A program of the Richard and Susan Smith Family Foundation

- **Edward Chouchani, Ph.D.**
  Assistant Professor of Cancer Biology
  Dana-Farber Cancer Institute

  "Systematic Chemical Manipulation Of Redox Sensitive Cysteines To Regulate Inflammatory Processes"

  Key Words: Mass spectrometry, Cysteine, Chemoproteomics

Mammalian tissues engage in specialized physiology that is regulated through reversible covalent modification of protein cysteine residues. Despite the widespread importance of redox regulation of tissue physiology, there is a persistent lack of information regarding the specific protein modifications that explain the molecular basis for these processes in vivo.

My lab recently developed a mass spectrometric (MS) technology for the first comprehensive and quantitative mapping of the mouse cysteine redox proteome in vivo. For the first time, we defined hundreds of protein cysteine modification networks that underlie distinct physiological responses across different tissues. Our "big picture" aim is to leverage this newfound regulatory landscape for an overarching mechanistic and therapeutic goal: systematic functional annotation and manipulation of redox regulated cysteines on proteins that play major roles in human diseases of aging. To do so, we will combine new MS methods, and chemical and biochemical approaches, to systematically develop covalent pharmacological manipulators of these redox regulated cysteines. Herein, we will prioritize newfound regulatory cysteines present on proteins that control macrophage cytokine production and inflammasome activation. Through systematic development of covalent chemotypes targeting these residues, we aim to engineer first-in-class manipulators for disease-relevant proteins that are currently undrugged. Successful completion of our aims will define mechanisms of redox regulation of effector proteins that control cytokine production and inflammasome activity, while developing new therapeutic chemotypes for treatment of inflammatory diseases.

- **Marcelo Dietrich, M.D.**
  Associate Professor
  Yale School of Medicine

"Opioid-Producing Neurons that Mediate the Attachment of Infants to their Mothers"

Key Words: Development, Behavior, Emotions, Neuronal circuits, Mother-Child bond

---

Children's bonds with caregivers in early childhood drive their physiological, emotional, and behavioral development. During the early postnatal period, mothers provide infants with their basic physiological needs, such as warmth, nutrition, and sensorial stimulation. The emotional bond between infants and their mothers ensures these physiological needs are met. Disruptions in mother-infant bonding—as it occurs

- **Jenna Galloway, Ph.D.**
  Assistant Professor of Orthopaedic Surgery
  MGH Center for Regenerative Medicine

  "Identifying the molecular and cellular determinants of exercise-driven tendon remodeling"

  Key Words: Musculoskeletal system, Tendon, Progenitor cells, Exercise

---

Tendons transduce force from muscles to bone, enabling movement. Emb

- **Sebastian Lourido, Ph.D.**
  Assistant Professor of Biology
  Whitehead Institute for Biomedical Research

"Controlling the developmental transitions of a eukaryotic pathogen"

Key Words: Transcriptional regulation, Microbiology, Parasitology, Toxoplasma gondii, High-throughput genetics, Functional genomics

---

A defining feature of eukaryotic parasites is their ability to restructure their cell biology to promote key transitions along their complex life cycles. Apicomplexan parasites depend on such developmental transitions to propagate between tissues and hosts and survive as the most widespread parasitic infections on earth. We propose to develop high-throughput approaches to investigate the molecular origin of key developmental transitions. Our recent work uncovering the master regulator of chronic differentiation suggests that relatively simple gene-expression networks underlie major developmental decisions in these parasites. We now pec 2 ra41 (c 2)-61 (c 2)-61 (a)-09(t)-52 (i)55(o) Td[(d

- **Sarah McMenamin, Ph.D.**
  Assistant Professor
  Boston College

"Mechanisms by which shape is specified and remembered during development and regeneration of the zebrafish fin"

Key Words: Regeneration, Positional information, Positional memory, Developmental disorders, Limb malformations, Zebrafish fins, Fin regeneration

---

To build an organ such as a limb or a fin, developing tissues must use positional information to generate appropriate shapes. Changes in these relationships underlie certain congenital malformations. Moreover, in order to regenerate following an amputation, tissues must re-deploy positional information. Nonetheless, the nature of positional information is incompletely understood; this lack of understanding limits