Metabolomics Workshop

ASMS Reboot 2020

Organizers: Miriam Sindelar and Tim Garrett

The metabolomic interested group workshop was held on June 2 from 12-1:30 pm (EST) during the ASMS reboot. The workshop was chaired by Miriam Sindelar and Tim Garrett. The workshop title was "Metabolomics in Core Facilities" We arranged to have a panel of 4 experts that included Gary Patti of Washington University in St. Louis, Nichole Reisdorph of the University of Colorado, Justin Cross of Memorial Sloan Kettering Cancer Center and Caroline Lewis of the Massachusetts Institute of Technology. We have each panelist 2 questions and asked them to provide a 5 min answer to those questions to help stimulate discussion. The workshop was attended by over 160 people. The questions and answer aspect of the workshop went very well. We did not have attendees ask their questions live, but instead asked them to input the questions into the chat area so that that workshop organizers could ask the panelist the questions. The questions and presentation slide deck are provided with this summary.

Overview

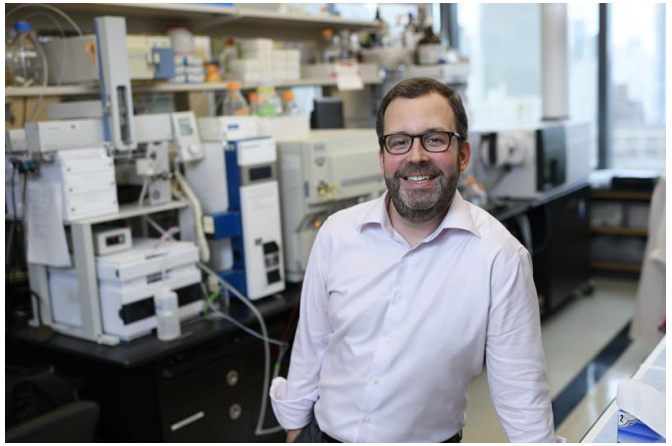
- Metabolomics core facilities are growing rapidly with almost every major institution offering services
- This has expanded access, discovery, and applications
- At the same time, metabolomics is rapidly growing with new developments in technology (both MS and chromatography), data filtering, statistics and software
- Managing a core in a rapidly growing field is both exciting and challenging
- In this workshop, we will discuss several questions about core facilities with key experts opinion

