UCI University of California, Irvine

CENTER FOR EPIGENETICS AND METABOLISM

NEWSLETTER SPRING 2020

CEM MEMBERS

Pierre Baldi, Ph.D.
Tallie Z. Baram, M.D., Ph.D.
Bruce Blumberg, Ph.D.
Emiliana Borrelli, Ph.D.
Rémi Buisson, Ph.D.
John Chaput, Ph.D.
Xing Dai, Ph.D.
Michelle Digman, Ph.D.
Tim Downing, Ph.D.
Enrico Gratton, Ph.D.
Klemens Hertel, Ph.D.
Peter Kaiser, Ph.D.
Kai Kessenbrock, Ph.D.
Devon Lawson, Ph.D.
Andrej Luptak, Ph.D.
Selma Masri, Ph.D.
Ali Mortazavi, Ph.D.
Nick Pannunzio, Ph.D.
Suzanne Sandmeyer, Ph.D.
Paolo Sassone-Corsi, Ph.D.
Marcus Seldin, Ph.D.
Yongsheng Shi, Ph.D.
Rob Spitale, Ph.D.
Joan Steffan, Ph.D.
Leslie Thompson, Ph.D.
Marcelo Wood, Ph.D.
Kyoko Yokomori, Ph.D.

QUARTER HIGHLIGHTS

- Over 140 guests attended **Epigenetics Day**, held on December 6th, 2019
- The CEM hosted four seminar speakers: **Bambos Kyriacou, Ph.D., John Hawley, Ph.D., Colin Goding, Ph.D.,** and **Katja Lamia, Ph.D.**
- **Shogo Sato, Ph.D.** received the NARSAD Young Investigator Grant
- **Giulia Giammo** was appointed the NIH T32 Cancer Biology and Therapeutics Training Grant
- **Robert Lewis** was awarded the Dr. Lorna Carlin Scholar Award
- The **Masri Laboratory** received an R01 Grant from NIH/NCI and an ACC Seed Grant
- **Emiliana Borrelli, Ph.D.** delivered the plenary lecture at the Neuroscience Symposium in Italy
- A **Kaiser Laboratory** publication was selected as the Methods and Resources JBC Resources Paper of 2019
- Research from the **Kessenbrock Laboratory** was featured in UCI News
- The **Sassone-Corsi**, **Buisson**, **Seldin**, and **Pannunzio Laboratories** welcomed new postdoctoral research fellows
- The CEM is in preparation of the **Epigenetic Control of Cellular Plasticity Symposium** to be held on October 8th and 9th, 2020

AWARDS AND GRANTS

NARSAD YOUNG INVESTIGATOR GRANT

Shogo Sato, Ph.D., a postdoctoral researcher in the Sassone-Corsi Laboratory, was the recipient of the 2020 – 2022 NARSAD Young Investigator Grant. This grant provides two years of funding to promising investigators to either extend their research fellowship training or to begin careers as independent research faculty.

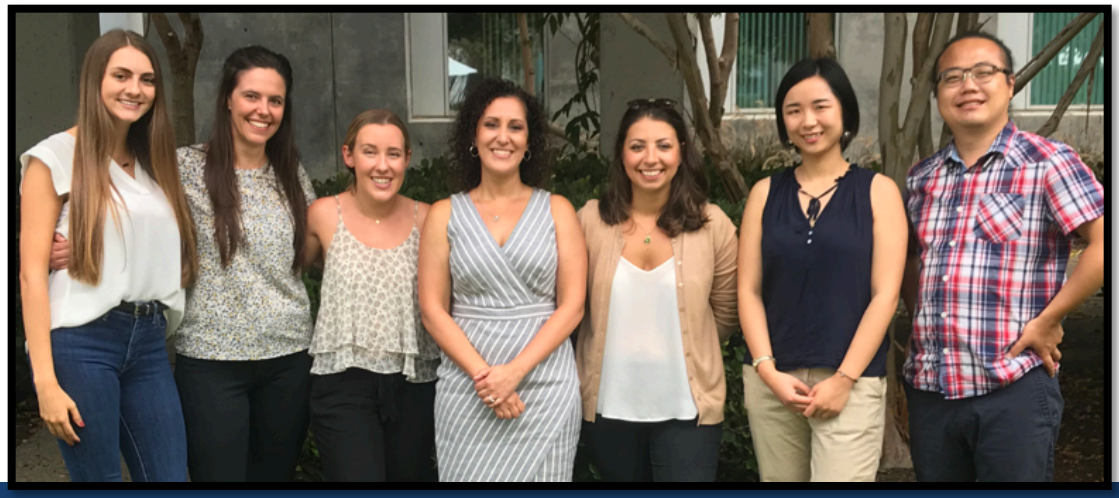
NIH T32 CANCER BIOLOGY AND THERAPEUTICS TRAINING GRANT

Giulia Giammo, a Ph.D. student and member of the Masri Laboratory, was appointed to the NIH T32 Cancer Biology and Therapeutics Training Grant.

