Virtual IARPA TEI-REX Proposers' Day

Dr. Robert Bruce Hayes, CHP, PE
Associate Professor
Nuclear Engineering Department
North Carolina State University

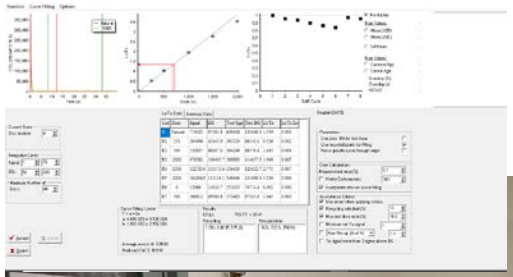
Radiological Detection and Nuclear Assay

Wed, Sept 29

Electron Paramagnetic Resonance (EPR)

- A free radical is simply an unpaired electron
- Identical physics to that of NMR but EPR sees free radicals rather than free protons
- EPR is a nondestructive means to measure free radicals in a solid.

TL/OSL




RISØ TL/OSL READER MODEL DA-20
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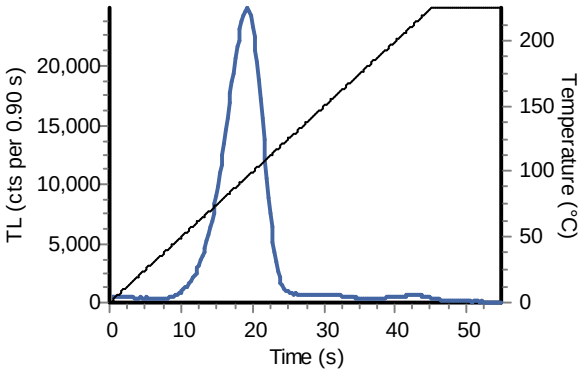
TL (cts per 0.90 s)
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10
20
30
40
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Time (s)
200
150
100
50
0
Temperature (°C)

EPR biodosimetry examples

- Antlers which unlike horns are annually shed by fauna allowing regional biodosimetry
- Walrus tusks which can give results on underwater nuclear activities with which they have contacted or other arctic conditions
- Shells, mollusks and snails can provide regional historical radiological conditions
- Plastic materials can be used but generally have low sensitivity and short (days to weeks) half lives and vary from one material to another

Thermal and Optically Stimulated Luminescence Biodosimetry Examples

- All insulator materials on a person which have a crystalline structure
  - This does require samples to be largely translucent
- Silica type materials including natural quartz, quartzite, feldspars and zircons
  - Dirt from money including both paper and coin
    - This requires silica components which have been light shielded
  - Natural rocks
    - This requires the accumulated natural background is small or comparable to the dose of interest

Solid State Biodosimetry

based on published research

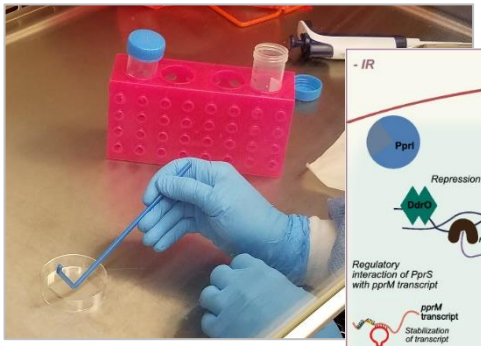
EPR

- Tooth enamel biopsy
  - Requires dentist rather than phlebotomist/nurses
- Confectionary
  - Requires edibles
- Fingernails
  - Low sensitivity and transients
- Buttons
  - Not well characterized

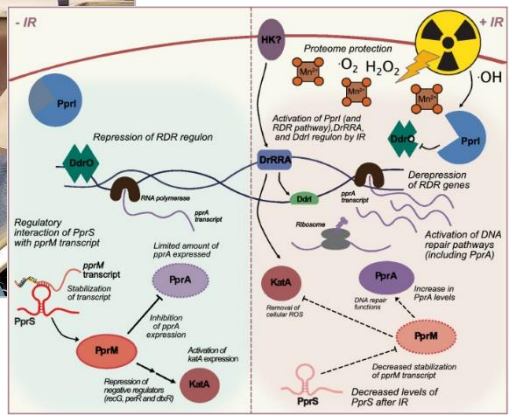
TL/OSL

- Watch PC board
  - Destructive unless reassembling watch
  - Sample preparation requires further research
- Surface mount resistors in personal electronics
  - High sensitivity but requires sufficient electronic components and is in principle destructive

