., Boutin, J. A., Harper, J. W., Brice, A., Guedin, D., Gautier, C. A., Corti, O. (2019) The PINK1 kinase-driven ubiquitin ligase Parkin promotes mitochondrial protein import through the presequence pathway in living cells. *Scientific Reports*. 9(1):11829
- Gottlieb, C.D.*, Thompson, A.C.S.*, **Ordureau, A.**, Harper, J.W., Kopito, R.R. (2019) Acute unfolding of a single protein immediately stimulates recruitment of ubiquitin protein ligase E3C (UBE3C) to 26S proteasomes. *J Biol Chem*. 294 (45), 16511-16524
- Najafov, A., Mookhtiar, A.K., Luu, H.S., **Ordureau, A.**, Pan, H., Amin, P.P., Li, Y., Lu, Q., Yuan, J. (2019) TAM Kinases Promote Necroptosis by Regulating Oligomerization of MLKL. *Molecular Cell*. 75(3):457-468
- An, H., **Ordureau, A.**, Paulo, J.A., Shoemaker, C.J., Denic, V., Harper, J.W. (2019) TEX264 is an ER-resident ATG8-interacting protein critical for endoplasmic reticulum remodeling during nutrient stress. *Molecular Cell*. 74(5):891-908.
 - Featured in a Spotlight of Trends in Biochemical Science as well as Editor's Corner of Autophagy
- Heo, J.M., **Ordureau, A.**, Swarup, S., Paulo, J.A., Shen, K., Sabatini, D.M., Harper, J.W. (2018) RAB7A phosphorylation by TBK1 promotes mitophagy via the PINK-PARKIN pathway. *Science Advances*. Nov 21;4(11)
- **Ordureau, A.**, Paulo, J.A., Zhang, W., Ahfeldt, T., Zhang, J., Cohn, E.F., Hou, Z., Heo, J.M., Rubin, L.L., Sidhu, S.S., Gygi, S.P., Harper, J.W. (2018) Dynamics of PARKIN-Dependent Mitochondrial Ubiquitylation in Induced Neurons and Model Systems Revealed by Digital Snapshot Proteomics. *Molecular Cell*. 70(2) 211-227
- Harper, J.W., **Ordureau, A.**, Heo, J.M. (2018) Building and decoding ubiquitin chains for mitophagy. *Nat Rev Mol Cell Biol*. 19(2):93-108
- Mohideen, F., Paulo, J.A., **Ordureau, A.**, Gygi, S.P., Harper, J.W. (2017) Quantitative Phospho-proteomic Analysis of TNF α /NF κ B Signaling Reveals a Role for RIPK1 Phosphorylation in Suppressing Necrotic Cell Death. *Mol Cell Proteomics*. 16(7):1200-1216.
- Wang, B., Jie, Z., Joo, D., **Ordureau, A.**, Liu, P., Gan, W., Guo, J., Zhang, J., North, B.J., Dai, X., Cheng, X., Bian, X., Zhang, L., Harper, J.W., Sun, S.C., Wei, W. (2017) TRAF2 and OTUD7B govern a ubiquitin-dependent switch that regulates mTORC2 signalling. *Nature*, 545(7654):365-369.
- Liu L, Michowski W, Inuzuka H, Shimizu K, Nihira NT, Chick JM, Li N, Geng Y, Meng AY, **Ordureau A**, Kołodziejczyk A, Ligon KL, Bronson RT, Polyak K, Harper JW, Gygi SP, Wei W, Sicinski P. (2017) G1 cyclins link proliferation, pluripotency and differentiation of embryonic stem cells. *Nat Cell Biol*. 19(3):177-188.
- Rose C.M.*, Isasa M.*, **Ordureau A.**, Prado M.A., Beausoleil S.A., Jedrychowski M.P., Finley D.J., Harper J.W., Gygi S.P. (2016). Highly Multiplexed Quantitative Mass Spectrometry Analysis of Ubiquitylomes. *Cell Systems* 3(4):395-403
- Brown, N. G.*, VanderLinden, R.*, Watson, E. R.*, Weissmann, F., **Ordureau, A.**, Wu, K.-P., Zhang, W., Yu, S., Mercredi, P.Y., Harrison, J.S., Davidson, I.F., Qiao, R., Lu, Y., Dube, P., Brunner, M.R., Grace, C.R., Miller, D.J., Haselbach, D., Jarvis, M.A., Yamaguchi, M., Yanishevski, D., Petzold, G., Sidhu, S.S., Kuhlman, B., Kirschner, M.W., Harper, J.W., Peters, J.M., Stark, H., Schulman, B.A. (2016). Dual RING E3 Architectures Regulate Multiubiquitination and Ubiquitin Chain Elongation by APC/C. *Cell* 165(6), 1440–1453.

