BIOGRAPHICAL SKETCH

NAME: Teruel, Mary

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
Duke University, Durham, NC	Postdoctoral	12/2000	Cell Biology
Stanford University, Stanford, CA	Ph.D.	01/1996	Aeronautical Engineering
Stanford University, Stanford, CA	M.S.	08/1989	Aeronautical Engineering
University of Pennsylvania, Philadelphia, PA	B.S.	05/1985	Mechanical Engineering

A. Personal Statement

The overarching goal of my research is to understand how cells control terminal cell differentiation, a process which is essential for tissue development, maintainance, and regeneration in all multicellular organisms. My lab uses live-cell imaging approaches to uncover the critical signaling events, transcriptional control principles, and role of the cell cycle in regulating the differentiation process. As model systems, we are particularly focused on adipogenesis and neurogenesis. Below are examples of papers my laboratory has published:

1. Zhao ML, Rabiee AR, Kovary KM, Bahrami-Nejad Z, Taylor B, **Teruel MN.** (2020). Molecular competition in G1 controls when cells simultaneously commit to terminally differentiate and exit the cell-cycle. ***Cell Reports*** 2020 Jun 16; 31(11):107769. PMID: 32553172.
2. Bahrami-Nejad Z*, Zhao ML*, Tholen S, Hunderdosse D, Tkach KE, van Schie S, Chung M, and **Teruel MN.** (2018). A transcriptional circuit filters oscillating circadian hormonal inputs to regulate fat cell differentiation. ***Cell Metabolism*** Apr 3, 27(4):854-868.e8. PMID: 29617644. *equal contribution. *Highlighted in* ***Nature, NIH Research Matters****, and by the* ***Faculty of 1000****.*
3. Ahrends R, Ota A, Kovary KM, Kudo T, Park BO, **Teruel MN.** (2014). Controlling low rates of cell differentiation through noise and ultra-high feedback. ***Science*** Jun 20; 344:1384-9. PMID: 24948735. *Awarded an Editors' Choice rating by the signaling editors of* ***Science.***
4. Park BO, Ahrends R, **Teruel MN.** (2012). Consecutive positive feedback loops create a bistable switch that controls preadipocyte to adipocyte conversion. ***Cell Reports*** Oct 25; 2(4): 976-90. Epub 2012 Oct. 11. PMID: 23063366.

B. Positions and Honors

Positions and Employment

2020 – present Assistant Professor, Dept. of Biochemistry & the Drukier Institute of Children's Health, Weill Cornell Medical College, Cornell University

2020 - 2021 Member of Scientific Committee for the 21st International Conference on Systems Biology: ICSB 2021, Hartford, CT, USA.

2019-present Member of the Editorial Board of ***PLOS Biology***

2019 Member of Scientific Committee for the 20th International Conference on Systems Biology: ICSB 2019, Okinawa, Japan.

2017 - 2020 Member of the NIH P50 Stanford Diabetes Research Center

2016 - 2020 Assistant Professor (by Courtesy), Dept. of Bioengineering, Stanford University, Stanford, CA.

2015 - 2020 Faculty Fellow, Stanford Institute for Chemistry, Engineering, and Medicine for Human Health (CHEM-H)

