Encouraging rigorous and reproducible research

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Fulbright Scholar to the Czech Republic 2025

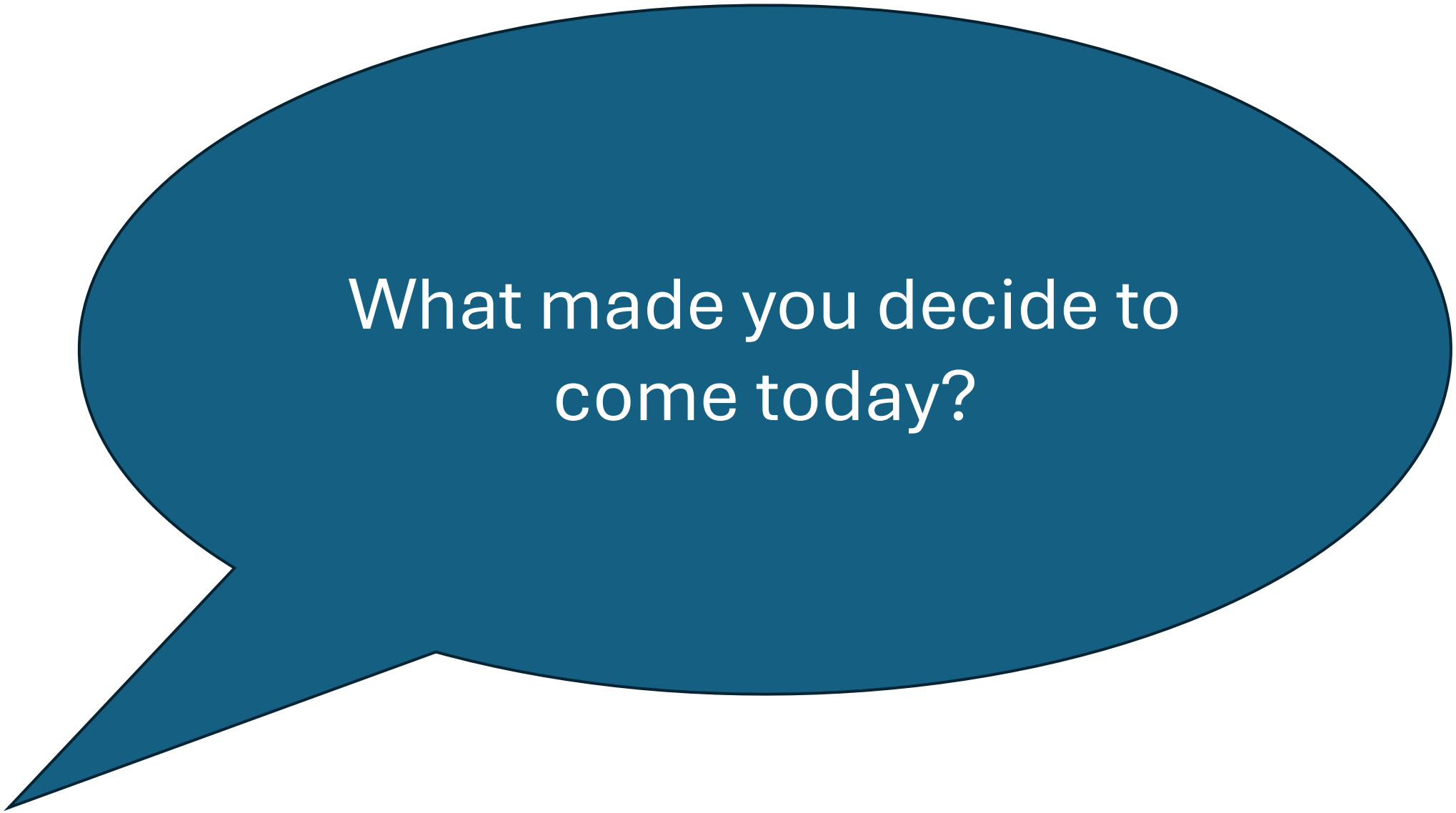
Funded by NIH and the Fulbright Commission