DR. LORNA CARLIN SCHOLAR AWARD

Robert Lewis, a Ph.D. student and member of the Borrelli Laboratory, received the Dr. Lorna Carlin Scholar Award.

FACULTY NEWS



MASRI LABORATORY

R01 GRANT

The **Masri Laboratory** received an R01 Grant from NIH/NCI to explore how the disruption of the intestinal circadian clock impacts colorectal cancer. Using organoid technology, the Masri Laboratory will define the crosstalk between the circadian transcriptional machinery and Wnt/Beta-Catenin signaling impinging on intestinal stem cells.

ANTI-CANCER CHALLENGE (ACC) SEED GRANT

The ACC Seed Grant was awarded to the **Masri Laboratory** from the Chao Family Comprehensive Cancer Center to study how disruption of the circadian clock in the intestine impacts metabolism and inflammation.

NEUROSCIENCE SYMPOSIUM

Emiliana Borrelli, Ph.D. delivered the Plenary Lecture at the Neuroscience Symposium in Perugia, Italy on September 28th, 2019 with co-plenary speaker, Eric Kandel (Columbia University).

PUBLICATIONS

Frontiers for Young Minds
The Body's Clock: Timekeeping with Food
Sassone-Corsi Laboratory

CORE CONCEPT Published: December 10, 2019

The Body's Clock: Timekeeping With Food

Authors
Carolina M. Greco
Kevin B. Koronowski
Paolo Sassone-Corsi

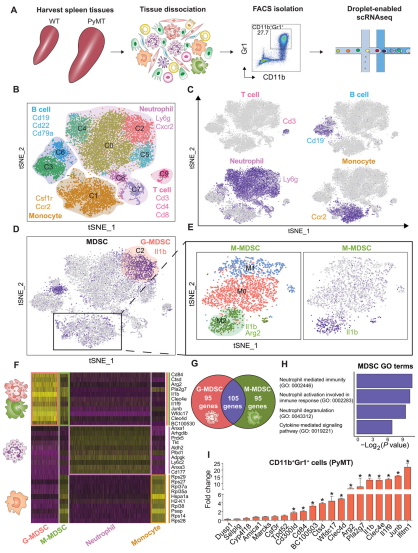
Young Reviewers
Sienna

ABSTRACT

Have you ever asked yourself why you have energy during the day and feel tired at night? What if I told you that there is a part of your body that is secretly controlling these feelings without you knowing? Well there is! It is called your biological clock or circadian rhythm, and it is ticking away inside you right now. What is really amazing is that your biological clock collects information from the outside world, such as sunlight and food, and sets your body's time to match it. The times when you choose to eat might move your body's clock forwards or backwards, and what you eat can make your clock stronger or weaker. Eating and sleeping are great, but your biological clock does so much more for you. The good news is all you need to do is listen to it and it will help keep you healthy.

https://kids.frontiersin.org/article/10.3389/frym.2019.00141

Defining the Emergence of Myeloid-Derived Suppressor Cells in Breast Cancer Using Single-Cell Transcriptomics
Kessenbrock Laboratory



RESEARCH RESOURCES | TUMOR IMMUNOLOGY

Defining the emergence of myeloid-derived suppressor cells in breast cancer using single-cell transcriptomics

Hamad Alshetaiwi[1,2], Nicholas Pervolarakis[3], Laura Lynn McIntyre[4], Dennis Ma[1], Quy Nguyen[1], Jan Akara Rath[5], Kevin Nee[1], Grace Hernandez[6], Katrina Evans[6], Leona Torosian[1], Anushka Silva[1], Craig Walsh[4] and Kai Kessenbrock[1,*]

[1]*Department of Biological Chemistry, University of California, Irvine, Irvine, CA 92697, USA.*
[2]*Department of Pathology, University of Hail, Hail 2440, Saudi Arabia.*
[3]*Center for Complex Biological Systems, University of California, Irvine, Irvine, CA 92697, USA.*
[4]*Department of Molecular Biology and Biochemistry, University of California, Irvine, Irvine, CA 92697, USA.*
[5]*Ludwig Institute for Cancer Research, University of Lausanne, Epalinges 1066, Switzerland.*
[6]*Department of Physiology and Biophysics, University of California, Irvine, Irvine, CA 92697, USA.*
↵*Corresponding author. Email: kai.kessenbrock@uci.edu
– Hide authors and affiliations