2014 - 2020 Member of the Stanford Cancer Institute

2013 - 2020	Co-Investigator and Director of the Technology Core, Stanford NIH Center for Systems Biology (P50)
2012 - 2020	Member of the Stanford Cardiovascular Institute
2012 - 2020	Assistant Professor, Dept. of Chemical & Systems Biology, Stanford University, Stanford, CA.
2007 - 2011	Senior Research Scientist, Dept. of Chemical & Systems Biology, Stanford University.
2007 - 2009	Visiting Scientist with Professor Ruedi Aebersold, Institute for Molecular Systems Biology, ETH Zürich, Zürich, Switzerland.
2001 - 2007	Senior Research Scientist, Dept. of Molecular Pharmacology, Stanford University.
2001 - 2005	Microscopy, Imaging, and Analysis Consultant for the Alliance for Cellular Signaling.
1998 - 2000	Postdoctoral Fellow, Dept. of Cell Biology, Duke University, Durham, NC.
1995 -1998	Microscopy Engineer, Dept. of Cell Biology, Duke University, Durham, NC.
1989 - 1995	Research Assistant with Prof. John Eaton, NASA Ames Research Center and the Dept of Mechanical Engineering, Thermosciences Division, Stanford University.
1988 - 1989	Research Assistant with Prof. Robert MacCormack, Dept. of Aeronautics & Astronautics, Stanford University. Computation of Hypersonic Duct Flow.
1988	Research Assistant with Prof. Peter Banks, Dept. of Electrical Engineering, Stanford University. Shuttle Electrodynamic Tether System Project
1986 - 1987	Test Engineer, Kronos Incorporated, Waltham, MA.
1985 - 1986	Helicopter Structural Test Engineer, Kaman Aerospace Corporation, Bloomfield, CT

Honors

2018	Recipient of the Stanford McCormick/Gabilan Award given to a faculty member at Stanford for their work in supporting the mentoring, training and encouragement of women pursuing the study of medicine, in teaching medicine, and engaging in medical research.
2018	Recipient of the inaugural Diabetes Knowledge Award (DKA) awarded by the Stanford Diabetes Research Center for the most impactful, original diabetes-related publication from Stanford in 2017-2018.
2013 – present	Stanford Gabilan Fellow
2007	Biochemical Journal Young Investigator Award
2000 - 2006	National Institutes of Health (NGHRI) Quantitative Mentored Career Development Award
1998 - 2001	National Institutes of Health Postdoctoral Fellowship
1989 – 1993	National Air and Space Administration (NASA) Graduate Student Fellowship

B. Contribution to Science

1. Adipogenesis

I have a deep interest that my basic science findings can someday be used to treat human disease, and this is a main motivation for my focus on adipogenesis and adipocyte function since defects in these lead to insulin resistance, diabetes, cardiovascular disease, and many types of cancer. My interest in adipocytes started with the development of a bioinformatics and fluorescence imaging approach to comprehensively identify proteins downstream of PI3K signaling which regulates insulin action and glucose uptake capability (Park,...Teruel, ***Molecular Cell,*** 2007). In a series of papers, my laboratory developed and experimentally validated the first quantitative molecular model of adipogenesis, based on stochastic differential equations, explaining how adipocyte progenitor cells undergo terminal differentiation, and how mammalian cells can adjust the fraction of cells that differentiate (Park,...,Teruel, ***Cell Reports*** 2012; Ahrends,...,Teruel, ***Science***, 2014; Bahrami-Nejad,...,Teruel, ***Cell Metabolism***, 2018). My lab has also developed novel targeted proteomics approaches that allow us to validate our in vitro findings, as well as to identify new regulatory mechanisms, in mouse models and in human patients (Ota,...,Teruel, ***Journal of Lipid Research***, 2015). Of note, our recent paper (Bahrami-Nejad et al, ***Cell Metabolism,*** 2018) won the inaugural Diabetes Knowledge Award awarded by the Stanford Diabetes Center for the most impactful, original diabetes-related publication from Stanford in 2017-2018 and also was chosen by the NIH National Institute of Diabetes and Digestive and Kidney Disease (NIDDK) to be highlighted in ***NIH Research Matters***. Our recent publication (Zhao,...,Teruel, ***Cell Reports*** 2020) describes our work to understand how the cell cycle controls adipogenesis and to begin to uncover the molecular mechanisms explaining why mice deficient in the cyclin-dependent kinase inhibitors p21 and p27 have 6-fold increases in fat mass, as well as impaired glucose tolerance and insulin sensistivity.

