OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

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| --- |
| NAME: Chaix, Amandine |
| eRA COMMONS USER NAME (credential, e.g., agency login): achaix |
| POSITION TITLE: Staff Scientist |

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) | END DATE MM/YYYY | FIELD OF STUDY |
| Paris XI University, Paris | BS | 06/2003 | Cell Biology & Physiology |
| Ecole Normale Superieure de Cachan, Paris | OTH | 06/2004 | Biochem & Biological Engineering |
| Univ. of Sciences of Luminy, Marseille | PHD | 09/2010 | Biology |
| The Salk Institute, La Jolla, CA | Postdoctoral Fellow | 10/2017 | Circadian Rhythms & Metabolism |

### A. Personal Statement

The overarching goal of my research is to explore the dynamic relationship between nutrition and the circadian clock in health and disease in order to develop new therapeutic strategies to increase healthspan and well-being across lifespan in humans. As a postdoctoral fellow and a staff scientist in Dr. Panda’s laboratory at The Salk Institute for Biological Studies, I explored the interaction between circadian rhythms and metabolic homeostasis. I have shown that consolidating food intake to 8-12h during the dark phase, a dietary intervention called time-restricted feeding (TRF), can protect diet-induced obesity mice from body weight gain and metabolic dysfunctions without differences in activity or food consumption [1]. In particular, TRF for over one year preserved metabolic health, muscle mass as well as motor coordination suggesting that TRF could delay age-related physiological decline. I have further shown that clock mutant mice with higher risk of metabolic disease are protected from obesity and metabolic dysfunction under TRF [2] suggesting that the temporal control of food intake plays a key role in TRF-mediated health benefits. As an Assistant Professor in the Nutrition and Integrated Physiology department at the University of Utah, I will investigate the benefits and mechanisms of TRF as an intervention (1) to prevent atherosclerosis and cardiovascular disease using benchmark pre-clinical mouse models of atherosclerosis (AHA funded project), and (2) to increase healthspan and lifespan in middle-aged obese mice on a western diet (NIA funded project). I will also leverage my expertise in metabolism and human clinical trials of TRE to expand my research directions.

1. Chaix A, Lin T, Le HD, Chang MW, Panda S. Time-Restricted Feeding Prevents Obesity and Metabolic Syndrome in Mice Lacking a Circadian Clock. Cell Metab. 2019 Feb 5;29(2):303-319.e4. PubMed PMID: [30174302](http://www.ncbi.nlm.nih.gov/pubmed/30174302/).
2. Chaix A, Zarrinpar A, Miu P, Panda S. Time-restricted feeding is a preventative and therapeutic intervention against diverse nutritional challenges. Cell Metab. 2014 Dec 2;20(6):991-1005. PubMed PMID: [25470547](http://www.ncbi.nlm.nih.gov/pubmed/25470547/); PubMed Central PMCID: [PMC4255155](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255155/).

### B. Positions and Honors

Positions and Employment

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| --- | --- |
| 2006 - 2010 | Lecturer, Department of Biochemistry & Physiology, University of Sciences of Luminy, Marseille |
| 2006 - 2010 | PhD Student, University of Sciences of Luminy and Marseille Cancer Center, Marseille |
| 2011 - 2017 | Postdoctoral Fellow, The Salk Institute, La Jolla, CA |
| 2018 - | Staff Scientist, The Salk Institute, La Jolla, CA |

Other Experience and Professional Memberships

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| --- | --- |
| 2002 - 2003 | Undergraduate Researcher, Institute of Pharmacology and Structural Biology, Toulouse, France |
| 2003 - 2004 | Master Student Researcher, Cell Stress Laboratory, Marseille, France |
| 2004 - 2005 | Master Student Researcher, Signalling, Hematopoiesis and Mechanism of Oncogenesis laboratory, Marseille, France |
| 2012 - | Member, Society for Research on Biological Rhythms |
| 2017 - | Member, American Heart Association |