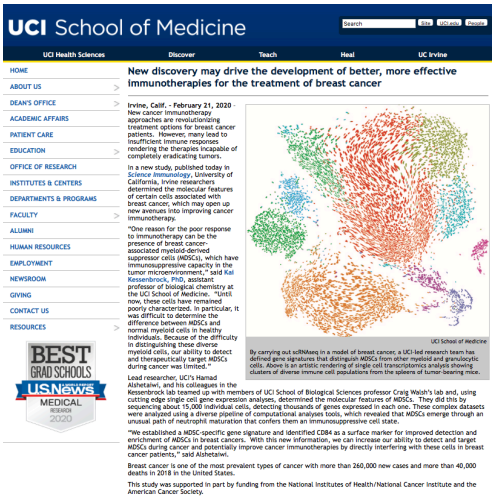
Science Immunology 21 Feb 2020:
Vol. 5, Issue 44, eaay6017
DOI: 10.1126/sciimmunol.aay6017

https://immunology.sciencemag.org/content/5/44/eaay6017/tab-figures-data

PUBLICATIONS

Defining the Emergence of Myeloid-Derived Suppressor Cells in Breast Cancer Using Single-Cell Transcriptomics

Kessenbrock Laboratory



UCI School of Medicine

UCI Health Sciences | Discover | Teach | Heal | UC Irvine

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BEST GRAD SCHOOLS U.S.News MEDICAL RESEARCH 2020

New discovery may drive the development of better, more effective immunotherapies for the treatment of breast cancer

Irvine, Calif. - February 21, 2020 - New cancer immunotherapy approaches are revolutionizing treatment options for breast cancer patients. However, many lead to insufficient immune responses rendering the therapies incapable of completely eradicating tumors.

In a new study, published today in *Science Immunology*, University of California, Irvine researchers determined the molecular features of certain cells associated with breast cancer, which may open up new avenues into improving cancer immunotherapy.

"One reason for the poor response to immunotherapy can be the presence of breast cancer-associated myeloid-derived suppressor cells (MDSCs), which have immunosuppressive capacity in the tumor microenvironment," said Kai Kessenbrock, PhD, assistant professor of biological chemistry at the UCI School of Medicine. "Until now, these cells have remained poorly characterized. In particular, it was difficult to determine the difference between MDSCs and normal myeloid cells in healthy individuals. Because of the difficulty in distinguishing these diverse myeloid cells, our ability to detect and therapeutically target MDSCs during cancer was limited."

UCI School of Medicine

By carrying out scRNAseq in a model of breast cancer, a UCI-led research team has defined gene signatures that distinguish MDSCs from other myeloid and granulocytic cells. Above is an artistic rendering of single cell transcriptomics analysis showing clusters of diverse immune cell populations from the spleens of tumor-bearing mice.

Lead researcher, UCI's Hamad Alshetaiwi, and his colleagues in the Kessenbrock lab teamed up with members of UCI School of Biological Sciences professor Craig Walsh's lab and, using cutting edge single cell gene expression analyses, determined the molecular features of MDSCs. They did this by sequencing about 15,000 individual cells, detecting thousands of genes expressed in each one. These complex datasets were analyzed using a diverse pipeline of computational analyses tools, which revealed that MDSCs emerge through an unusual path of neutrophil maturation that confers them an immunosuppressive cell state.

"We established a MDSC-specific gene signature and identified CD84 as a surface marker for improved detection and enrichment of MDSCs in breast cancers. With this new information, we can increase our ability to detect and target MDSCs during cancer and potentially improve cancer immunotherapies by directly interfering with these cells in breast cancer patients," said Alshetaiwi.

Breast cancer is one of the most prevalent types of cancer with more than 260,000 new cases and more than 40,000 deaths in 2018 in the United States.

This study was supported in part by funding from the National Institutes of Health/National Cancer Institute and the American Cancer Society.

https://www.som.uci.edu/news_releases/discovery-drives-better-immunotherapies-for-breast-cancer.asp

Proteomics links ubiquitin chain topology change to transcription factor activation

Kaiser Laboratory

Molecular Cell

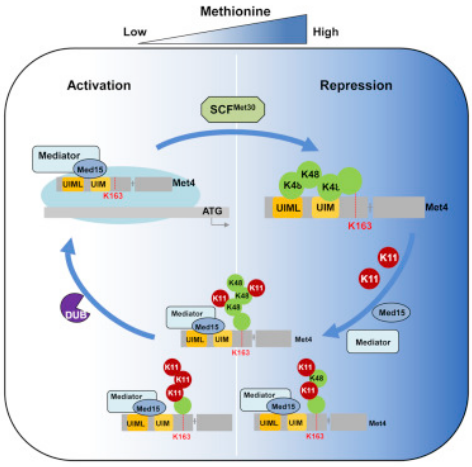
Volume 76, Issue 1, 3 October 2019, Pages 126-137.e7