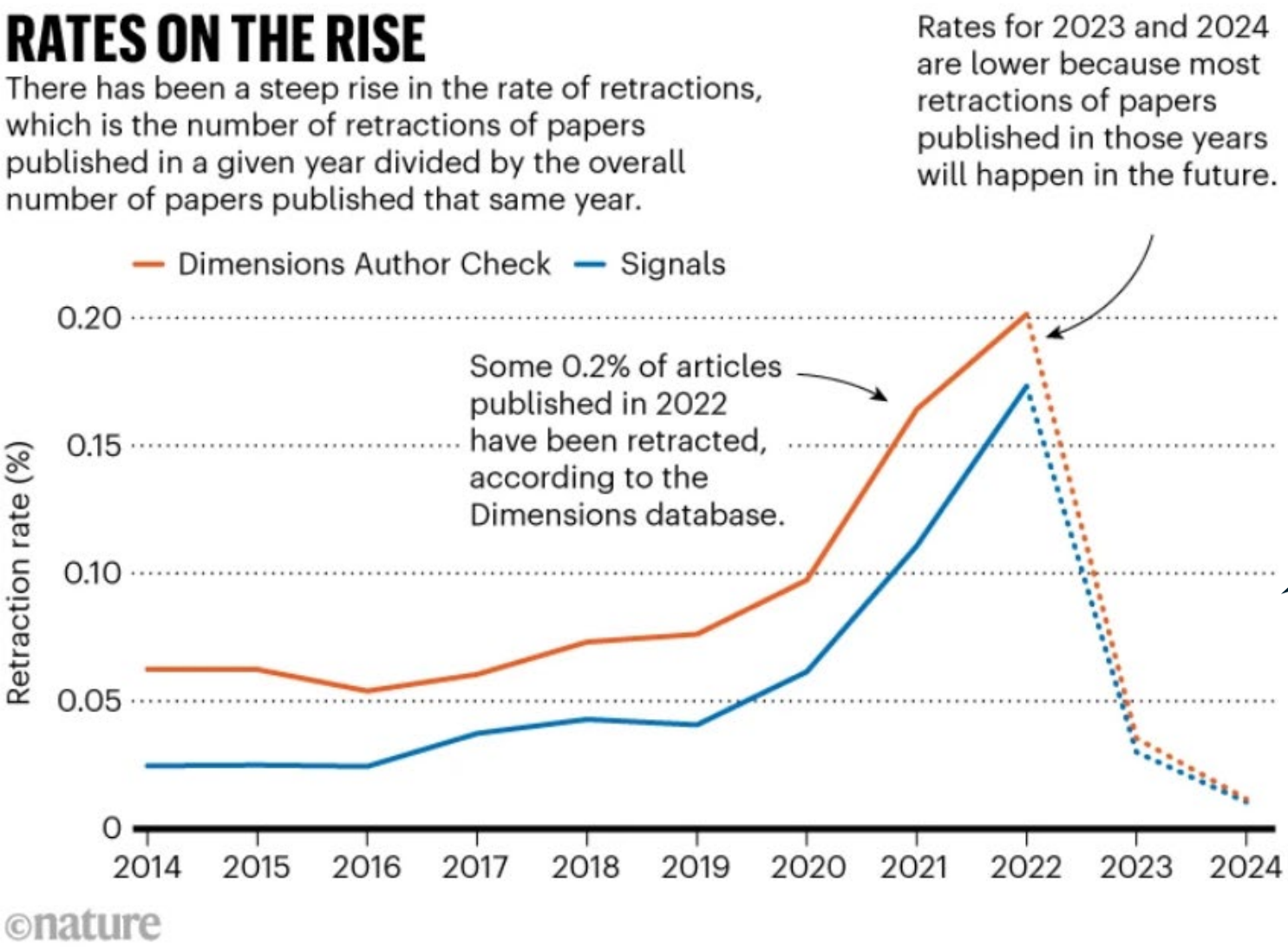
Overview

- Why are we here?
- What are the causes of the reproducibility crisis?
- What are some solutions?
- Ways to create a lab environment that encourages rigor and reproducibility

How I got here…….