Curt Hewitt, PhD – SigSci/UT Team



In vitro modeling of skin microbiome



In vivo characterization of radiation response (Villa et al., 2021)

Project Overview

- Our approach focuses primarily on genomic and proteomic signatures based on signatures in the human microbiome and virome as well as similar signatures from the host
- We utilize a proprietary *in vitro* model system to establish signatures and appropriate time frames early in the project, followed by *in vivo* studies to validate models
- Adopt a multi-omic approach to assess various signatures of low dose radiation exposure and employ statistical frameworks to integrate data and predict exposure states from non-invasive or trace samples

Teaming Overview and Capabilities

- SigSci has experience in human forensic analysis, microbiome analysis, genomics, proteomics, and biomarker discovery efforts following exposure to CBRNE threats
- The Contreras lab has experience in characterizing RNA-mediated regulation pathways that are affected by radiological exposures at relevant doses relevant to TEI-REX
- Institutional access to IRB, animal facilities/IACUC, and laboratories focused on genomic, proteomic, and other small molecule/metabolomic analysis
- SigSci has performed as a prime contractor on numerous IARPA programs including Proteos, FunGCAT, MAEGLIN, and multiple seedling efforts

Teaming Needs

- Open to collaborators with experience in:
  - Biodosimetry and radiation biology
  - Radiation dosimetry/health physics
  - Novel "-omics" approaches to integrate into a multi-omisc approach
  - Access to relevant samples

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Biophysical and biophotonic characterization of biological alterations caused by ionizing radiation

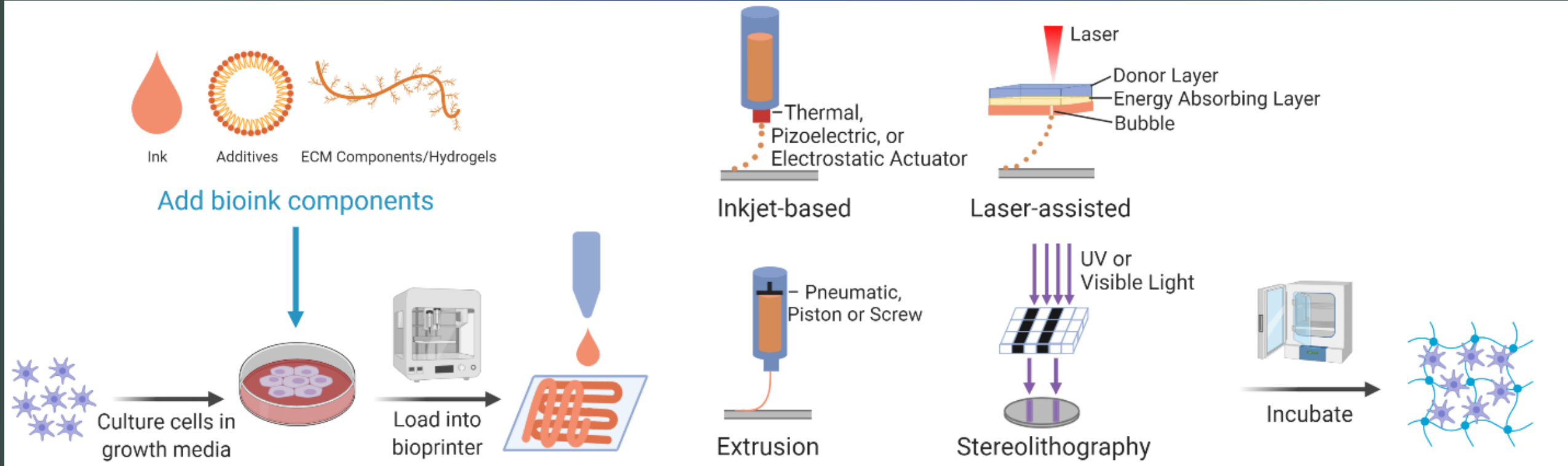
Yun Chen

Laboratory of
MEOW (Mechanical Engineering of Wet-materials)

Dept. of Mechanical Engineering
Whiting School of Engineering
Center for Cell Dynamics
Johns Hopkins School of Medicine

JOHNS HOPKINS
MEDICINE

Bioprinting = Placing Cells and ECM in Precision (as how they are in tissues)