Metabolomics in Core Facilities
Panelists

Gary Patti
WashU, St. Louis

Nichole Reisdorph
University of Colorado

Caroline Lewis
MIT, Boston



Justin Cross
MSKCC, New York

Questions

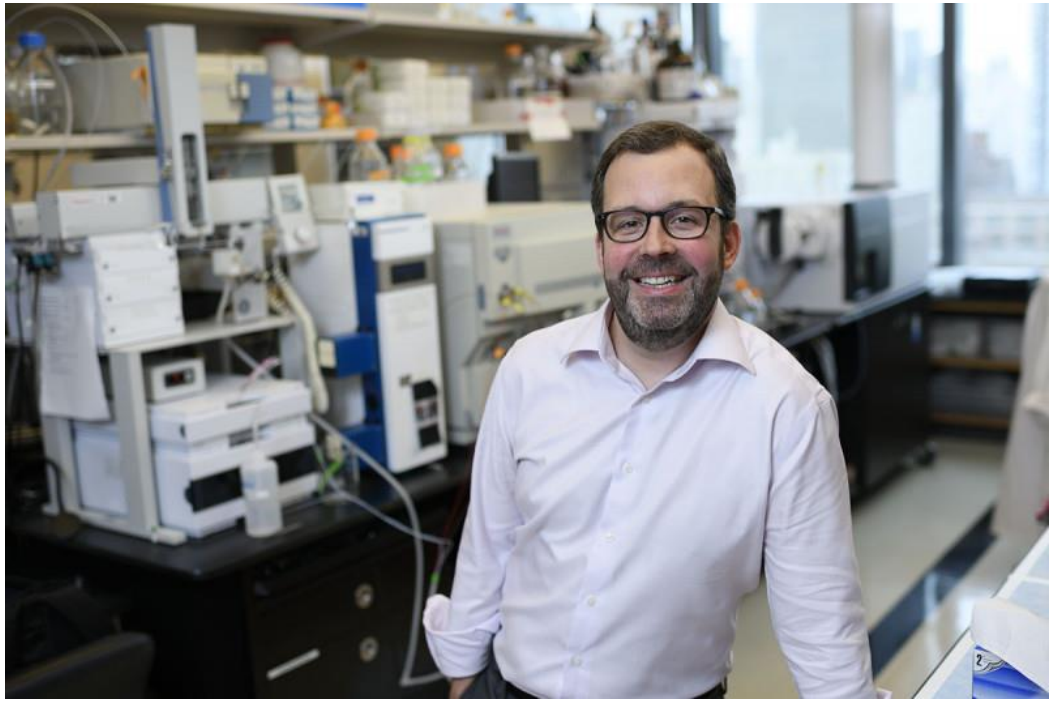
A)	How do you manage expectations of customers?	**Justin Cross**
A)	When does a simple analysis need to become a scientific collaboration?	
B)	How do you decide if you take on a project or do you have to analyze all samples that are ordered for analysis?	**Caroline Lewis**
B)	What are some challenges for running a metabolomic core facility? What is a key for success?	
C)	Are they specific practices that should be adopted for core facilities in metabolomics?	**Nichole Reisdorph**
C)	What advances in metabolomics do you think have been very important in the past few years?	
D)	When and why do you take on untargeted metabolomics projects when a researcher approaches with a collaboration?	**Gary Patti**
D)	How do you handle the issue of unknowns?	

Participants

- **Justin Cross**

Director, Donald B. and Catherine C. Marron Cancer Metabolism Center

Memorial Sloan Kettering Cancer Center, New York



A) How do you manage expectations of customers?

The -omics in Metabolomics is a problem – try to get the messaging right, from the very first interaction

They know their science best, we know the technology best

- *Don't assume they know what they want and don't jump straight in… take some time, discuss their question, explain what's possible.*
- *Explain this will be a substantial commitment of resources and people's time (theirs and yours), it requires some planning.*
- *If you're meeting investigators halfway, also expose them to some of the analytical challenges, educate them on the decisions we still need to make.*
- *Make them participants and expect engagement in return – if this starts to look like 'outsourced science' consider reducing the scope.*

No tubes without an experiment plan

- *Design the experiment or study together – groups; replicates; time points; controls; for clinical, discuss available metadata.*
- *The details matter: define some positive and negative controls, sample collection, sample prep, which methods? Which metabolites?*
- *Require extra samples you can use to test the analytical system before working with an entire batch.*
- *Define the scope: key molecules, format of the results - extending beyond this is a separate discussion and a separate timeline.*

Avoid spray and pray at all costs

- *Do pilots, check coverage, confirm key assumptions.*
- *No large studies without a smaller one first.*
- *No untargeted without a targeted study targeted first.*

A) When does a simple analysis need to become a scientific collaboration?

If you're managing expectations, it likely already is a collaboration

- *You're an expert in what you do and you are contributing your expertise to their exciting project.*
- *If you're proactively taking a steering, advisory role in the project you are already a collaborator and most people will recognize that.*

Interesting, cutting-edge research will almost always become a collaboration eventually, even if it doesn't start that way

- *Reviewer requested experiments come with higher stakes, time pressures and are not always feasible.*
- *Try to anticipate and plan ahead, but stand up for what is reasonable/possible, and request the time you need to be sure.*

The lab's core assays have their place, we love them

- *Start with simple, with assays you're already confident in.*
- *It builds experience, validates the experimental approach, builds confidence in the project, and working together – then branch out if needed.*