- Running a molecular biology research lab (>20 years)
- Testing 60% of the sewage in Colorado for COVID for 3 years
- Running a graduate program since 2018
  - Leading Rigor & Reproducibility Workshops (4 years)
  - Helping faculty and students deal with conflict (6 years)
  - Teaching Rigorous Research Methods course (>10yrs)
- Being contracted to conduct an experiment for a law firm


What made you decide to come today?



Why?

Van Noorden Nature 2025

Factors Contributing to Irreproducibility

What strategies do you currently use to ensure your research is reproducible?

Some good ways to improve reproducibility

Randomization & Blinding

Pre-registration/ Planning

Templates / SOPs / Checklists

Training in best practices
- Statistics
- Data management
- Software
- Instrument calibration

Publishing negative results / replication studies

Electronic lab notebooks

Data Management Plan

Transparent reporting
- data and resources
- methods & protocols

Version control
- Protocols
- Reagents
- Cell lines
- Plasmids
- Datasets
- Analyses
- Code

Authentication of resources
- Antibodies
- Primers
- Plasmids
- Strains
- Cell lines

Much of this is not new to you!

So why is the problem not going away?

The “Hidden Curriculum”

Knowledge about best practices for rigorous & reproducible research is primarily conveyed through informal means such as mentoring and lab culture