- Zhang, W.*, Wu, K.-P.*, Sartori, M.A., Kamadurai, H.B., **Ordureau, A.**, Jiang, C., Mercredi, P.Y., Murchie, R., Hu, J., Persaud, A., Mukherjee, M., Li, N., Doye, A., Walker, J.R., Sheng, Y., Hao, Z., Li, Y., Brown, Y.K., Lemichez, E., Chen, J., Tong, Y., Harper, J.W., Moffat, J., Rotin, D., Schulman, B.A., and Sidhu, S.S (2016). System-Wide Modulation of HECT E3 Ligases with Selective Ubiquitin Variant Probes. *Molecular Cell* 62, 121–136.
- Heo, J.H., **Ordureau, A.**, Paulo, J.A., Rinehart, J., and Harper, J.W. (2015) The PINK1-PARKIN Mitochondrial Ubiquitylation Pathway Drives a Program of OPTN/NDP52 Recruitment and TBK1 Activation to Promote Mitophagy. *Molecular Cell* 60, 7–20.
- Huttlin, E.L., Ting, L., Bruckner, R.J., Gebreab, F., Gygi, M.P., Szpyt, J., Tam, S., Zarraga, G., Colby, G., Baltier, K., Dong, R., Guarani, V., Vaites, L.P., **Ordureau, A.**, Rad, R., Erickson, B.K., Wuhr, M., Chick, J., Zhai, B., Kolippakkam, D., Mintseris, J., Obar, R.A., Harris, T., Artavanis-Tsakonas, S., Sowa, M.E., De Camilli, P., Paulo, J.A., Harper, J.W., and Gygi, S.P. (2015). The BioPlex Network: A Systematic Exploration of the Human Interactome. *Cell* 162, 425-440.
- Pickrell, A.M.*, Huang, C.H.*, Kennedy, S.R., **Ordureau, A.**, Sideris, D.P., Hoekstra, J.G., Harper, J.W., and Youle, R.J. (2015). Endogenous Parkin Preserves Dopaminergic Substantia Nigral Neurons following Mitochondrial DNA Mutagenic Stress. *Neuron* 87, 371-381.
- **Ordureau, A.**, Munch, C., and Harper, J.W. (2015). Quantifying ubiquitin signaling. *Molecular Cell* 58, 660-676.
- **Ordureau, A.**, Heo, J.M., Duda, D.M., Paulo, J.A., Olszewski, J.L., Yanishevski, D., Rinehart, J., Schulman, B.A., and Harper, J.W. (2015). Defining roles of PARKIN and ubiquitin phosphorylation by PINK1 in mitochondrial quality control using a ubiquitin replacement strategy. *Proc Natl Acad Sci USA* 112, 6637-6642.
- Cirulli, E.T., Lasseigne, B.N., Petrovski, S., Sapp, P.C., Dion, P.A., Leblond, C.S., Couthouis, J., Lu, Y.F., Wang, Q., Krueger, B.J., Ren, Z., Keebler, J., Han, Y., Levy, S.E., Boone, B.E., Wimbish, J.R., Waite, L.L., Jones, A.L., Carulli, J.P., Day-Williams, A.G., Staropoli, J.F., Xin, W.W., Chesi, A., Raphael, A.R., McKenna-Yasek, D., Cady, J., Vianney de Jong, J.M., Kenna, K.P., Smith, B.N., Topp, S., Miller, J., Gkazi, A., Consortium, F.S., Al-Chalabi, A., van den Berg, L.H., Veldink, J., Silani, V., Ticozzi, N., Shaw, C.E., Baloh, R.H., Appel, S., Simpson, E., Lagier-Tourenne, C., Pulst, S.M., Gibson, S., Trojanowski, J.Q., Elman, L., McCluskey, L., Grossman, M., Shneider, N.A., Chung, W.K., Ravits, J.M., Glass, J.D., Sims, K.B., Van Deerlin, V.M., Maniatis, T., Hayes, S.D., **Ordureau, A.**, Swarup, S., Landers, J., Baas, F., Allen, A.S., Bedlack, R.S., Harper, J.W., Rouleau, G.A., Brown, R., Harms, M.B., Cooper, G.M., Harris, T., Myers, R.M., and Goldstein, D.B. (2015). Exome sequencing in amyotrophic lateral sclerosis identifies risk genes and pathways. *Science* 347, 1436-1441.
