Worms need microbes too: microbiota, metabolism and ageing in *Caenorhabditis elegans*

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Animals typically live in close association with commensal and symbiotic microbes. Recent studies have revealed that the status of gut microbiota can influence nutrition-related syndromes such as obesity and type-2 diabetes, and perhaps ageing. However, to-date we know very little about how such interactions are regulated. The suspected role of host-microbiota interactions in human diseases and the regulation of metabolism is largely derived from observational studies, and it is often difficult to establish whether changes in microbiota are cause or effect of pathology. Currently we lack understanding of how microorganisms can precisely regulate the response of key components in metabolic health. Therefore, it is important to understand how these microbial communities determine human physiology, and if they can be targeted by drugs to improve human health. Of particular interest is the role of microbiota in mediating effects on drugs targeted at metabolic disease and ageing. In this talk we assess how microbiota may be manipulated (via pharmacology, diet or gene manipulation) in order to alter metabolism, immunity, health and aging in the host. We will focus on the nematode *Caenorhabditis elegans* that in combination with one microbial species is an excellent, defined model system to investigate the mechanisms of host-microbiota interactions in the context of ageing, particularly given the combined power of worm and microbial genetics.

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■ Education

2003 BSc Biochemistry, University of Porto, Portugal
2004 MSc Biology of Ageing, Universite Paris VII Denis Diderot, Paris, France
2007 PhD Biochemistry, Universite Paris VII Denis Diderot, Paris, France

■ Career

2007-08: Postdoctoral researcher, Universite Paris VII, with Prof. Bertrand Friguet. *Zinc supplementation in elderly subjects*.
2008-13: Postdoctoral fellow, University College London, UK with Prof. David Gems. *Anti-ageing drugs in C. elegans*.
2013: Lecturer in metabolism and metabolic disease, University College London, UK
2014: Sir Henry Dale Royal Society/Wellcome Trust Research Fellow, Department of Structural and Molecular Biology, University College London, U.K. *Exploring the gut microbial action of metformin: targeting the gut microbiota to treat metabolic disease*

■ Major Research Interest

Host-microbe interactions, Biological mechanisms of ageing, Drug metabolism

■ Selected Recent Publications

1) Cabreiro, F., Au, C., Leung, K.Y., Vergara-Irigaray, N., Cocheme, H.M., Noori, T., Weinkove, D., Schuster, E., Greene, N.D., and Gems, D. Metformin retards aging in *C. elegans* by altering microbial folate and methionine metabolism. **Cell** 153, 228-239, 2013

2) Cabreiro, F., and Gems, D. Worms need microbes too: microbiota, health and aging in *Caenorhabditis elegans*. **EMBO molecular medicine** 5, 1300-1310, 2013

3) Coburn, C., Allman, E., Mahanti, P., Benedetto, A., Cabreiro, F., Pincus, Z., Matthijssens, F., Araiz, C., Mandel, A., Vlachos, M., et al. Anthranilate fluorescence marks a calcium-propagated necrotic wave that promotes organismal death in *C. elegans*. **PLoS biology** 11, e1001613, 2013

4) Leung, K.Y., De Castro, S.C., Cabreiro, F., Gustavsson, P., Copp, A.J., and Greene, N.D. Folate metabolite profiling of different cell types and embryos suggests variation in folate one-carbon metabolism, including developmental changes in human embryonic brain. **Molecular and cellular biochemistry** 378, 229-236, 2013

5) Valentini, S., Cabreiro, F., Ackerman, D., Alam, M.M., Kunze, M.B., Kay, C.W., and Gems, D. Manipulation of in vivo iron levels can alter resistance to oxidative stress without affecting ageing in the nematode *C. elegans*. **Mechanisms of ageing and development** 133, 282-290, 2012

6) Cabreiro, F., Burnett, C., Valentini, S., Goss, M., Somogyvari, M., Piper, M.D., Hoddinott, M., Sutphin, G.L., Leko, V., McElwee, J.J., *et al*. Absence of effects of Sir2 overexpression on lifespan in *C. elegans* and *Drosophila*. **Nature** 477, 482-485, 2011

7) Cabreiro, F., Ackerman, D., Doonan, R., Araiz, C., Back, P., Papp, D., Braeckman, B.P., and Gems, D. Increased life span from overexpression of superoxide dismutase in Caenorhabditis elegans is not caused by decreased oxidative damage. **Free radical biology & medicine** 51, 1575-1582, 2011

8) Cocheme, H.M., Quin, C., McQuaker, S.J., Cabreiro, F., Logan, A., Prime, T.A., Abakumova, I., Patel, J.V., Fearnley, I.M., James, A.M., et al. Measurement of H_2O_2 within living *Drosophila* during aging using a ratiometric mass spectrometry probe targeted to the mitochondrial matrix. **Cell metabolism** 13, 340-350, 2011

9) Cabreiro, F., and Gems, D. Treating aging: progress toward dietary restriction mimetics. **F1000 biology reports** 2, 76, 2010

10) Cabreiro, F., Picot, C.R., Perichon, M., Friguet, B., and Petropoulos, I. Overexpression of methionine sulfoxide reductases A and B2 protects MOLT-4 cells against zinc-induced oxidative stress. **Antioxidants & redox signaling** 11, 215-225, 2009

11) Cabreiro, F., Picot, C.R., Perichon, M., Castel, J., Friguet, B., and Petropoulos, I. Overexpression of mitochondrial methionine sulfoxide reductase B2 protects leukemia cells from oxidative stress-induced cell death and protein damage. **The Journal of biological chemistry** 283, 16673-16681, 2008