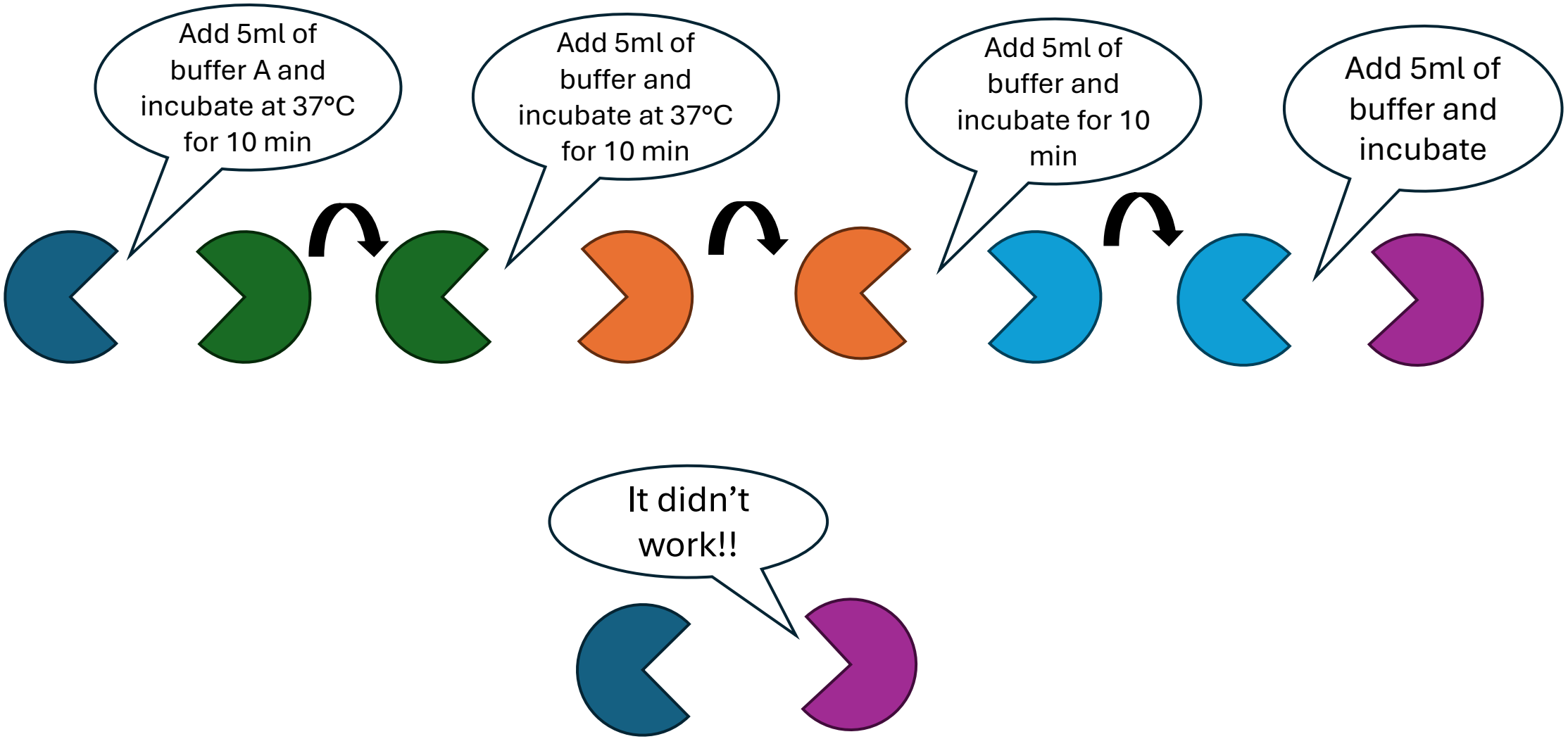
J. Nat. Prod. 2024, 87, 5, 1487-1492

Have you experienced a situation where a trainee made a mistake because they hadn’t picked up on an unwritten rule or convention?

Problems with Implicit Learning

- Assumed to occur naturally (but rarely assessed)
- Inconsistency:
  - Students receive different implicit lessons depending on their prior research experiences/opportunities
- Gaps in knowledge:
  - Important skills and knowledge may be omitted
- Ethical Concerns:
  - Students may unknowingly adopt unethical or questionable behaviors
- Lack of Awareness:
  - Students may be unaware of the lessons they are learning, making it difficult to critically evaluate them, *or accurately pass them on*

tichá pošta


Add 5ml of buffer A and incubate at 37°C for 10 min
Add 5ml of buffer and incubate at 37°C for 10 min
Add 5ml of buffer and incubate for 10 min
Add 5ml of buffer and incubate
It didn't work!!

How do you know your trainees are learning the right way to do things?

Supplement with EXPLICIT training!

- Formal workshops and training
- Written documentation and guidelines
  - SOPs
  - Code of Conduct
- Incorporate discussion of R&R into lab culture
  - Lab meetings
  - Journal clubs
  - One-on-one meetings
- Pay attention
  - Check lab notebooks
  - Review protocols
  - Ask questions
  - Look at the raw data

TRUST BUT VERIFY!

We double check ALL critical tasks.

Make the Right Way Easier than the Wrong Way

- People want to do the right thing
- BUT if it's a lot easier to do the wrong thing
- AND there's no immediate consequence
- OR they don't value the right thing
- They will do the wrong thing……
  - Even when they know it's the wrong thing

People will only recycle if you make it easy.....

Colorado

Academie Ved

Make the Right Way Easier than the Wrong Way

- Provide the necessary tools and training
  - Onboarding Check Lists
- Create accessible SOPs, Templates, Protocols, Manuals
- Automate doing the right thing
  - Version control, templates
- Make someone responsible for tedious tasks
- Allow/create extra time for it
- Notice and reward desired behavior
- Make your expectations and values clear
  - Code of Conduct / Lab Guidebook

Examples from the Sewer…….