Dig deeper when you see the opportunity, do justice to the time and resources you're already invested

- *Talk, read, plot: your data is beautiful – use it!*
- *Don't assume the collaborator knows how to get the best out of the data, work with them to the end.*
- *Biology rarely works as we expect – data we collect puts us in a position to make discoveries and find the unexpected, so seize the moment!*
- *Meaningful scientific contributions are almost always recognized, and every experiment makes us better equipped for the next opportunity.*

Justin Cross, Memorial Sloan Kettering Cancer Center

Participants

- **Caroline Lewis**

Director Metabolite Profiling Core Facility

Whitehead Institute

MIT, Boston

B) How do you decide if you take on a project or if you have to analyze all the samples that are ordered for an analysis?

- Depends! Internal or external? Institute expectations?
- Internal….not much of a choice, but:
  - Always discuss the project thoroughly with the researcher, know exactly what their biological question is
  - Hypothesis driven? Fishing expedition?
  - Try to guide the project if you see holes or problems with experimental design
  - Suggest pilot experiments to help avoid running unnecessary samples
  - Are the researchers going to “walk-up” to the instrument, or will the analysis require staff time?
- External:
  - Again will depend on the model of the Core and Institute expectations
  - Is project interesting and of importance?
  - If capacity of core is limited, say no
  - If experimental design is poor, say no

B) What are some key challenges for running a metabolomics core facility? What is a key for success?

- Challenges:
  - Everything we're talking about today!
  - Staying on top of new technologies and method development
  - Turn around time
  - Standardization

- Key to Success:
  - Don't be afraid to play with your model until you find something that works
  - Good people!!!!!!
  - Networking: Discuss with other colleagues who are facing similar challenges
  - Communication

Participants

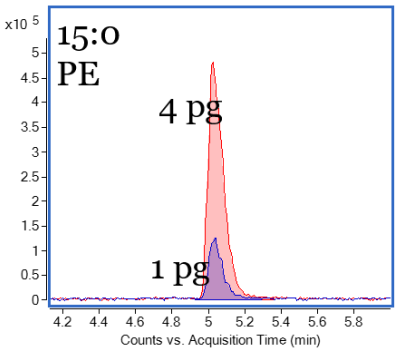
- **Nichole Reisdorph**

Associate Professor, Department of Pharmaceutical Sciences

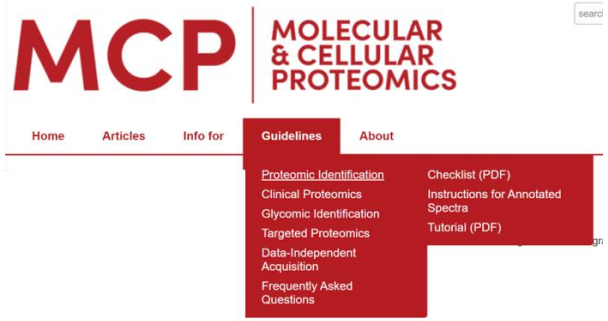
Director, Skaggs School of Pharmacy Mass Spectrometry Facility

University of Colorado

C) Are there specific practices that should be adopted for core facilities in metabolomics?



- Standardized reporting and publications guidelines
  - Eg. Molecular Cellular Proteomics
  - Metabolomics Society should have initiative soon (feel free to volunteer!)
  - Eg. Reporting confidence levels for annotated/identified molecules
  - Outside of metabolomics journals too
- Routine use of spiked internal standards for QC purposes, with results reported (%CV for mass, RT, and abundance)
- Analysis of standards, such as NIST, to benchmark new methods and platforms and as part of monthly routine



C) What advances in metabolomics do you think have been very important in the past few years?