Honors

|  |  |
| --- | --- |
| 2006 - 2009 | Dual Research & Teaching Predoctol Fellowship, French Ministry of Education and Research |
| 2009 - 2010 | Predoctoral Fellowship, French Association for Cancer Research (ARC) |
| 2010 | Best PhD Thesis Prize 2010, Aix-Marseille University, France |
| 2011 | PhD‐to­‐postdoc Transition Fellowship, French Society of Haematology |
| 2012 | Mentor-Based Postdoctoral Fellowship, American Diabetes Association (ADA) |
| 2013 | Award for Promise in Research, Philippe Foundation Inc., NY, USA |
| 2014 | Research Merit Award, Society for Research on Biological Rhythms (SRBR) |
| 2014 | People’s Choice Presentation Award, The Salk Institute |
| 2014 | Selected Short Talk, Society for Research on Biological Rhythms annual meeting, Big Sky, MO |
| 2016 | Travel Award to Keystone Symposium, Society of Research Fellows , The Salk Institute |
| 2016 | Salk Women & Science Research Award, The Salk Institute |
| 2016 | Selected Short Talk, Keystone symposium Metabolism, Transcription and Disease, Snowbird, UT |
| 2017 | Travel Award, "Metabolism In Action" meeting, Copenhagen, The Salk Institute |
| 2017 | Poster Award, "Metabolism In Action" meeting, Copenhagen, Denmark, Novo Nordisk |
| 2017 | Invited Speaker, SLEEP meeting, Boston, MA |
| 2017 | Selected Short Talk, Cell symposium on Metabolic disease therapies, San Diego, CA |
| 2017 | Invited Chair, Cell symposium on Metabolic disease therapies, San Diego, CA |
| 2018 - 2021 | Career Development Award, American Heart Association (AHA) |
| 2019 | Invited Seminar Speaker, Colorado State University |
| 2019 | Invited Speaker, Nutrition meeting, Baltimore, MD |
| 2019 | Invited Speaker, Society for the Study of Ingestive Behavior annual meeting, Netherlands |

