Welcome
DHS and LPI Ignite Colloquium

• F. Javier Nieto, Dean, CPHHS
• Richard B. van Breemen, Director, LPI

Moderators:
• Marie Harvey, Associate Dean, CPHHS
• Mark Leid, Associate Dean, COP
• Luiz Bermudez, Associate Dean, CVM
Ignite Agenda and Timeline

3:30 – 3:45 Welcome

3:45 – 4:25  Session I
            5 presentations; Q&A
            5 presentations; Q&A

4:25 – 5:00  Session II
              5 presentations; Q&A
              5 presentations; Q&A

5:00 – 6:00  Reception: wine, beer, hors d’oeuvres
Model organism for cost-effective lifespan studies:

- *Nothobranchius furzeri* (~3-4 months)
- *Nothobranchius guentheri* (~12 months)
- Shortest-lived vertebrate model
- Whole animal, longitudinal studies

Current data:

- Active avoidance test (learning, memory)
- Anxiety test
- Locomotor test
- Fecundity
- Metabolomics
- Organ pathology
- PCR
- Protein analysis
- Sirtuin activity

Kate Petersen Shay, PhD
Experimental Approach for Health Span Testing:

1. Get ACUP approval
2. Hatch fish and raise to maturity (4 weeks of age)
3. Create diet with experimental compound/deficiency
4. Begin experimental diet or treatment in adulthood
5. Collect data over life span
6. Challenge or intervention
7. Breed fish and collect eggs
8. Raise F₁ generation for epigenetics

Endpoints:
- Cognitive studies
- Lifespan length
- Pathology
- Molecular Biology Endpoints

kate.shay@oregonstate.edu
Exosomes as key players in cancer

Mean: 132.0 ± 1.9 nm
Mode: 109.1 ± 2.7 nm
Exosomes of chemoresistant cells induce drug resistance in naive cells.

Malignant exosomes manipulate immunity:
- Increase deposition of calcium by healthy osteoblasts.
QUALITY, ACCESS AND COST OF HEALTH CARE FOR VETERANS

The total Veteran Population is predicted to decline from 20.0 million in 2017 to 13.6 million in 2037

Annual % Change 2017 - 2037

- Total: -1.9%
- Male: -2.3%
- Female: +0.7%

Race and Ethnicity

Minority Veterans are predicted to increase from 23.2 percent of the total Veteran population in 2017 to 32.8 percent in 2037. Hispanic Veterans will increase from 7.4 percent in 2017 to 11.2 percent in 2037. Minorities are all races/ethnicities except non-Hispanic White Veterans.
Care Coordination and Outcomes in the VA Expanded Choice Program

- **Three-year project plan**
- Using a mixed methods approach, with emphasis on care coordination for primary care and specialty care across inpatient and outpatient care
- Assess new processes being put in place for quality governance, integrated care management, and health information exchange
- Examine the impact of the expanded Community Care program on access to care, quality of care, and duplication of services provided compared to services provided under usual care at VA facilities
- **Partnerships** with internal and external stakeholders, and with clinical, care coordination, and quality experts
Eczema affects >30 million people/year.

The most common and chronic form of it is atopic dermatitis (AD).

Patients with barrier defects develop asthma and allergic rhinitis.

Identifying Lipid deficiency in AD and supplementing custom lipid formulation (Precision medicine).

Normal skin barrier

Abnormal skin barrier

Tape stripping → Sampling discs collection → Lipid Extraction → Lipidomics analysis (Mass Spectrometry)
Cure the uncurable: Melanoma

1. New animal model- • Spontaneous • Acute UVB induced
2. Reduced latency and more aggressive-drug validation
3. New target-BRAF: CRAF dimerization

Keratinocyte-> melanocyte crosstalk

Oregon ranks 3rd in nation

Kris and Agestinis, 2012; Hyter and Indra., 2013

Nature Reviews Cancer volume 16, pages 345-358 (2016) Shain and Bastian

Activation of cell→ cell signaling and perturbation of tumor microenvironment in absence of keratinocytic RXRa during UV induced melanomagenesis

