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TEI-REX Proposers Day

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

1 Genome Sciences — University of Washington

2 UW Medicine — Department of Radiation Oncology

3 Spectragen Informatics

IARPA

Team Capabilities

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

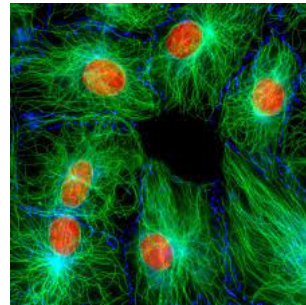| Team Members	Affiliation	Radiation biology	In vitro and in vivo models associated with radiation exposure	Analytical biochemistry	Biomarker discovery	Biodosimetry	Machine learning and Artificial Intelligence	Radiation dosimetry/health physics	Statistics	Program management
Michael MacCoss	UW Genome 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

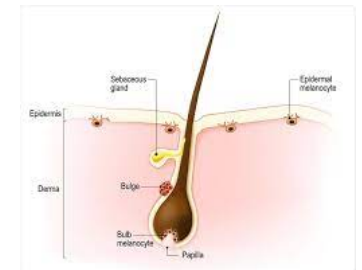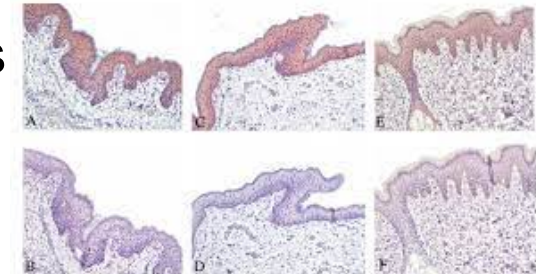- C57BL/6
- Nude mice

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
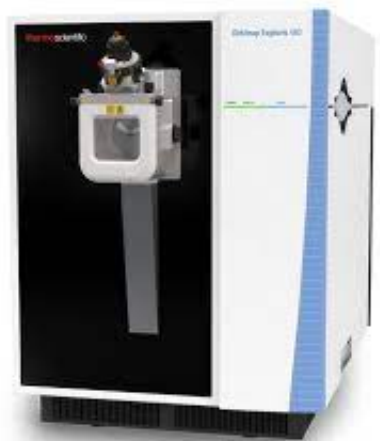
Elekta Synergy Linear Accelerator

XSTRAHL small animal radiation research platform

Scanditronix MC50 Cyclotron

Mass Spectrometry

7 high performance MS instruments

Including:

Exploris 480

Fusion Lumos

Orbitrap Eclipse

Advanced Orbitrap instruments:

Narrow overlapping isolation window DIA

Enables comprehensive and unbiased sampling of precursor ions

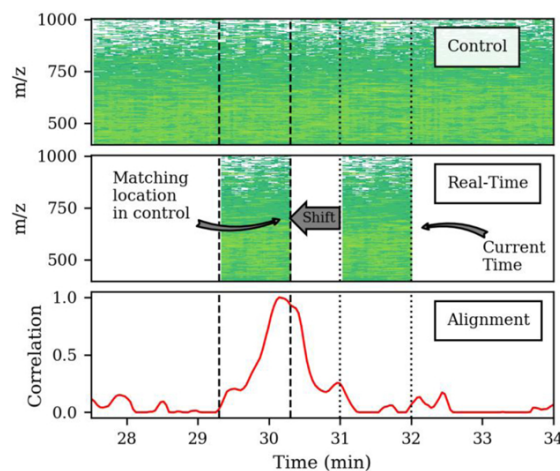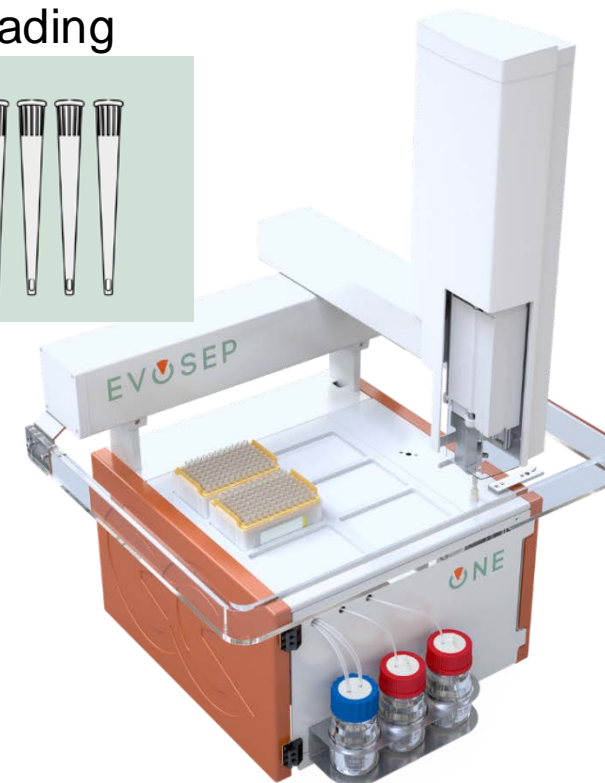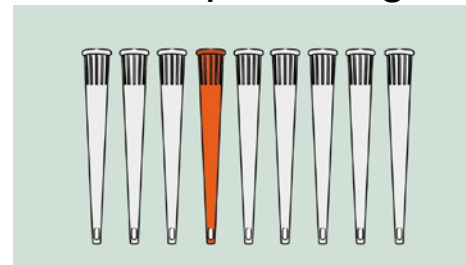PRM: Highly multiplexed targeted proteomics