PRE-BIOPRINTING

1. Cell selection

2. Bioink selection:
mix cells with hydrogel, a water-based biomaterial

3. Morphological design:
load bioink into bioprinter print nozzle for seeding in a specific pattern, layer by layer

PROCESSING

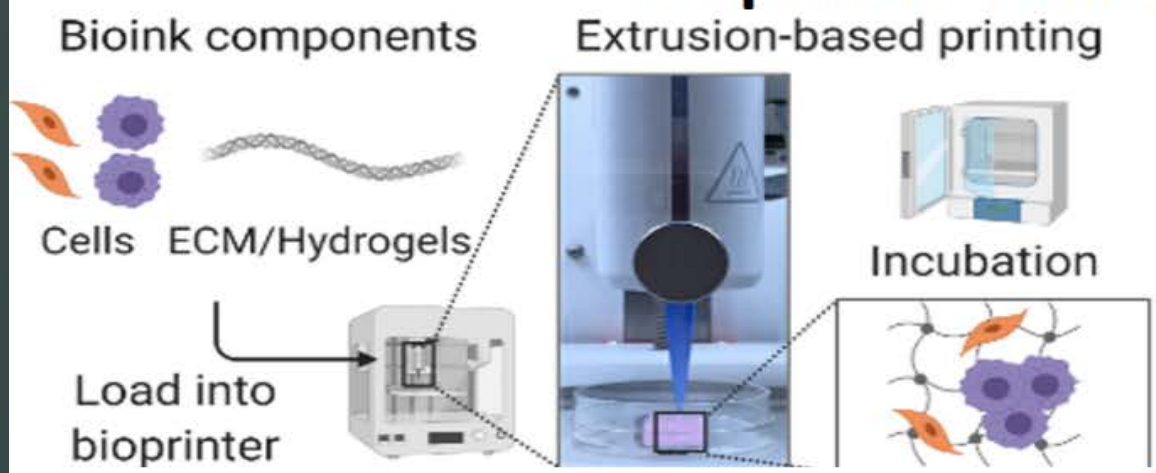
4. Selection of fabrication technique:
extrusion-based, inkjet-based bioprinting, laser-assisted, and stereolithography

