Center for Redox Biology and Medicine

Wake Forest University School of Medicine

Co-Director, Cristina M. Furdui, PhD, Department of Internal Medicine, Section on Molecular Medicine
Co-Director, Leslie B. Poole, PhD, Department of Biochemistry

Mission

The CRBM core mission is to coordinate and facilitate cross-campus, inter-departmental, and multidisciplinary educational and research programs that have the common goal of advancing knowledge and improving the health of everyone, particularly patients suffering from diseases with disrupted redox balance such as **cancer, aging, infectious diseases/sepsis, obesity-associated diabetes, and cardiovascular diseases**.

CRBM's bench-to-bedside and back research fosters development of cutting-edge redox-based diagnostics, new redox therapeutics, and innovative solutions for preservation of clinical specimens to facilitate discovery of clinically relevant biomarkers.

Priorities

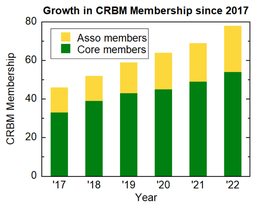
- Leverage local and national resources and work with other Centers around the Enterprise to advance the core mission.
- Promote equity, diversity and inclusion in all research and training activities.
- Provide support for pilot studies to encourage new, interdisciplinary collaborations leading to extramural funding.
- Create cutting-edge education and seminar programs to expand the international recognition of the institution in redox biology and medicine.

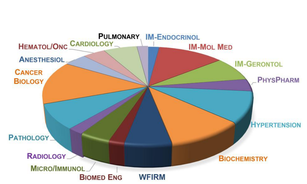
Leadership

- Co-Directors Cristina Furdui and Leslie Poole are world leaders in the expanding field of redox biology, and co-lead the center with an Executive Committee of five other faculty members **@ WFUSM**: Suzanne Craft, PhD; W. Todd Lowther, PhD; Donald A. McClain, MD, PhD; and **@ WFU**: Gloria Muday, PhD; S. Bruce King, PhD.

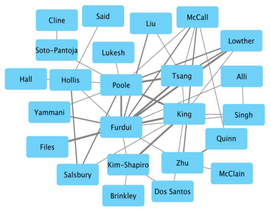
Membership

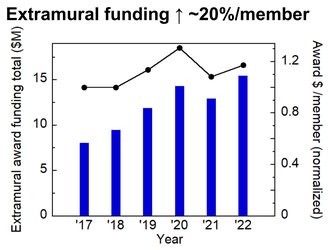
- Membership continues to grow, from 33 faculty members in 2017 to **54** (Atrium Health/WF), representing **18 clinical and academic departments**. Associated faculty (**24**) are from WFU basic sciences and regional institutions.





- Members are highly collaborative (inter-action network of a subset below), and bring in substantial extramural research support, which has grown 1.9X in 6 years.





The Science of Redox Biology

- Chemical reactions involving electron transfers (reduction and oxidation, i.e. redox reactions) are intricately associated with life and health.
- Oxidizing species (collectively referred to as ROS, or Reactive Oxygen Species) are natural signals that regulate and balance the energy state of cells/organs/body.
- In excess, ROS may divert normal signaling pathways and damage molecules, leading to impairment and disease.

Education and Training

- **CRBM** provides an educational environment for redox-related research activities across multiple institutions
- **CRBM** supports and encourages research and career mentoring for redox biology trainees at all levels
- **NIH/NIGMS T32 Training Program in Redox Biology and Medicine** is currently in its 5th year
  - Started in 2019, this program has supported 13 PhD candidates (~2 years each), 7 of whom have graduated
  - Averages: 5.2 years to degree (PhD), and 4.6 publications per fellow, including in high-impact journals.

Center Activities (selected)

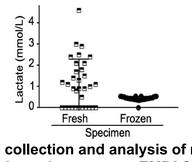
- **Annual Retreat (full day),** with guest speaker, talks & posters
- **@WakeRedox Seminar Series**
- **RBM T32 Training Program Activities, enriching the research environment:**
  - Chalktalks (2 sessions/year)
  - Course in Redox Biology and Medicine
  - Alumni visits to enhance awareness of the diversity of scientific careers
- **Annual Call for Pilot Grants**, 7 of the 25 CRBM-funded pilot studies has already resulted in extramural funding support.
- **Working Groups and Workshops**
  - Metabolomics and Inflammation Working Group (regularly, Mon 1 PM)
  - Workshops: e.g., Redox Innovations (half-day), interest group with redox- and IP-related projects seeking collaborations

Innovative Research Project Spotlight

Redox Trapping for Preservation of Clinical Specimens (Furdui, Files *et al*)

Limiting artifactual oxidation of specimens is critical to:
- reduce pre-analytical variability.
- enable discovery of redox biomarkers.
- improve **clinical diagnosis**, enable **patient-tailored treatments**, and improve **prediction of outcomes**.

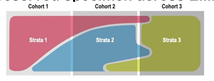
Data showing loss of inter-patient variability for lactate and loss of information upon specimen freezing.



Phase I
- Utilize patented chemical reagents to develop a new blood stabilizing formulation.
- Validate the new formulation for improved collection and analysis of blood compatible with advanced research technologies.

Phase II

Scale-up collection and analysis of redox preserved specimen across EMPACT NETWORK

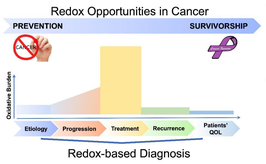


EMPACT: EMbedded **P**rec ision in **A**cute **C**are **T**rials

Study participants will be enrolled by **Cohort** (**1**: infection; **2**: sepsis 3; **3**: septic shock) and post-hoc adjudicated for Strata.

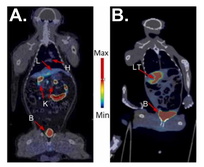
IMPACT: Redox-based diagnosis could be critical to understand heterogeneity that is associated with the pathogenesis and resolution of sepsis in humans.

New ROS PET Imaging Radiotracers (Solingapuram Sai *et al*)



Biomed Pharmacother. 2022;156:113937.

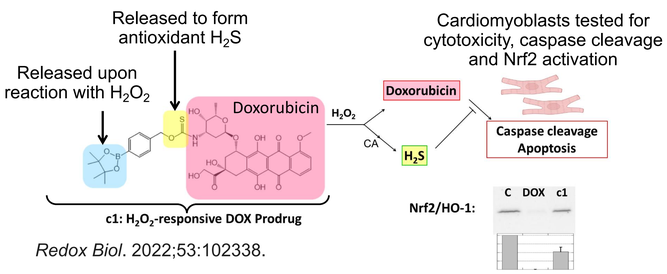
- Ascorbate-based PET radioligand, [^{18}F]KS1 can measure ROS.
- Dual action: at tracer concentrations, it tracks ROS and at pharmacologic concentrations, it kills tumor cells.



PET/CT images 90 min post-injection of [^{18}F]KS1 in a **A.** healthy and **B.** irradiated hepatic-tumor bearing rhesus monkey. Arrows indicate L: liver, H: heart, K: kidneys, B: bladder, and LT: liver tumor.

IMPACT: Novel redox PET imaging radiotracers are broadly applicable to cancer and other diseases with inflammatory mechanisms of evolution enabling early detection and therapeutic intervention.

Mitigation of doxorubicin (Dox)-induced cardiotoxicity (Lukesh, Poole *et al)*



Redox Biol. 2022;53:102338.

IMPACT: Novel prodrug, imparting tumor-selective activation by ROS delivering both DOX and H_2S; a highly promising and synergistic strategy for combating DOX-induced cardiotoxicity in cancer survivors.