- Li, N., Fassel, A., Chick, J., Inuzuka, H., Li, X., Mansour, M.R., Liu, L., Wang, H., King, B., Shaik, S., Gutierrez, A., **Ordureau, A.**, Otto, T., Kreslavsky, T., Baitsch, L., Bury, L., Meyer, C.A., Ke, N., Mulry, K.A., Kluk, M.J., Roy, M., Kim, S., Zhang, X., Geng, Y., Zagozdzon, A., Jenkinson, S., Gale, R.E., Linch, D.C., Zhao, J.J., Mullighan, C.G., Harper, J.W., Aster, J.C., Aifantis, I., von Boehmer, H., Gygi, S.P., Wei, W., Look, A.T., and Sicinski, P. (2014). Cyclin C is a haploinsufficient tumour suppressor. *Nat Cell Biol* 16, 1080-1091.
- **Ordureau, A.**, Sarraf, S.A., Duda, D.M., Heo, J.M., Jedrychowski, M.P., Sviderskiy, V.O., Olszewski, J.L., Koerber, J.T., Xie, T., Beausoleil, S.A., Wells, J.A., Gygi, S.P., Schulman, B.A., and Harper, J.W. (2014). Quantitative proteomics reveal a feedforward mechanism for mitochondrial PARKIN translocation and ubiquitin chain synthesis. *Molecular Cell* 56, 360-375.
 - *Commentary:* Stolz, A., & Dikic, I. (2014). PINK1-PARKIN interplay: down to ubiquitin phosphorylation. *Mol. Cell*, 56(3), 341–342.
- **Ordureau, A.**, and Harper, J.W. (2014). Cell biology: balancing act. *Nature* 510, 347-348.
- Emmerich, C.H., **Ordureau, A.**, Strickson, S., Arthur, J.S., Pedrioli, P.G., Komander, D., and Cohen, P. (2013). Activation of the canonical IKK complex by K63/M1-linked hybrid ubiquitin chains. *Proc Natl Acad Sci USA* 110, 15247-15252.
- **Ordureau, A.**, Enesa, K., Nanda, S., Le Francois, B., Peggie, M., Prescott, A., Albert, P.R., and Cohen, P. (2013). DEAF1 is a Pellino1-interacting protein required for interferon production by Sendai virus and double-stranded RNA. *J Biol Chem* 288, 24569-24580.
- Enesa, K., **Ordureau, A.**, Smith, H., Barford, D., Cheung, P.C., Patterson-Kane, J., Arthur, J.S., and Cohen, P. (2012). Pellino1 is required for interferon production by viral double-stranded RNA. *J Biol Chem* 287, 34825-34835.
- Gleason, C.E., **Ordureau, A.**, Gourlay, R., Arthur, J.S., and Cohen, P. (2011). Polyubiquitin binding to optineurin is required for optimal activation of TANK-binding kinase 1 and production of interferon beta. *J Biol Chem* 286, 35663-35674.
- Nanda, S.K., Venigalla, R.K., **Ordureau, A.**, Patterson-Kane, J.C., Powell, D.W., Toth, R., Arthur, J.S., and Cohen, P. (2011). Polyubiquitin binding to ABIN1 is required to prevent autoimmunity. *J Exp Med* 208, 1215-1228.
- Nichols, R.J., Dzamko, N., Morrice, N.A., Campbell, D.G., Deak, M., **Ordureau, A.**, Macartney, T., Tong, Y., Shen, J., Prescott, A.R., and Alessi, D.R. (2010). 14-3-3 binding to LRRK2 is disrupted by multiple Parkinson's disease-associated mutations and regulates cytoplasmic localization. *Biochem J*. 430, 393-404.
- **Ordureau, A.***, Smith, H.*, Windheim, M., Peggie, M., Carrick, E., Morrice, N., and Cohen, P. (2008). The IRAK-catalysed activation of the E3 ligase function of Pellino isoforms induces the Lys63-linked polyubiquitination of IRAK1. *Biochem J*. 409, 43-52.

(*) Indicates equal contribution by authors.

Full bibliography with article citations: [Alban Ordureau](#)