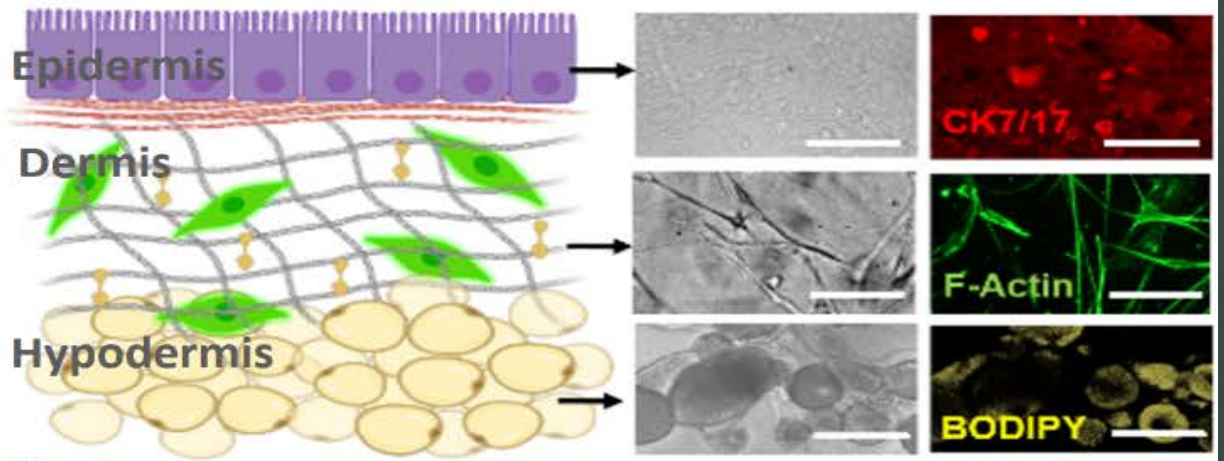
POST-BIOPRINTING

5. Stabilize bioprinted constructs with crosslinking

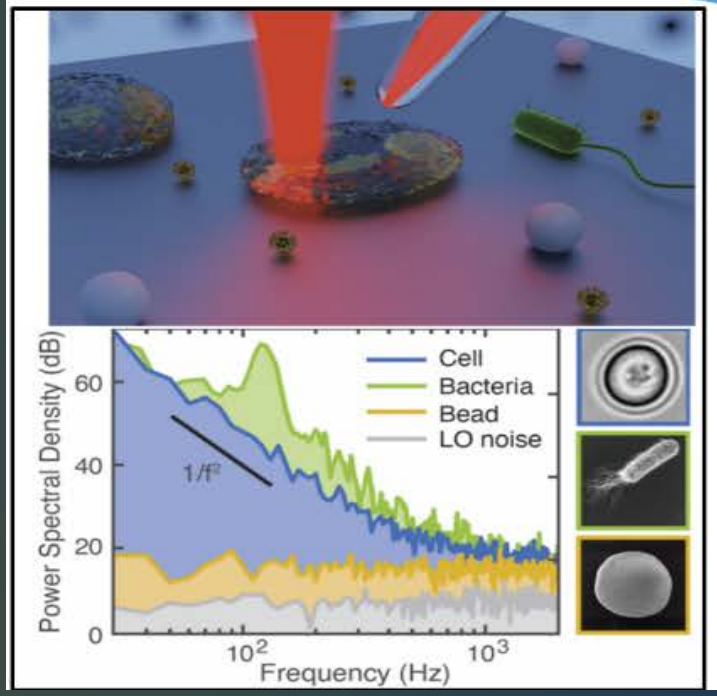
6. Further modifications:
removal of sacrificial inks, seed with cells