Arup K. Indra, Pharmacy

Chagani et al, 2017 BMC Cancer
Fighting infection with vitamin D and other natural compounds

Nanofiber bandages and sutures


Adrian F. Gombart, Linus Pauling Institute, Department of Biochemistry & Biophysics
Fighting fat with natural compounds


Q & A
Investigating colloid transfusion in horses

- Transfusion with equine plasma provides albumin to horses with low blood protein
  - Can cost owners hundreds to thousands of dollars
- We suspect the positive impact is minimal and transient
- We wish to collaborate to trace albumin transfused into horses to determine its persistence in the vascular space

Erica McKenzie BVMS, PhD. DACVIM, DACVSMR
Sarah Schale DVM (presenting)
Colloid osmotic pressure

- Average 19.1 ± 2.1 mmHg in 27 healthy horses
- Average 10.4 ± 2.2 mmHg in 8 sick horses pre-treatment
  - Transfusion induced a maximum mean increase of 2.2 ± 1.8 mmHg within 4 hours

Please contact erica.mckenzie@oregonstate.edu if interested in collaborating.
Discovery of Chemoprevention Agents that Upregulate the Antioxidant Response Element (ARE) via Keap1/Nrf2

- ARE genes code for cytoprotective Phase I enzymes such as GST, COMT and UGTs.
- Induction of the ARE prevents cellular damage.
- Covalent modification of Keap1 cysteines by xenobiotics inhibits ubiquitination of Nrf2 by the Keap1/Nrf2/Cul3 complex.
- Less ubiquitination of Nrf2 means less degradation by the proteasome.
- Elevated Nrf2 upregulates the ARE.
- Examples of dietary chemoprevention agents include sulforaphane (broccoli) and isoliquiritigenin (licorice).
- The van Breemen group at the LPI uses mass spectrometry to discover new chemoprevention agents using mass spectrometry.
2-Step MS-Based Discovery of Chemoprevention Agents

1. MALDI MS of Keap1+Test Extract

- Keap1 mass increases if covalent modification occurs

van Breemen Linus Pauling Institute OSU

2. LC-MS Screening of Active Extract (example: Hops)

- Peak diminished for component reacting with Keap1

Electrospray LC-MS

- Xanthohumol removed by covalent reaction with Keap1

m/z 353

Retention time (min)

m/z 71,877 72,418

Relative abundance

m/z 65,000 71,000 77,000

60 50 40

KEAP1 + solvent

KEAP1 + sample

Hop Extract

Extract + Keap1

Xanthohumol

Isoxanthohumol

25.9
Emily Ho, PhD

Areas of expertise: nutrient metabolism, diet/gene interactions, epigenetics, cancer prevention, inflammation & immune function

Current ongoing projects:
1. Benefits of zinc in human health across the lifespan
   • Zinc status and its effects microbiome and age-related immune dysfunction.
   • Genetic & epigenetic function of zinc during development and sensitization to environmental toxins

2. Dietary factors for in cancer prevention (prostate and breast cancer)
   • Dietary epigenetic modulators, such as sulforaphane, for prostate and breast cancer prevention- chromatin/non-coding/DNA methylation
   • Metabolomic biomarkers
Moore Family Center for Whole Grain
Foods, Nutrition & Preventive Health

Healthy Diets & Food

Foods, Nutrients & Preventive Health

Community Nutrition & Public Health Practice

Integration

Establish links between nutrition and health
Develop methods for measurement
Identify influencing factors
Evaluation interventions to change
Translate research into practice
Analytical Service Core Laboratory (ASCL) at LPI

Chemical Assays
- Clinical or animal specimens; food analysis (Vitamin A, C, D, E, K, flavonoid)
- Oxidative damage assessment (Isoprostane, glutathione, 8-oxo-dG, MDA, plastiquinone)
- Lipidomics (oxidized lipids, phospholipids, sphingolipids, fatty acids)
- Metabolomics (amino acids, TCA metabolites, glycolysis)
- Stable isotope tracer studies