a) Park WS, Heo WD, Whalen JH, O'Rourke NA, Bryan HM, Meyer T, **Teruel MN.** (2008). Identification of PIP3-regulated proteomes from C.elegans to human by model prediction and live imaging. ***Molecular Cell*** May 9;30(3):381-92. PMID:18471983

b) Park BO, Ahrends R, **Teruel MN**. (2012). Consecutive positive feedback loops create a bistable switch that controls preadipocyte to adipocyte conversion. ***Cell Reports*** Oct 25; 2(4): 976-90. Epub 2012 Oct. 11. PMID: 23063366

c) Ahrends R, Ota A, Kovary KM, Kudo T, Park BO, **Teruel MN.** (2014). Controlling low rates of cell differentiation through noise and ultra-high feedback. ***Science*** Jun 20; 344:1384-9. PMID: 24948735. *Awarded an Editors' Choice rating by signaling editors of **Science.***

d) Ota A, Kovary KM, Wu OH, Ahrends R, Costa MJ, Shen W, Feldman BJ, Kraemer FB, **Teruel MN.** (2015). Using SRM mass spectrometry to profile nuclear protein abundance differences between adipose tissue depots of insulin resistant mice. ***Journal of Lipid Research*** May; 56(5):1068-78. Epub Apr 3. PMID: 25840986.

2. **Circadian Control of Cell Differentiation and Tissue Regeneration**

Glucocorticoid and other differentiation-inducing hormones are secreted in mammals in circadian oscillations. Loss of this circadian oscillation pattern during stress and disease correlates with increased fat mass and obesity in humans, raising the intriguing question of how hormone secretion dynamics affect the process of adipocyte differentiation. In Bahrami-Nejad *et al* (***Cell Metabolism,*** 2018), we used live, single-cell imaging of the key adipogenic transcription factors CEBPB and PPARG, endogenously tagged with fluorescent proteins, and discovered that pulsatile circadian hormone stimuli are rejected by the adipocyte differentiation control system. In striking contrast, equally strong persistent signals trigger maximal differentiation. We identify the mechanism of how hormone oscillations are filtered as a combination of slow and fast positive feedback centered on PPARG. Furthermore, we confirmed in mice that flattening of daily glucocorticoid oscillations significantly increases the mass of subcutaneous and visceral fat pads. Our results provide a molecular mechanism for why stress, Cushing's disease, and other conditions for which glucocorticoid secretion loses its pulsatility may lead to obesity. Given that oscillating hormones are ubiquitous in mammals, the temporal filtering mechanism we discovered likely represents a general principle for the control of cell differentiation.

a) Bahrami-Nejad Z*, Zhao ML*, Tholen S, Hunderdosse D, Tkach KE, van Schie S, Chung M, and **Teruel MN.** (2018). A transcriptional circuit filters oscillating circadian hormonal inputs to regulate fat cell differentiation. ***Cell Metabolism*** Apr 3, 27(4):854-868.e8. *equal contribution. *Highlighted in **Nature**, the **Faculty of 1000, and NIH Research Matters**.*

b) Tholen S, Kovary KM, Rabiee A, Bielczyk-Maczyńska E, Yang W, **Teruel MN.** Flattened circadian glucocorticoid oscillations cause obesity due to increased lipid turnover and lipid uptake. ***BioRxiv*** DOI 10.1101/2020.01.02.893081.

