

BIOGRAPHICAL SKETCH

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NAME: Michalis Agathocleous

eRA COMMONS USER NAME (credential, e.g., agency login): magath

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Cambridge, U.K.	BA	2000-2003	Medical Sciences
University of Cambridge, U.K.	Ph.D.	2003-2007	Neurobiology
University of Cambridge, U.K.	Fellow	2007-2011	Neurobiology
University of Texas Southwestern, TX	Fellow	2012-2017	Immunology

A. Personal Statement

My laboratory studies the metabolism of hematopoietic stem cells (HSCs) and its impact on leukemia initiation. By studying HSC metabolism and leukemia cell metabolism in parallel, we hope to understand how normal metabolic control maintains homeostasis and enables regeneration, and how aberrant metabolic control leads to cancer. We are also investigating the impact of physiological challenges on stem cell function and cancer initiation.

We have developed rare cell metabolomics methods to profile the metabolome of somatic stem cells for the first time. Using those methods, we discovered that each hematopoietic stem and progenitor cell type is metabolically distinct, and that almost all detected metabolites have cell-type specific enrichment patterns. Most of these metabolites have not been previously implicated in stem and progenitor cell function, raising the possibility that they have novel roles in hematopoiesis and leukemia. We have shown that ascorbate (Vitamin C) accumulates in HSCs and that it promotes the activity of the tumor suppressor enzyme TET2, which oxidizes methylated cytosine on DNA. Ascorbate depletion promotes stem cell function and myeloid leukemia. Therefore, a dietary metabolite can directly impact the stem cell epigenome, regeneration and cancer initiation *in vivo*.

B. Positions and Honors**Positions**

12/2017 - present Assistant Professor, Children's Medical Center Research Institute, and Department of Pediatrics, University of Texas Southwestern Medical Center.

Honors and Awards

2000-2006 Junior, Senior and Research Scholar, Trinity College Cambridge.
2007-2011 Research Fellow, Gonville and Caius College Cambridge.
2011-2014 Research Fellow, Royal Commission for the Exhibition of 1851.
2017 Cancer Prevention and Research Institute of Texas (CPRIT) Scholar
2019 Alex's Lemonade Stand Foundation 'A' Award for childhood cancer research.
2019 American Cancer Society Pilot Award

C. Selected publications

Research Papers

- 1) Agathocleous M, Meacham CE, Burgess RJ, Piskounova E, Zhao Z, Crane GM, Cowin BL, Bruner E, Murphy MM, Chen W, Spangrude GJ, Hu Z, DeBerardinis RJ, Morrison SJ: Ascorbate regulates haematopoietic stem cell function and leukaemogenesis, **Nature** 549:476 (2017).
- 2) Piskounova E, Agathocleous M, Murphy MM, Hu Z, Huddlestun SE, Zhao Z, Leitch AM, Johnson TM, DeBerardinis RJ, Morrison SJ: Oxidative stress inhibits distant metastasis by human melanoma cells, **Nature** 527:186 (2015).
- 3) Love NK, Keshavan N, Lewis R, Harris WA, Agathocleous M: A nutrient-sensitive restriction point is active during retinal progenitor cell differentiation, **Development** 141:697 (2014).
- 4) Agathocleous M, Love NK, Randlett O, Harris JJ, Liu J, Murray AJ, Harris WA: Metabolic differentiation in the embryonic retina, **Nature Cell Biology** 14:859 (2012).

Reviews

- 1) Burgess RJ*, Agathocleous M*, Morrison SJ: Metabolic regulation of stem cell self-renewal and differentiation, **J Internal Medicine** 276:12 (2014) *equal contribution.
- 1) Agathocleous M, Harris WA: Metabolism in physiological cell proliferation and differentiation, **Trends in Cell Biology** 23:484 (2013).
- 2) Agathocleous M, Harris WA: From progenitors to differentiated cells in the vertebrate retina, **Annu. Rev. Cell Dev. Biol.** 25:45 (2009).

Full bibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/54152437/?sort=date&direction=descending>