Bioprinted Skin-Mimetic Tissues

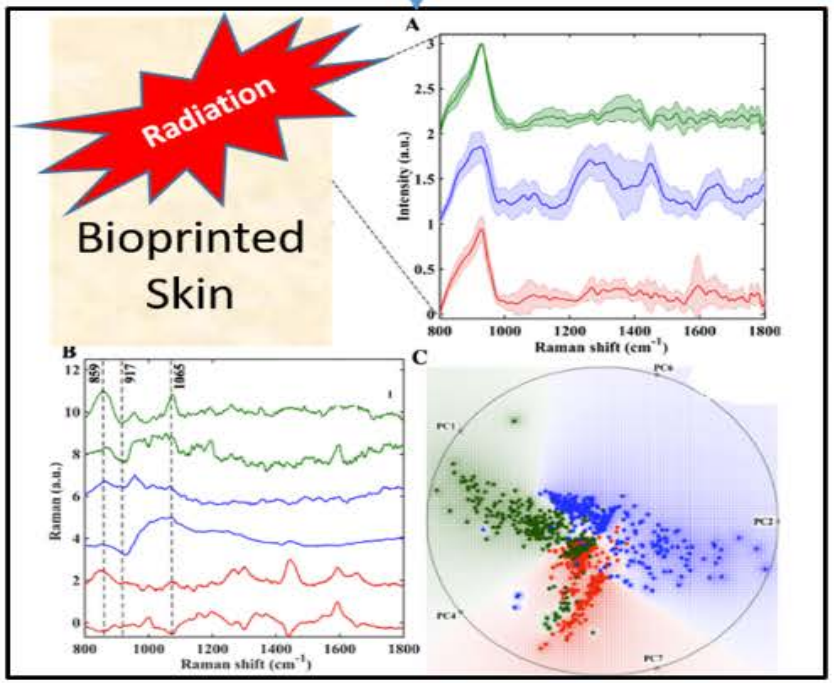




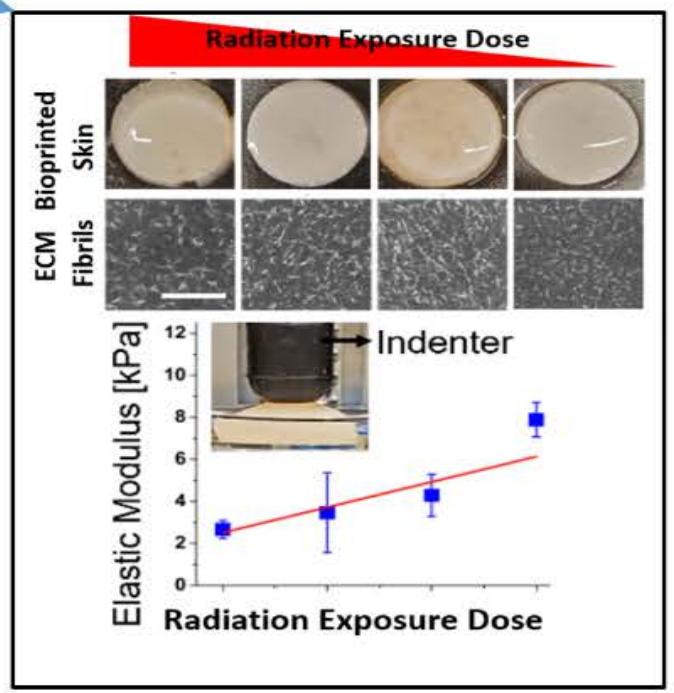
Cytoplasmic Macromolecular Motion



Raman Spectroscopy



Tissue Viscoelasticity Measurement



Turning Science Into Solutions

Advancing Biodosimetry Technologies

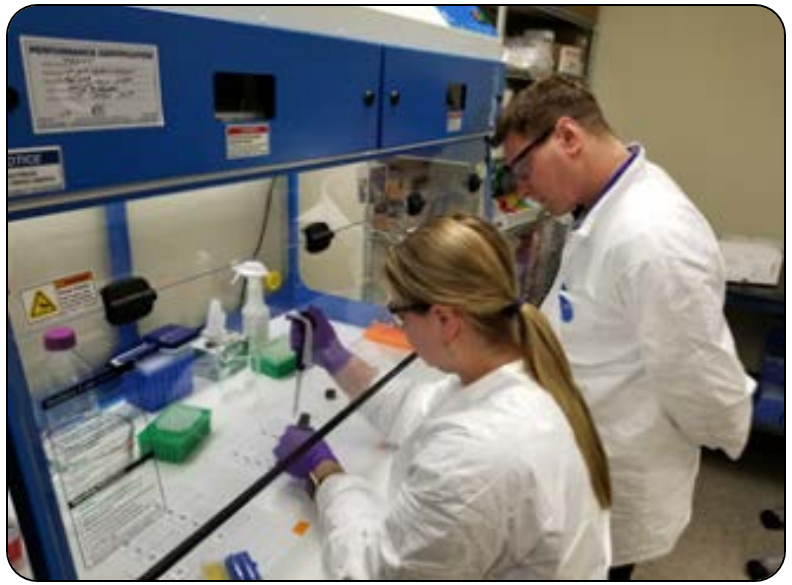
Sept 2021

About Us

Mission → Turning Science Into Solutions

What we do: Technology development to strengthen national security and emergency preparedness

- Partnership-based model to apply emerging technologies to government priorities
- Primary focus is development of biodosimetry and R/N response technologies



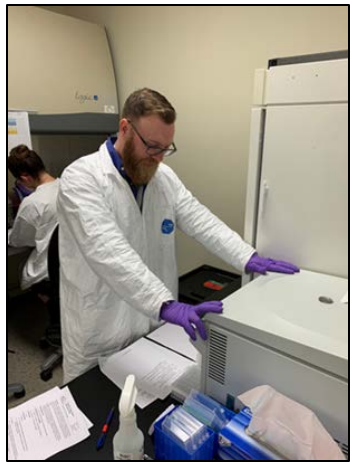
Corporate Highlights

- Founded to perform advanced development of radiation diagnostics
- Team experienced in assay & instrument development, verification, validation, clinical and non-clinical research & deployment
- Extensive network of biodosimetry development partners
- Small business with established program management, contracts, and subcontracts management systems needed for USG contractor
- FDA-compliant Quality Management System
- Federal Acquisition Regulation compliant accounting system

Our People

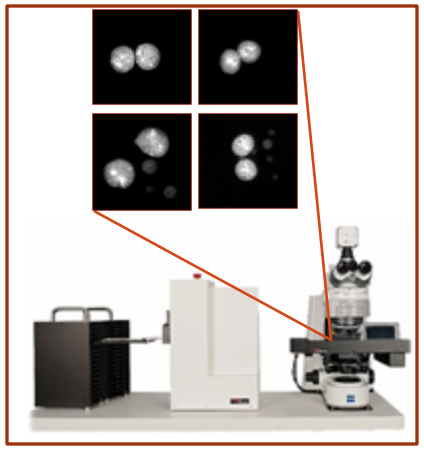
ASELL's team brings a diverse skillset with deep biodosimetry experience

- Experienced team with wide breadth and depth of experience in technology development
- > 75% with advanced degrees
  - Molecular biology, biochemistry, chemical engineering, mathematics, biomedical engineering, systems engineering, electrical engineering
- Expertise:
  - Protein, molecular, and cell-based assay development, verification and validation
  - Algorithm development/machine learning
  - Test and evaluation
  - Ionizing radiation
  - Large and small animal models
  - Systems engineering & automation
  - Clinical research
  - Program management
  - Federal contracting
  - Regulatory affairs
  - Quality assurance