3. **Cell Cycle Control of Terminal Cell Differentiation.**

A main focus of our current work is on how tissues control the critical balance between proliferating progenitors and post-mitotic differentiated cells during the differentiation process. As part of the terminal cell differentiation process, progenitor cells must undergo permanent cell cycle exit. Failure of terminally differentiated cells to exit the cell cycle and to maintain the post-mitotic state can lead to a variety of diseases and is a hallmark of cancer. However, how cell cycle exit and differentiation are mechanistically coupled was not understood and has been a black box due to a lack of critical tools. To solve this long-standing question in terminal cell differentiation, we developed a method that allows us for the first time to simultaneously monitor in the same progenitor cell the moment when the cell irreversibly commits to terminally differentiate together with its progression through the cell cycle[6]. Using this approach, we show that there is a precise time when cells commit to terminally differentiate and that this time is exclusively during the G1 phase of the cell cycle. Importantly, we identify the molecular mechanism for permanent cell cycle exit by showing that the moment cells commit to differentiate, they rapidly self-amplify PPARG and this switch mechanism triggers a parallel rapid increase in p21 that causes permanent cell cycle exit. We go on to show that a permanent increase in p21 is required to maintain a postmitotic and healthy differentiated state. Finally, the terminal differentiation control mechanism we discovered led to a new paradigm how tissues can balance their need to control both the levels of differentiated and progenitor cells during the differentiation process. Our in vitro studies can thus explain the conundrum why mice lacking the CDK inhibitor p21 along with a homolog inhibitor p27 have a 6-fold increase in fat mass[17]. Finally, our results have implications for neurogenesis, myogenesis, and terminal cell differentiation processes in general by providing a framework of how the size of terminally differentiated tissues and maintenance of the progenitor pool can be synergistically controlled by varying the relative strengths of mitogen and differentiation stimuli.

a) Zhao ML, Rabiee AR, Kovary KM, Bahrami-Nejad Z, Taylor B, **Teruel MN.** (2020). Molecular competition in G1 controls when cells simultaneously commit to terminally differentiate and exit the cell-cycle. ***Cell Reports*** 2020 Jun 16; 31(11):107769.

4. **Understanding how feedback and noise can control mammalian cell fate-decisions.**
The advent of single cell approaches has made it clear that noise (cell-to-cell variability) is inherent in all cell populations, but how noise originates, propagates, and affects cell signaling outcome has been largely unexplored. Our goal is to identify and understand the different mechanisms that can be used to stabilize noisy signaling systems and how noise can be modulated to resolve the conflict that noise is harmful for analog signaling but at the same time is needed for robust control of binary cell-fate decision signaling. In Abell *et al*, **(*PNAS,*** 2011), we applied a novel combined mass spectrometry and modeling strategy to the calcium signaling system to understand how eukaryotic cells can prevent signaling failure despite the inherent noise in expression of individual signaling components. In Ahrends *et al* (***Science***, 2014), we used computational modeling and quantitative proteomics to show that noise, combined with multiple feedback loops in the regulatory circuits, enables the stable and infrequent differentiation required to homeostatically maintain tissue size. In Shi *et al* (***Molecular Cell***, 2017), we developed a quantitative mass spectrometry approach to understand variation in ribosomal composition in stem cells. In Kovary *et al* (***Molecular Systems Biology*****,** 2018), we developed single-cell mass spectrometry and imaging strategies to more accurately measure the variation of proteins between individual cells and found it to be much less than has been assumed in the literature. We discovered that covariation provides a key mechanism for fractional activation of population-level binary signaling outputs and were able to use our results to develop a model of how covariance and number of pathway components can be used to increase the variation in a signaling system in order to balance opposing needs for low noise in accurate single-cell analog signaling and high noise for accurate population-level binary signaling.

a) Abell E, Ahrends R, Bandara S, Park BO**, Teruel MN.** (2011). Parallel adaptive feedback enhances reliability of the Ca2+ signaling system. ***Proc Natl Acad Sci U S A*** Aug 30;108(35):14485-90. Epub 2011 Aug 15. *Awarded a "Must Read" and "Exceptional" rating by the Faculty of 1000.*

b) Ahrends R, Ota A, Kovary KM, Kudo T, Park BO, **Teruel MN.** (2014). Controlling low rates of cell differentiation through noise and ultra-high feedback. ***Science*** Jun 20; 344:1384-9. PMID: 24948735. *Awarded an Editors' Choice rating by signaling editors of* ***Science.***

c) Shi Z, Fujii K, Kovary KM, Genuth NR, Röst HL, **Teruel MN**, Barna M. (2017). Heterogeneous Ribosomes Preferentially Translate Distinct Subpools of mRNAs Genome-wide. ***Molecular Cell*** Jul 6;67(1):71-83.e7. Epub 2017 Jun 15. PubMed PMID: 28625553.

d) Kovary KM, Taylor B, Zhao ML, and **Teruel MN.** (2018). Expression variation impairs analog and enables binary signaling control. ***Molecular Systems Biology*** May 14;14(5):e7997. PMID: 29759982.