### C. Contribution to Science

Full list of publications

<https://www.ncbi.nlm.nih.gov/myncbi/amandine.chaix.1/bibliography/public/>

1. Circadian rhythms, dietary interventions and metabolic fitness: The circadian clock is an internal timing system that orchestrates physiology and behavior in a 24 h periodicity. Genetic or behavioral disruptions of the clock increase the risk of obesity and metabolic diseases in mice and humans. Reciprocally, metabolic imbalance is associated with dampened circadian rhythms (b). We observed that mice fed a high fat diet have a disrupted daily eating pattern, raising the possibility that the timing of food consumption could contribute to the development of diet-induced obesity and associated metabolic diseases. Indeed, consolidating eating during the dark phase by time-restricted feeding (TRF) prevents and reverts body weight gain and metabolic disorders on various energy dense diets (c,d) without changes in activity or food intake. Furthermore, TRF can override compromised rhythms in clock mutant mice and restore metabolic homeostasis by inducing a rhythmic coherent activation of nutrient-sensing and physiological cellular stress response pathways to maintain cellular homeostasis (a). These comprehensive studies on TRF have laid the ground to further investigation of TRF in humans.
   1. Chaix A, Manoogian ENC, Melkani GC, Panda S. Time-Restricted Eating to Prevent and Manage Chronic Metabolic Diseases. Annu Rev Nutr. 2019 Aug 21;39:291-315. PubMed PMID: [31180809](http://www.ncbi.nlm.nih.gov/pubmed/31180809/); PubMed Central PMCID: [PMC6703924](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6703924/).
   2. Chaix A, Lin T, Le HD, Chang MW, Panda S. Time-Restricted Feeding Prevents Obesity and Metabolic Syndrome in Mice Lacking a Circadian Clock. Cell Metab. 2019 Feb 5;29(2):303-319.e4. PubMed PMID: [30174302](http://www.ncbi.nlm.nih.gov/pubmed/30174302/).
   3. Chaix A, Zarrinpar A, Miu P, Panda S. Time-restricted feeding is a preventative and therapeutic intervention against diverse nutritional challenges. Cell Metab. 2014 Dec 2;20(6):991-1005. PubMed PMID: [25470547](http://www.ncbi.nlm.nih.gov/pubmed/25470547/); PubMed Central PMCID: [PMC4255155](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255155/).
   4. Hatori M, Vollmers C, Zarrinpar A, DiTacchio L, Bushong EA, Gill S, Leblanc M, Chaix A, Joens M, Fitzpatrick JA, Ellisman MH, Panda S. Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. Cell Metab. 2012 Jun 6;15(6):848-60. PubMed PMID: [22608008](http://www.ncbi.nlm.nih.gov/pubmed/22608008/); PubMed Central PMCID: [PMC3491655](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3491655/).
2. Circadian rhythms, microbiome and metabolic homeostasis: The gut microbiome plays an essential role in energy balance and metabolic homeostasis. With Dr. Zarrinpar, MD. Ph.D., we investigated the influence of the dynamic of the gut microbiome on metabolic homeostasis. We showed that the gut microbiome undergoes daily oscillations that are affected by diet and feeding pattern (b). In a follow up study, we showed that antibiotic-induced microbiome deletion (AIMD) dramatically alters whole-body glucose homeostasis by altering gut luminal secondary metabolites and signaling (a).
   1. Zarrinpar A, Chaix A, Xu ZZ, Chang MW, Marotz CA, Saghatelian A, Knight R, Panda S. Antibiotic-induced microbiome depletion alters metabolic homeostasis by affecting gut signaling and colonic metabolism. Nat Commun. 2018 Jul 20;9(1):2872. PubMed PMID: [30030441](http://www.ncbi.nlm.nih.gov/pubmed/30030441/); PubMed Central PMCID: [PMC6054678](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC6054678/).
   2. Zarrinpar A, Chaix A, Yooseph S, Panda S. Diet and feeding pattern affect the diurnal dynamics of the gut microbiome. Cell Metab. 2014 Dec 2;20(6):1006-17. PubMed PMID: [25470548](http://www.ncbi.nlm.nih.gov/pubmed/25470548/); PubMed Central PMCID: [PMC4255146](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4255146/).
3. Normal and oncogenic signaling of the receptor tyrosine kinase c-Kit in mast cells: Oncogenic activation of c-Kit is found in various tumors and leukemia. As described for other oncogenes, the wild type (W) and constitutively active forms of the receptor can trigger distinct signal transduction cascades (c). During my Ph.D. I studied the mechanisms of the differential signaling between WT and oncogenic c-Kit receptor tyrosine kinase (d). I showed that STAT5 pathway was selectively activated in mastocytoma cell lines and required for their proliferation (b). I also showed that constitutive Kit could recruit a new set of interacting partners that modulate its oncogenic properties (a). My work has identified pathways that are selectively activated in tumor cells representing attractive new therapeutic targets.
   1. Chaix A, Arcangeli ML, Lopez S, Voisset E, Yang Y, Vita M, Letard S, Audebert S, Finetti P, Birnbaum D, Bertucci F, Aurrand-Lions M, Dubreuil P, De Sepulveda P. KIT-D816V oncogenic activity is controlled by the juxtamembrane docking site Y568-Y570. Oncogene. 2014 Feb 13;33(7):872-81. PubMed PMID: [23416972](http://www.ncbi.nlm.nih.gov/pubmed/23416972/).
   2. Chaix A, Lopez S, Voisset E, Gros L, Dubreuil P, De Sepulveda P. Mechanisms of STAT protein activation by oncogenic KIT mutants in neoplastic mast cells. J Biol Chem. 2011 Feb 25;286(8):5956-66. PubMed PMID: [21135090](http://www.ncbi.nlm.nih.gov/pubmed/21135090/); PubMed Central PMCID: [PMC3057865](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3057865/).
   3. Yang Y, Létard S, Borge L, Chaix A, Hanssens K, Lopez S, Vita M, Finetti P, Birnbaum D, Bertucci F, Gomez S, de Sepulveda P, Dubreuil P. Pediatric mastocytosis-associated KIT extracellular domain mutations exhibit different functional and signaling properties compared with KIT-phosphotransferase domain mutations. Blood. 2010 Aug 19;116(7):1114-23. PubMed PMID: [20484085](http://www.ncbi.nlm.nih.gov/pubmed/20484085/).
   4. Simon C, Dondi E, Chaix A, de Sepulveda P, Kubiseski TJ, Varin-Blank N, Velazquez L. Lnk adaptor protein down-regulates specific Kit-induced signaling pathways in primary mast cells. Blood. 2008 Nov 15;112(10):4039-47. PubMed PMID: [18753636](http://www.ncbi.nlm.nih.gov/pubmed/18753636/).
4. Educational approach: Part of the training to become a “professeur agrege” (tenured teaching position at College level) in France is to be involved in an educational/outreach project. With a colleague, over the 3 years of our Ph.D., we focused our interest on inquiry-based learning as an educational approach. To that end, we conceptualized, designed, executed, and evaluated a 3 day inquiry-based learning and hands-on workshop on glycemia and diabetes. The protocol of the workshop (objectives, teaching materials, lab materials and protocols, agenda, instructions, and evaluation criteria (b)) as well as the evaluation of the teaching approach (a) were published in two separate manuscripts in Advances in Physiological. The workshop successfully improved student awareness and understanding of the scientific reasoning and the research process.
   1. Mingueneau M, Chaix A, Scotti N, Chaix J, Reynders A, Hammond C, Thimonier J. A multidisciplinary guided practical on type I diabetes engaging students in inquiry-based learning. Adv Physiol Educ. 2015 Dec;39(4):383-91. PubMed PMID: [26628664](http://www.ncbi.nlm.nih.gov/pubmed/26628664/).
   2. Mingueneau M, Chaix A, Scotti N, Chaix J, Reynders A, Hammond C, Thimonier J. Hands-on experiments on glycemia regulation and type 1 diabetes. Adv Physiol Educ. 2015 Sep;39(3):232-9. PubMed PMID: [26330044](http://www.ncbi.nlm.nih.gov/pubmed/26330044/).

### D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

18CDA34110292, AHA

Chaix, Amandine (PI)

07/01/18-06/30/21

Benefits and mechanisms of time-restricted feeding as an intervention against atherosclerosis and cardiovascular disease

Role: PI

R01AG065993-01 , NIA

Chaix, Amandine (PI)

09/15/19-05/31/24

Mechanisms by which time-restricted feeding (TRF) delays the onset of age-related declines in health, cognition, and circadian rhythms.

The major goal of this project is to describe the healthspan and lifespan benefits of TRF in wild type mice on a western diet as well as determine the underlying mechanisms.

Role: PI