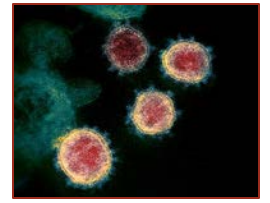
Example Dosimetry Initiatives

Meeting National Security Objectives



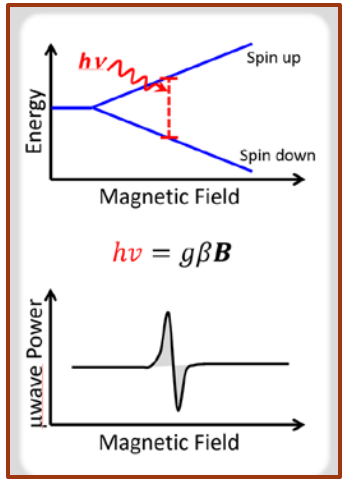
Quantitative Biodosimetry

- Quantitative, high-throughput diagnostic test (400,000 tests in 7 days) using cytokinesis-block micronucleus assay without lab-specific calibration curves
- Innovations in chemistries, cell culture formulations, image analysis and data processing algorithms
- Technology development, clinical and non-clinical studies/validation, regulatory submissions



Triage Biodosimetry

- Evaluating soluble, cell surface, and intracellular protein and hematologic biomarkers in NHP and human models
- Deployable instrument with unique imaging technology and neural network-based image processing requiring only single fingerstick sample
- Integration of instrument and biomarkers with novel biodosimetry algorithm will enable rapid, qualitative field screening for radiological exposure



Novel Electron Spin Resonance Dosimetry

- Supporting innovative spectrometer and associated technology development
- Overcoming challenges of background signatures, differentiating mix-field radiation, and rapid measurement of low dose radiation
- Leading to field-portable ESR technology for triage applications

Our Approach to TEI-REX

- Current assessment suggests the solution will likely require integration of multiple biomarkers and technologies
- Actively engaging our network of biodosimetry collaborators and evaluating emerging biomarkers and detection technologies
- Seeking interested technology partners with emerging biodosimetry solutions with promising approaches to meet specific TEI-REX objectives
- If you wish to discuss how we might collaborate, please contact Michael Ehret at mehret@asell.com

Turning Science Into Solutions

1

Genome Sciences
UNIVERSITY OF WASHINGTON

IARPA

TEI-REX Proposers Day

Michael MacCoss[1], William Noble[1], Ning Cao[2], Eric Ford[2],
Daniel Chelsky[3], Paul Rudnick[3]

2

UW Medicine
DEPARTMENT OF RADIATION ONCOLOGY

3

SPECTRAGEN INFORMATICS

Team Capabilities

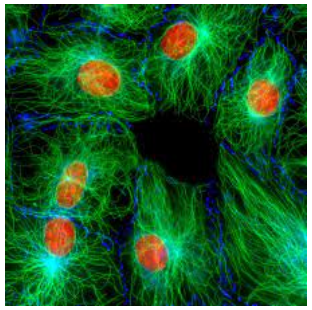
UW/Spectragen team addresses all key capabilities for TEI-REX program

Team Members	Affiliation	Radiation biology	In vitro and in vivo models associated with radiation exposure	Analytical biochemistry	Biomarker discovery	Biodosimetry	Machine learning and Artificial Intelligence	Radiation dosimetry/health physics	Statistics	Program management
Michael MacCoss	UW Genome Sciences			x	x					
Paul Rudnick	Spectragen Informatics			x	x					x
Daniel Chelsky	Spectragen Informatics			x	x					x
William Noble	UW Computer Sciences				x		x		x	
Ning Cao	UW Radiation Oncology	x	x	x		x		x		
Eric Ford	UW Radiation Oncology	x	x	x		x		x		

Model Systems

Mouse

IR exposed:



Fibroblasts

- Primary dermal cells
- NIH/3T3
- L929

Skin/fur

- C57BL/6
- Nude mice

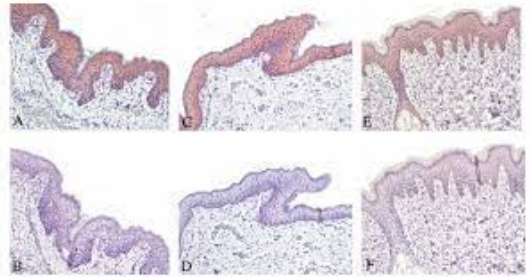
Human

IR exposed:

Fibroblasts

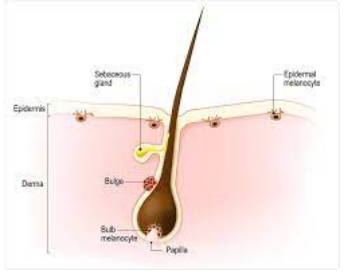
- Primary dermal cells
- Fibroblast cell lines

Human surgical skin samples



Non-IR exposed:

Human hair, hair follicles, skin adhesive disc sampling

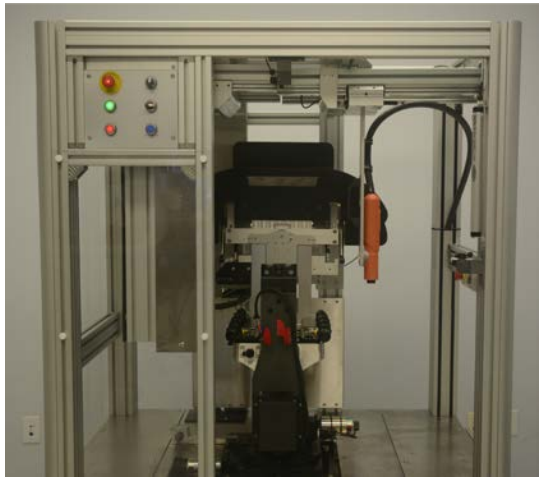


Proteomics experience with other species including rat and pig

Radiation Biology

- State of the Art Facility
- Full small animal and cell culture treatment platform
- Range of IR sources:
  - 225 kV x-rays
  - 6 MV x-rays
  - 10-50 MeV photons
  - High linear energy transfer fast neutrons

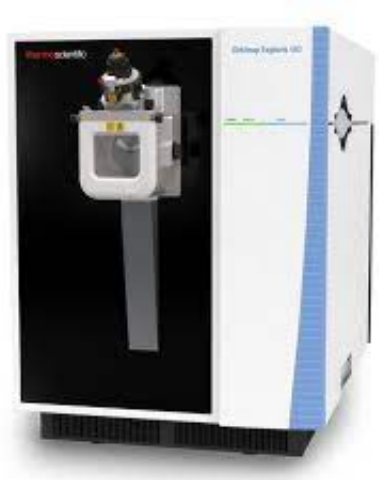
Elekta Synergy
Linear Accelerator



XSTRAHL small animal radiation research platform

Scanditronix MC50 Cyclotron

Mass Spectrometry



7 high performance MS instruments

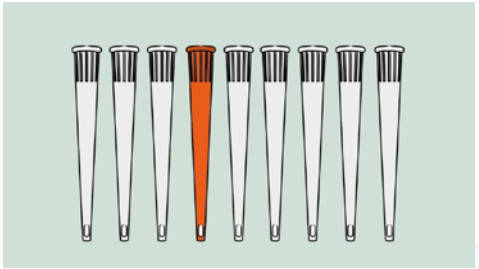
Including:

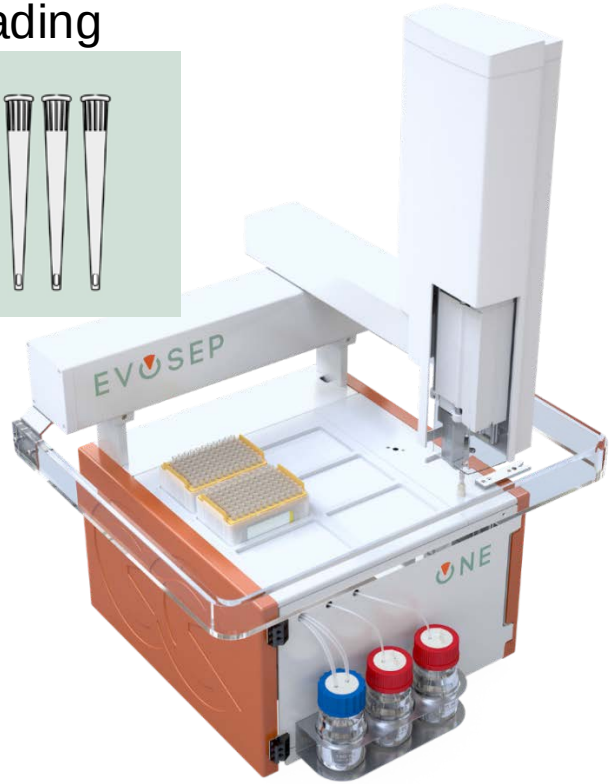
Exploris 480

Fusion Lumos

Orbitrap Eclipse

EvoTip loading

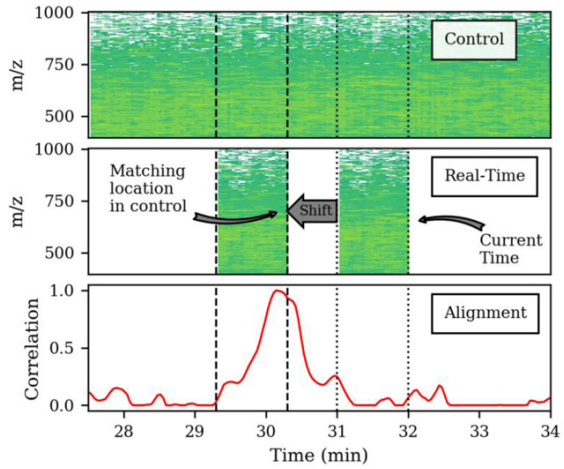




Advanced Orbitrap instruments:

Narrow overlapping isolation window DIA

Enables comprehensive and unbiased sampling of precursor ions



PRM: Highly multiplexed targeted proteomics

5,000 peptides quantified in 1h run

Enabled by real-time chromatographic alignment

EvoSep One:

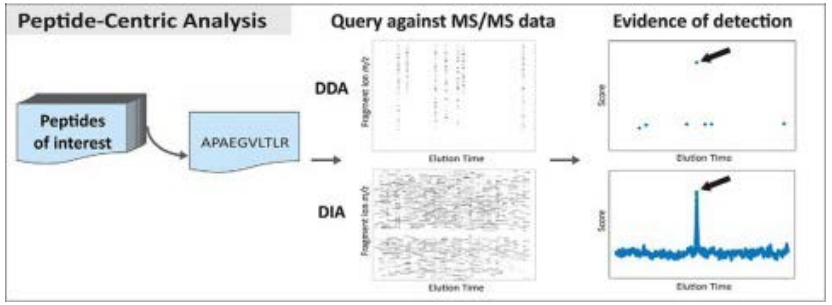
Rapid high-performance separation

500 sample/month throughput

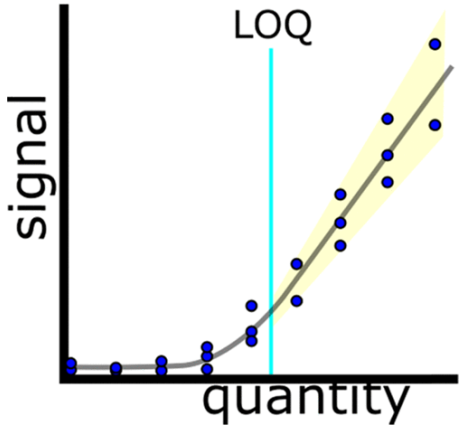
Machine Learning & Statistics

17-year collaboration between the Noble and MacCoss labs

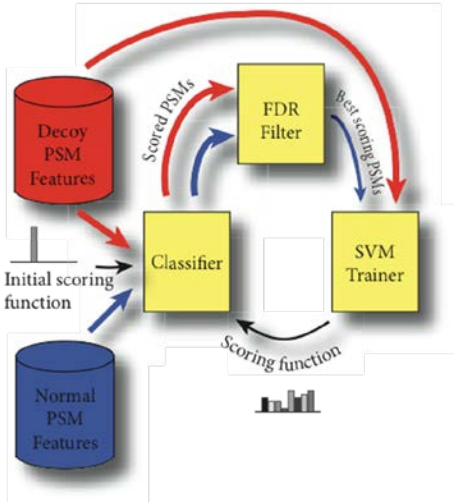
- 25 joint publications on the use of machine learning for the analysis of proteomics data
- Co-developed several of the most widely used tools
  - Percolator, Crux, Tide, accurate FDR control, etc…
  - Peptide-centric analysis for DIA
  - Analytical figures of merit, etc…



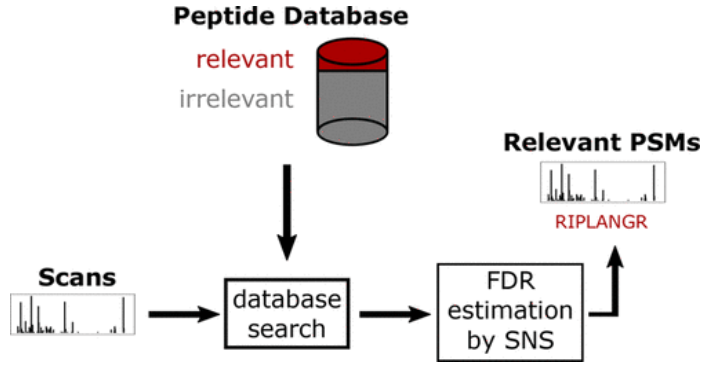
Peptide-centric proteomic analysis



Matrix-matched calibration curves for analytical figures of merit in quantitative proteomics



Percolator Algorithm



Accurately assigning peptides to spectra when only a subset of peptides are relevant