- Development of databases/libraries with MS/MS spectral data
  - More confidence in annotations and more true identification of compounds
  - In-house and on-line, NIH Metabolomics Common Fund
- Technological Advances: eg. Ion Mobility
- Lipidomics: Appreciating challenges and improved lipid annotation
- Platforms are more robust = Larger studies
  - Increasing chances of reaching statistical significance.
  - Can develop and test metabolomics-specific bioinformatics strategies
- Cross disciplinary studies, especially in microbiome and nutrition
- Metabolites Standards Initiative coming out with new Confidence Levels

Participants

- **Gary Patti**

Michael and Tana Powell Professor

Professor of Chemistry

Professor of Medicine
Siteman Cancer Center

Nutrition, Obesity, Research Center

Director of Graduate Admissions

Washington University, St. Louis

D) When and why do you take on untargeted metabolomics projects when a researcher approaches with a collaboration?

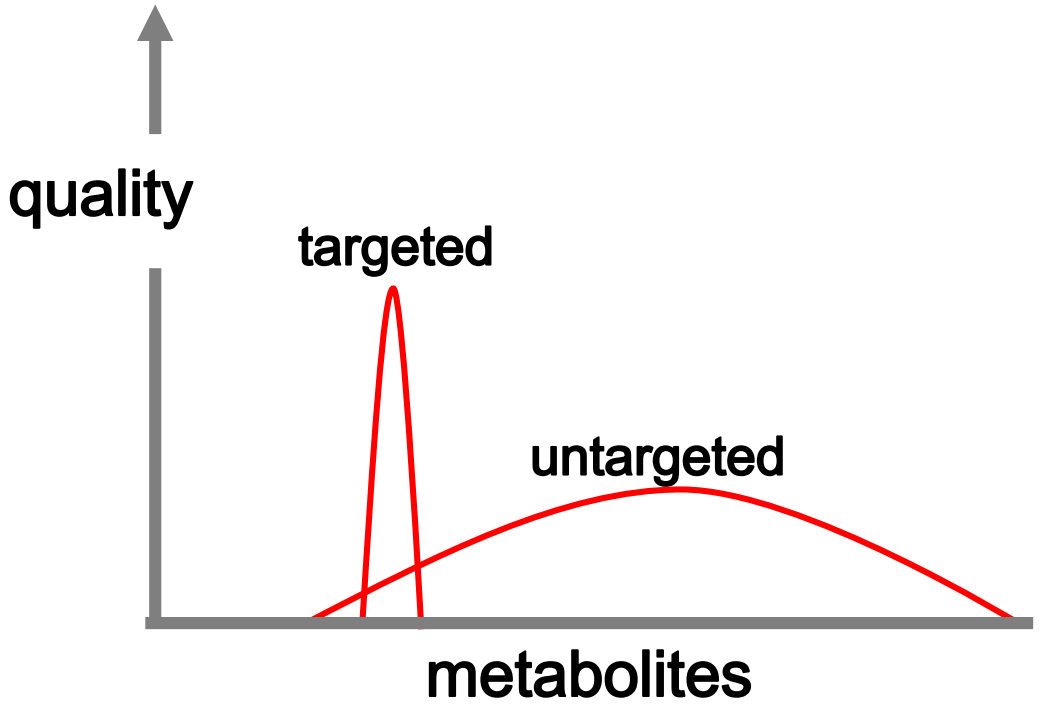
ENTHUSIASM TO COLLABORATE

- **untargeted**
- **no hypothesis**
- **early in project**
- **no funding**
- **pilot study**
- **low interest**
- **min expertise**

- **targeted**
- **defined model**
- **mature project**
- **funding**
- **publishable**
- **high impact**
- **expertise**

D) When and why do you take on untargeted metabolomics projects when a researcher approaches with a collaboration?

<u>MUST</u> UNDERSTAND PROJECT, GOALS, & THEIR METHODS



D) How do you handle the issue of unknowns?

IN OUR EXPERIENCES…

- most unknowns do not correspond to new metabolites
- collaborators do not like the uncertainty of unknowns
- characterizing an unknown requires major resources
- we try to avoid investigating unknowns collaboratively