Mass Spectrometry
- RT-PCR, microarray
- Flow cytometry
- Cell culture

Biological Assays
- API3000 TQ mass spectrometer
- Biotage solid phase extractor
- Tecan LLE
- Waters HPLC and UV fluorescence
- Shimadzu HPLC with Dual Wavelength UV Detector/Fluorescence
- Waters HPLC with Photodiode Array and ECD

http://lpi.oregonstate.edu/research/analytical-core-laboratories
mRNA therapeutics for cystic fibrosis

Airway (Apical)

Interstitium (Basolateral)

Chloride Efflux

Fluorescence (Ft/F0)

Radiance (psec/cm²/sr)

PEG Conjugated Lipid

Structural Lipid

Cholesterol

Cationic Lipid

Messenger RNA

1.0
1.1
1.2
1.3
1.4
1.5
1.6
70
120
170
220

0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180

+ amiloride
+ CFTR(inh)-172
+ ATP

Pre-Treatment
Day 1
Day 4
Day 8
Supramolecular assembly of NanoDrills for drug delivery

Hydrophobic Sequence
Amphiphilic Sequence
Hydrophilic Sequence

Comparative study

Mean Fluorescence Intensity

Emission wavelength (nm)

400 450 500 550 600

2F-RT = Fmoc-FF-(RADA)$_2$-Tat$^{48-59}$-CONH$_2$

3F-RT = Fmoc-FFF-(RADA)$_2$-Tat$^{48-59}$-CONH$_2$

4F-RT = Fmoc-FFFF-(RADA)$_2$-Tat$^{48-59}$-CONH$_2$

Cy-7 labeled 2F-RT Blank
Q & A
SESSION II
Sun Lab – OSU Pharmaceutical Sciences

- **Materials Chemistry/Engineering Laboratory**
  - Synthesis – Characterization – *in vitro* – *in vivo*

- **Novel Molecular Imaging Agents & Modalities**
Sun Bio-Nanomaterials Laboratory

- Enhancing Radiation Therapy through Nanotechnology

- Stimuli-responsive Drug Carriers
In older men, those with moderate to high levels of life event trajectories were about 40% more likely to die, covarying risk factors (Aldwin et al., 2011).

Those with consistently high or moderate appraisals of hassles intensity are also about 50% more likely to die (Jeong et al., 2014).

Hassle and life event trajectories have independent effects on mortality (Aldwin et al. 2014b).
Regulation Processes in Optimal Aging

Specific Aims
• (1) What are long-term self-regulation and adaptation patterns over 20 years?
  1a. Changes in self-regulation
  1b. Changes executive function
  1c. Changes in Inflammation
• (2) Do long-term patterns affect daily stress outcomes in daily diary study?
• (3) What are interrelationships among cognitive, biological, and psychological regulation?

Hypotheses

<table>
<thead>
<tr>
<th>Coping Effort</th>
<th>Cop. Efficacy</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>High</td>
<td>Efficient</td>
</tr>
<tr>
<td>Low</td>
<td>Challenged</td>
<td>Efficient</td>
</tr>
<tr>
<td>Strugglers</td>
<td>Helpless</td>
<td></td>
</tr>
</tbody>
</table>

• 2a. Efficient copers will show less stress reactivity in terms of daily cortisol
• 2b. Those who maintain exec function will have fewer stress-related daily memory problems
• 3a. Does self-regulation -> less inflammation -> maintenance of executive function, OR
• 3b. Does less inflammation -> maintenance of executive function -> better self-regulation?
• Do changes in methylation translate into changes in gene expression and protein abundance?

• Does genetic ablation of the clock in mammary exacerbate epigenetic changes?
Project 2: Effects of estrogen on intracellular circadian clocks in reproductive axis

Circadian Clocks in Reproduction and Cancer

Dr. Patrick Chappell, Dept. of Biomedical Sciences
patrick.chappell@oregonstate.edu

RNA-seq: What genes are selectively activated/repressed by E2 in each cell type?

Peptide assays: What does KP secretion look like under varying E2 conditions?