For a complete list of publications, please see:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40592858/?sort=date&direction=descending

SELECTED INVITED LECTURES

December 2020	Einstein-Mount Sinai Diabetes Research Center Seminar, NY, NY.
June 2020	**In**sights in **Si**gnaling **D**ynamics and **E**ncoding (InSiDE 2020) Virtual Seminar Series.
May 2020	Society for Research on Biological Rhythms Biennial Meeting, Amelia Island, Florida.
May 2020	University of Chicago, Committee on Molecular Metabolism and Nutrition Program (Students' Choice, invited by the graduate students in the program), Chicago, IL.
February 2020	Workshop on "The Dynamics of Collective Decisions", Wissenschaftskolleg, Berlin, Germany.
December 2019	American Society of Cell Biology (ASCB) Annual Meeting, Session on Systems and Synthetic Biology of Decoding Complex Cellular Rhythms, Washington DC.
November 2019	ICSB 2019 - 20th International Conference on Systems Biology, Chair and speaker of session on "Developmental Systems Biology", Okinawa, Japan.

October 2019	University of Cincinnati and Cincinnati Children's Hospital Research Foundation
March 2019	CHSL Meeting on Systems Biology: Networks, Cold Spring Harbor, NY.
February 2019	Winter Qbio Meeting 2019, Oahu, Hawaii
January 2019	Keystone Symposia on Signal Dynamics and Signal Integration in Development and Disease, Keystone, CO.
January 2019	University of Southern California (USC), Molecular & Computational Biology Program, Los Angeles, CA.
January 2019	Boston University, Dept. of Biomedical Engineering, Boston, MA
January 2019	Boston University, Dept. of Biochemistry, Boston, MA.
December 2018	Weill-Cornell School of Medicine, Dept. of Biochemistry, New York City, NY.
December 2018	American Society of Cell Biology (ASCB) Annual Meeting, Session on Systems and Synthetic Biology of Decoding Complex Cellular Rhythms, San Diego, CA.
December 2018	University of Michigan, Dept. of Biomedical Engineering, Ann Arbor, MI.
December 2018	UC Santa Cruz; Dept. of Molecular, Cell, and Developmental Biology; Santa Cruz, CA.
October 2018	UC Berkeley, Dept. of Bioengineering, Berkeley. CA.
July 2018	Green Center for Systems Biology and Dept. of Cell Biology, UT Southwestern, Dallas, TX.
July 2018	CSHL Course on Single Cell Analysis, Cold Spring Harbor, NY.
July 2018	The Francis Crick Institute, London, England.
May 2018	Quantitative Biology Seminar Series, UC San Diego, San Diego, CA. "Students' Choice". Invited by the graduate students in the UCSD Quantitative Biology PhD program.
May 2018	Solvay Workshop on "Dynamics of biological systems: Modelling genetic, signaling and microbial networks", The International Solvay Institutes, Brussels, Belgium.
March 2018	Dept. of Cell Biology/Institute of Cell Dynamics, Johns Hopkins University, Baltimore, MD.
February 2018	SysBio 2018: 8th Advanced Lecture Course on Systems Biology, Innsbruck, Austria.
January 2018	Dept. of Systems Biology, Harvard University, Cambridge, MA.
January 2018	Institute of Genomics and Systems Biology, University of Chicago, Chicago, IL.
November 2017	Institute of Systems Biology and Dept. of Biomedical Engineering, Yale University, New Haven, CT.
May 2017	1st Latin-American Systems Biology Conference, Mexico City, Mexico.
April 2017	Stanford Diabetes Research Symposium, Stanford, CA.
February 2017	Fifth Annual Winter Quantitative Biology (q-bio) Conference, Kauai, Hawaii.
January 2017	Keystone Symposia on Obesity and Adipose Tissue Biology, Keystone, CO.
January 2017	UCSF/Gladstone Institutes Seminar, UC San Francisco, San Francisco, CA.
November 2016	NIH/NIDDK Workshop on the Adipose Tissue Niche, Bethesda, MD.
October 2016	University of Mississippi Medical Center, Jackson, MS.August 2015 EMBO workshop on Cell and Developmental Systems, Arolla, Switzerland.
October 2016	Biozentrum/University of Basel, Basel, Switzerland.
July 2016	q-bio 2016: Quantitative and Systems Biology in Nashville Conference, Nashville, TN.
September 2015	14th Human Proteome Organization World Congress – HUPO 2015, Session on Protein Networks and Systems Biology, Vancouver, Canada.
June 2016	Japanese Society of Cell Biology Annual Meeting, Kyoto, Japan.
February 2016	Biophysical Society Annual Meeting, Symposium on Synthetic Biology and Systems Biology, Los Angeles, CA.
December 2015	American Society of Cell Biology (ASCB) Annual Meeting, Minisymposium on Signaling and Differentiation, San Diego, CA.
November 2015	Dept. of Biomedical Engineering, Georgia Tech and Emory University, Atlanta, Georgia.
October 2015	Keystone Symposium on Diabetes: New Insights into Molecular Mechanisms and Therapeutic Strategies, Kyoto, Japan.
July 2015	International Conference on the Systems Biology of Disease, German Cancer Institute, Heidelberg, Germany.
May 2015	Program in Vascular Biology, UCLA, Los Angeles, CA.
April 2015	Friedrich Miescher Institute (FMI) for Biomedical Research, Basel, Switzerland.
April 2015	EMBO|EMBL Symposium: Cellular Heterogeneity: Role of Variability and Noise in Biological Decision Making, Heidelberg, Germany.
March 2015	Society for Developmental Biology, West Coast Meeting, Yosemite, CA.
February 2015	Third Annual Winter Quantitative Biology (q-bio) Conference, Maui, Hawaii.
December 2015	American Society of Cell Biology Annual Meeting, Philadelphia, PA.

