High-throughput screening for osteocyte-mediated bone remodeling (OMBRE) regulatory compounds
At least half of fragility fractures occur in individuals with normal bone mass.

- Wainwright, JCEM 2005
Osteocyte-Mediated Bone Remodeling (OMBRE)
Agents that control OMBRE have therapeutic potential for treating skeletal diseases.
Knowledge Gaps: role of OMBRE in skeletal disease, OMBRE therapies

1. Are there current FDA-approved drugs that can be repurposed as OMBRE-regulators for treating skeletal diseases?

2. What are the side effects of currently used medications that regulate OMBRE on skeletal health?

3. Advance fundamental understanding of OMBRE to develop improved therapies for skeletal diseases.
This project aims to screen a library of FDA-approved small molecule compounds to identify agents that regulate OMBRE in vitro.

**Aim 1:** Validate functional OMBRE assays in a high-throughput screen (HTS) format.

- currently, there is no validated in vitro PLR assay

**Aim 2:** Perform high throughput screen for OMBRE regulatory compounds.

**Aim 3:** Identify and validate lead OMBRE-regulatory compounds for in vitro analysis.
Validate in vitro OMBRE HTS assay

Aim 1: Functional pH\textit{i} assay
   Gene expression screening

Identify OMBRE regulatory compounds

Aim 2: FDA-approved drug screening
Aim 3: Validate OMBRE-regulatory compounds
Deliverables

**Validate in vitro OMBRE HTS assay**

**Aim 1:** Functional pH Assay

Gene expression screening

Change in intracellular pH will be visually and quantitatively evaluated.
Validate in vitro OMBRE HTS assay

Aim 1: Functional pHi assay
Gene expression screening

Identify OMBRE regulatory compounds

Aim 2: FDA-approved drug screening
Aim 3: Validate OMBRE-regulatory compounds

Progress Update
Recruiting new hire for needed personnel efforts

Evaluating top candidates and will make an offer this week

Progress Update
Scheduling meeting with UCSF Small Molecule Development Center (SMDC)
**In vitro OMBRE assay**

**Aim 1:** Functional pH Assay

Gene expression screening

Using OCY454, Taqman array plates will screen genes known to be involved in OMBRE in vivo.

**Progress Update**

Explore new gene expression array reader for Taqman arrays

* core resource at the VA*
Milestones & Timeline

December 2017  Conference Call
Spring 2018  Spring Symposium @ UT
March 2018  Validate HTS OMBRE assays & Screening plan for FDA approved compound library
June 2018  Conference Call
August 2018  List of lead OMBRE regulatory compounds for in vitro validation
September 2018  Fall Symposium @ UCSF
November 2018  Final Report
Clinical Need and Industrial Relevance

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Steroid Use
Osteonecrosis
Osteoarthritis
Aging
Diabetes

OMBRE: Osteocyte-Mediated Bone Remodeling Core