CellPress

Article

Proteomics Links Ubiquitin Chain Topology Change to Transcription Factor Activation

Yanchang Li [1, 7], Eric B. Dammer [1, 2, 7], Yuan Gao [1, 7], Qiuyan Lan [3, 7], Mark A. Villamil [4, 7], Duc M. Duong [1, 2, 7], Chengpu Zhang [1, 7], Lingyan Ping [1, 3], Linda Lauinger [4], Karin Flick [4], Zhongwei Xu [1], Wei Wei [1], Xiaohua Xing [1], Lei Chang [1], Jianping Jin [5], Xuechuan Hong [3], Yunping Zhu [1], Junzhu Wu [3] ... Ping Xu [1, 3, 6, 8]



https://www.sciencedirect.com/science/article/abs/pii/S1097276519305040

PUBLICATIONS

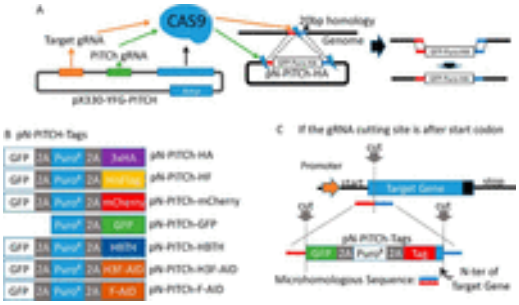
Microhomology Based CRISPR Tagging Tools for Protein Tracking, Purification, and Depletion

Kaiser Laboratory

Selected as the Methods and Resources JBC Paper of 2019

Microhomology-based CRISPR tagging tools for protein tracking, purification, and depletion

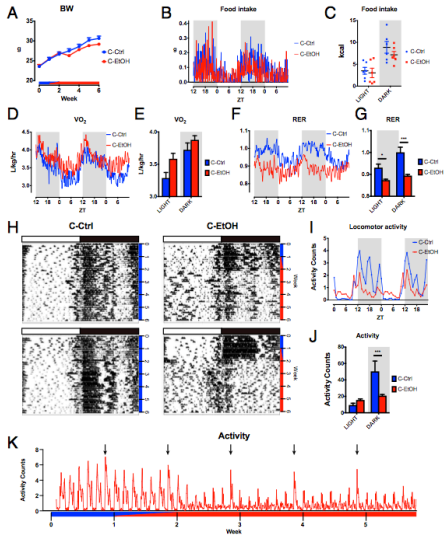
Da-Wei Lin[‡], Benjamin P. Chung[‡], Jia-Wei Huang[‡], Xiaorong Wang[§], Lan Huang[§] and Peter Kaiser[‡1]



https://www.jbc.org/content/294/28/10877.long

Distinct Metabolic Adaptation of Liver Circadian Pathways to Acute and Chronic Patterns of Alcohol Intake

Sassone-Corsi Laboratory



Distinct metabolic adaptation of liver circadian pathways to acute and chronic patterns of alcohol intake

Jonathan Gaucher, Kenichiro Kinouchi, Nicholas Ceglia, Emilie Montellier, Shahaf Peleg, Carolina Magdalen Greco, Andreas Schmidt, Ignasi Forne, Selma Masri, Pierre Baldi, Axel Imhof, and Paolo Sassone-Corsi

PNAS December 10, 2019 116 (50) 25250-25259; first published November 22, 2019
https://doi.org/10.1073/pnas.1911189116

https://www.pnas.org/content/pnas/116/50/25250.full.pdf

NEW POSTDOCTORAL RESEARCH FELLOWS

SASSONE-CORSI LABORATORY

- **Ebru Aras, Ph.D.** – University of Turkey
- **Shin-Ichi Inoue, Ph.D.** – Tohoku University of Japan

BUISSON LABORATORY

- **Elodie Bournique, Ph.D.** – University of Toulouse, France

SELDIN LABORATORY

- **Leandro Velez, Ph.D.** – University of Buenos Aires

PANNUNZIO LABORATORY

- **Jason Sterrenberg, Ph.D.** – Rhodes University, South Africa

UPCOMING EVENTS

2020 SYMPOSIUM

Epigenetic Control of Cellular Plasticity Symposium

October 8th - October 9th, 2020

Beckman Center of the National Academies of Science and Engineering

Irvine, CA

Confirmed Speakers:

Patrick Allard, Ph.D. *University of California, Los Angeles*
Juan Carlos Izpisua Belmonte, Ph.D. *Salk Institute*
Sharon Dent, Ph.D. *University of Texas*
Andrew Dillin, Ph.D. *University of California, Berkeley*
Martin Hetzer, Ph.D. *Salk Institute*
Axel Imhof, Ph.D. *University of Munich*
Michael Karin, Ph.D. *University of California, San Diego*
Andreas Ladurner, Ph.D. *University of Munich*
Karolin Luger, Ph.D. *University of Colorado*
Ashby Morrison, Ph.D. *Stanford University*
Danny Reinberg, Ph.D. *New York University*
Bing Ren, Ph.D. *University of California, San Diego*
Claire Rougeulle, Ph.D. *Paris Diderot University*
Yongsheng Shi, Ph.D. *University of California, Irvine*
Joanna Wysocka, Ph.D. *Stanford University*

UPCOMING EVENTS

2020 SYMPOSIUM

https://insermu1233.org

SEMINARS

Center for Epigenetics and Metabolism
Special Seminar

Charalambos P. Kyriacou, Ph.D.
University of Leicester,
Department of Genetics and Genome Biology
"Sharing clock genes: circadian and circatidal rhythms in flies and crustacea"

Monday, December 16th, 2019
11:00 am – 12:00 pm
Hitachi Lecture Hall

Center for Epigenetics and Metabolism
Special Seminar

John Hawley, Ph.D.
Australian Catholic University
Mary MacKillop Institute for Health

"A time to eat and a time to exercise"

Friday, January 17th, 2020
3:00 pm – 4:00 pm
Hitachi Lecture Hall

Center for Epigenetics and Metabolism
Special Seminar

Colin Goding, Ph.D.
University of Oxford
Ludwig Cancer Research

"Starvation and pseudo-starvation in cancer progression"

Tuesday, January 28th, 2020
4:00 pm – 5:00 pm
Sprague Hall, First Floor Conference Room

CANCER METABOLISM SEMINAR

UCI Health | Chao Family Comprehensive Cancer Center
A Comprehensive Cancer Center Designated by the National Cancer Institute

Katja Lamia, PhD
Associate Professor, Department of Molecular Medicine
Scripps Research

"Cryptochromes integrate circadian rhythms with metabolism and genome protection"

Friday, February 21, 2020
4:00 PM
Sprague Hall
Room 105

Light refreshments will be provided

For more information, contact Dr. Selma Masri at smasri@uci.edu

EPIGENETICS DAY 2019

Over 140 guests attended Epigenetics Day on December 6th, 2019 in Gross Hall

Keynote Speaker: Jim Kadonaga, *UCSD*

EPIGENETICS DAY 2019 PROGRAM

EPIGENETICS DAY

Center for Epigenetics and Metabolism at the University of California, Irvine

PROGRAM

10:00	Welcome
10:10 – 11:00	Opening Lecture **James Kadonaga**, University of California, San Diego *New Adventures in Chromatin Dynamics and Transcriptional Regulation*
11:00 – 11:30	**Kai Kessenbrock**, University of California, Irvine *Revealing cellular identities using integrated chromatin accessibility and transcriptome analysis in individual cells*
11:30 – 12:00	**Janine La Salle**, University of California, Davis *Imprinted snoRNA Loci and Circadian Entrainment*
12:00 – 12:50	Lunch
12:50 – 1:20	**Andrej Luptak**, University of California, Irvine *Aptamers and Ribozymes in Biology*
1:20 – 1:50	**Yinsheng Wang**, University of California, Riverside *Quantitative Proteomics for Interrogating Mechanisms of Epitranscriptomic Regulation*
1:50 – 2:20	**Rolf Bodmer**, Sanford Burnham Prebys Medical Discovery Institute *Lipotoxic Cardiomyopathy Inheritance Across Generations*
2:20 – 2:50	**Break**
2:50 – 3:20	**Olga Razorenova,** University of California, Irvine *Multi-Level Regulation of Metastasis by CDCP1 in Breast Cancer*
3:20 – 3:50	**Rémi Buisson,** University of California, Irvine *Molecular Mechanisms of APOBEC3A-induced Mutagenesis in Cancer*
3:50 – 4:20	**Peter Kaiser**, University of California, Irvine *Molecular Links between Methionine Metabolism, Cell Cycle, and Cancer*
4:20 – 4:50	**Cédric Blanpain,** Université Libre de Bruxelles *Tumor Transition States, Metastasis, and Resistance to Therapy*
5:00	Reception