October 2014	Cell Press Symposia: Systems Approach to Metabolic Diseases, Chicago, IL
July 2014	NIH National Centers for Systems Biology Annual Meeting, San Diego, CA.
June 2014	Sanofi/Aventis, Frankfurt, Germany.
February 2014	Second Annual Winter Quantitative Biology (q-bio) Conference, Kona, Hawaii.
October 2013	University of Chicago, Institute of Genomics and Systems Biology, Chicago, IL.
August 2013	Quantitative Biology (q-bio) 2013 Conference on Cellular Information Processing, St. Johns College, Santa Fe, NM.
June 2013	International Conference on the Systems Biology of Disease, German Cancer Institute, Heidelberg, Germany.
November 2012	Uppsala University, Department of Medical Cell Biology, Uppsala, Sweden.
November 2012	EMBL Symposium: From Functional Genomics to Systems Biology, Heidelberg, Germany.
July 2012	Kern Lipid Conference on Systems Biology and Cardiometabolic Diseases, Aspen, CO.
March 2012	U.S. Human Proteome Organization (HUPO) Annual Meeting, San Francisco, CA.

D. Research Support

Current

NIH 1 R01 DK106241 Teruel (PI) 6/1/15-5/31/21
"Controlling tissue size by noise and feedback"

NIH 1 RO1 DK101743 Teruel (PI) 2/1/15-1/31/21
"Controlling the rate of terminal cell differentiation: experiments and theory"

NIH RO1- DK114217 Feldman (PI) 7/1/18-6/30/22
"Integrated Systemic and Adipose Depot-Specific Regulation of Adipogenesis"
Role: Co-Investigator

Past

Stanford BioX Seed Grant Teruel (PI) 10/1/14-9/30/19
"Hormonal control of fat cell differentiation"

NIH 1 P50 GM107615-01 Ferrell (PI) 7/1/13 – 6/30/18
Role: Co-Investigator and Director of the Technology Core
"Systems Biology of Collective Cell Decisions"