5,000 peptides quantified in 1h run

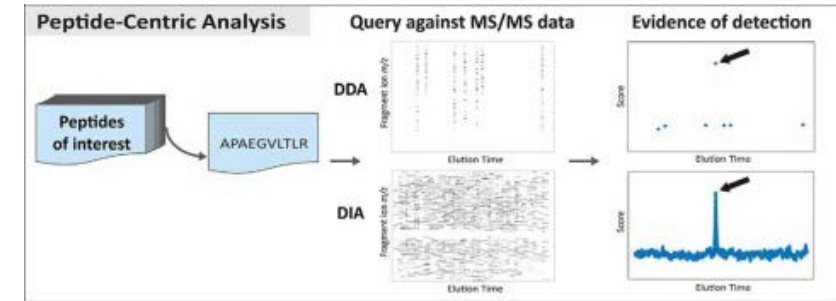Enabled by real-time chromatographic alignment

EvoTip loading

EvoSep One:

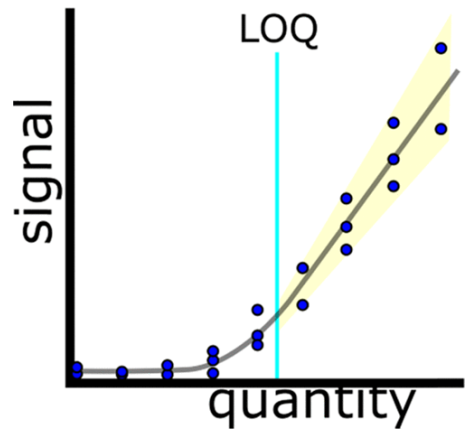Rapid high-performance separation

500 sample/month throughput

UW GS

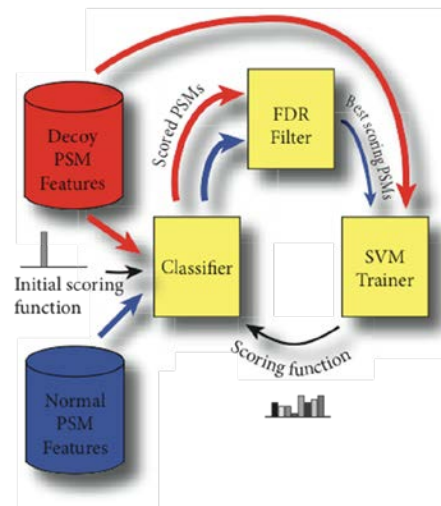**17-year collaboration between the Noble and MacCoss labs**

- 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
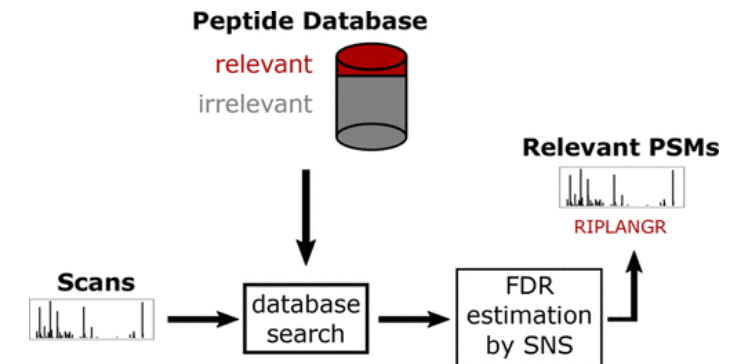 - Analytical figures of merit, etc…

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