A | B
---|---
KTaV-3 | KTaR-1
Mass Spectrometry-Based Screening Assays for Natural Product Lead Discovery

Pulsed Ultrafiltration Mass Spectrometer-Based Screening (PUF-MS)

Magnetic Microbead Affinity Selection Screening (MagMASS)

Application of MagMASS in Screening Botanical Extract/Library

High throughput screening in 96 well plate

- High Resolution MS
- Data analysis by XCMS online (Scripps)
- Peak area enrichment identified through chromatogram alignment of the assay and control

Artifact/background

- 423.1801 (not seen in the original extract used in the assay)
- 351.0849 – [C20H15O6] (3.44 ppm), Licoisoflavone B
- 423.1815 – [C25H27O6] (0.44 ppm), Licoisoflavone B

Compound identification:

1. Literature search for any available data
2. Isolation of hit compound and analysis by MS/MS and NMR

(Glycyrrhiza uralensis) extract

GU093118 graphic
Chunhuei Chi, MPH, Sc.D.
Professor, Global Health Program, & Health Management and Policy Program
Director, Center for Global Health, CPHHS
Affiliated Faculty Member: Applied Economics Program, and Public Policy Program

Area of Expertise

• Health System Financing
• Governance in Health Systems
• Global Health Governance
• Equity in Health, Health Care, and Financial Burden of Health Care
• Deliberative Process for Community Decision Making
• Health Systems Strengthening
• Comprehensive Health Development in MLICs
• Priority Setting in Health Systems
• Universal Health Care Systems

Research Questions and Ideas

• How to promote self-sufficiency in community health development in MLICs?
• Methods for gathering and aggregating community values and preferences for health system
• Alternative frameworks of community governance in health development
• Alternative frameworks of program planning and evaluation
• How to promote shared health agency in global health governance
Examples of works


Critical evaluation of international health programs: Reframing global health and evaluation

Authors

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International Symposium on Universal Healthcare
National NHI Systems of Focus: Taiwan, Canada, Chile, Japan, & S. Korea

Dates: May 24 & 25, 2018
Q & A
From Organ Development to Regeneration
Chrissa Kioussi
College of Pharmacy
modeling human disease

identifying molecular states

building gene networks

respecifying cell states
Dave Dallas, Assistant Professor, CPHHS

- Milk protein digestion and bioactive peptides
Lipid peroxidation causes increased phospholipid remodeling, especially phosphatidyl choline, causing choline depletion.

MORTALITY AND MORBIDITY

% Dead or Malformed of Total Embryo Count

- E–
- E+

$\rho < 0.0001$

Hours Post-Fertilization

- 24
- 48
- 72
- 120

- d
- c
- b

p < 0.0001
Even if the E– larvae looked OK, they had neurologic problems!

Possibly caused by the lack of methyl donors (choline) and dysregulation of epigenetic controls!
Anthocyanins
Phenolics
Antioxidants
  FRAP
  ORAC
Vitamins
  C, D, E, K, folate
Minerals
  Cu, Ca, Fe, Mg, K, Na
Amino acids
Procyanidins

Carotenoids
  Lycopene
  Lutein
  β-carotene
Fatty acids including omega-3’s
Sugars & sugar alcohols
Acids
Sterols
  β-sitosterol
  Campesterol
  Stigmasterol
Food Composition Lab – LPI
Bob.Durst@OregonState.edu (7-6490)

- Fruits
  - Cranberry
  - Cane berries
  - Apple/pear
  - Pomegranate
  - Aronia
  - Salal

- Vegetables
  - Tomato / purple tomato
  - Red/blue potato
  - Blue corn

- Foods
  - Honey
  - Dulse
  - Wines

- Research projects
  - NASA-Mars mission
  - Chitin
    - Prof. Greg Rohrer
  - Honeybee die-off
    - Prof. Sujaya Rao
  - Elderberry products
    - SBIR
Laboratory Animal Resources Center (LARC)

- Novel techniques
- Study design consultation
- Refinements
- Training

LARC@oregonstate.edu
Jennifer.Sargent@oregonstate.edu
Seeking C57BL/6 mice on a high fat diet and their controls!

- Ulcerative dermatitis
- Hypothesized to be compulsive disorder
- Behavior filming to capture grooming microstructure

Jennifer.Sargent@oregonstate.edu
Q & A
Thank you – Please join us at the reception!