Labels for samples printed the night before

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	
1	CSU Internal Identifier	IP Volume processed (ml)	total copies BCoV	total eluate volume (ul)	volume into extraction (ul)	final RNA volume	ul used in ddPCR	BCoV Copies/20ulWell	SARS -N1 Copies/20ulWell	F+ Copies/20ulWell	BCoV % recovery	SARS Copies/L	F+ copies/L	Droplets all over 10K?	BCoV>5%?	F+ pre
2	SA	40	40122.4198	890	140	60	8.2	85.0	15.7	1654.1	10%	18286.1	96174914.8	Y	Y	Y
3	SC	40	41569.927	710	140	60	8.2	50.4	9.8	1218.3	4.5%	9069.9	56511276.7	Y	N	Y
4	SD	40	40122.4198	710	140	60	8.2	70.2	20.9	1365.6	6%	19366.9	63343491.9	Y	Y	Y
5	SE	40	40122.4198	690	140	60	8.2	78.9	28.1	1684.2	7%	25339.9	75921364.5	Y	Y	Y
6	SF	40	41569.927	760	140	60	8.2	942.0	5.6	1356.1	90%	5572.5	67334205.3	Y	Y (too high)	Y
7	SG	40	40122.4198	740	140	60	8.2	98.3	2.6	3100.3	9%	2554.4	149882061.6	Y	Y	Y
8	SH	40	40122.4198	690	140	60	8.2	76.7	3.1	1016.8	7%	2755.9	45833999.6	Y	Y	Y
9	SI	40	40122.4198	690	140	60	8.2	71.2	25.6	1581.4	6%	23079.3	71285195.6	Y	Y	Y
10	SJ	40	40122.4198	740	140	60	8.2	96.1	16.6	2658.8	9%	16073.5	128540257.6	Y	Y	Y
11	SL	40	40122.4198	720	140	60	8.2	51.4	86.3	1005.8	5%	81151.8	47311660.3	Y	Y	Y
12	SN	40	40122.4198	720	140	60	8.2	61.5	15.8	1893.3	6%	14862.1	89058184.6	Y	Y	Y
13	SO	40	40122.4198	700	140	60	8.2	69.8	10.1	2258.3	6%	9202.8	103275302.8	Y	Y	Y
14	SP	40	40122.4198	690	140	60	8.2	59.3	2.8	2198.8	5%	2500.4	99120330.0	Y	Y	Y
15	SQ	40	41569.927	670	140	60	8.2	111.6	2.9	1178.1	9%	2512.0	51568688.9	Y	Y	Y
16	SR	40	40122.4198	660	140	60	8.2	82.2	6.2	1518.4	7%	5308.3	65470802.2	Y	Y	Y
17	SS	40	40122.4198	670	140	60	8.2	90.0	5.4	678.6	8%	4707.1	29704229.4	Y	Y	Y
18																
19																

Spreadsheet template for Data Entry and Analysis

- 20200914_Report
- 20200917_Intake
- 20200917_Report
- 20200921_Intake
- 20200921_Report
- 20200924_Intake

File/Sample Naming Conventions

POOP PROCESSING CHECKLIST 2021

Date										
Tech 1 Time In /Initials										
Tech 1 Time Out/Initials										
Tech 2 Time In/Initials										
Tech 2 Time Out/Initials										
Intake Form uploaded										
logged										
Eluate volumes entered into report										
Report read-me completed										
Eluate frozen and location logged										
Innovaprep in storage fluid and off										
BSC clean and tidy										
Biohazard waste autoclaved										
Bleached IP waste discarded										
RNA frozen and location logged										
Reagents and cold block at -20C										
Droplet reading scheduled										
Plate map accurate and uploaded										
Mastermix sheet accurate and uploaded										
Benches, centrifuge, pipettes wiped down										

How to Use This CheckList:
1. Enter Date and Time In upon arrival - initial as tech 1 or tech 2
2. Initial tasks as they are completed or some time before you leave
3. Enter time out and initial when you leave
4. Last one out is responsible for completing unchecked tasks

Poop processing check list

4/4/2025

Colorado State University Wastewater Testing Lab
Code of Conduct

Our students and staff work as a team, efficiently generating reliable data from wastewater to inform public health decisions for our community

Every week the Wastewater Testing Lab receives wastewater samples from manholes around the Colorado State University campus and from treatment plants up and down the Colorado Front Range. We are a dedicated team of students and staff trained to safely and efficiently process wastewater samples and provide reliable and accurate quantification of extracted nucleic acids. Our data is delivered to the Colorado Department of Public Health & Environment, and to Colorado State University Pandemic Preparedness team where it is used to monitor and respond to SARS-CoV-2 infection rates.

Our team is diverse, yet united in the mission of keeping our community healthy. Our success relies on a **welcoming, safe, respectful, equitable** and **professional environment**.

Lab Code of Conduct

Handling mistakes

- Everyone makes them
- If you don't know about them then you cannot fix them

"My post-docs don't make mistakes"

"You are not welcome here if you make the same mistake twice"

"The Lost Data"

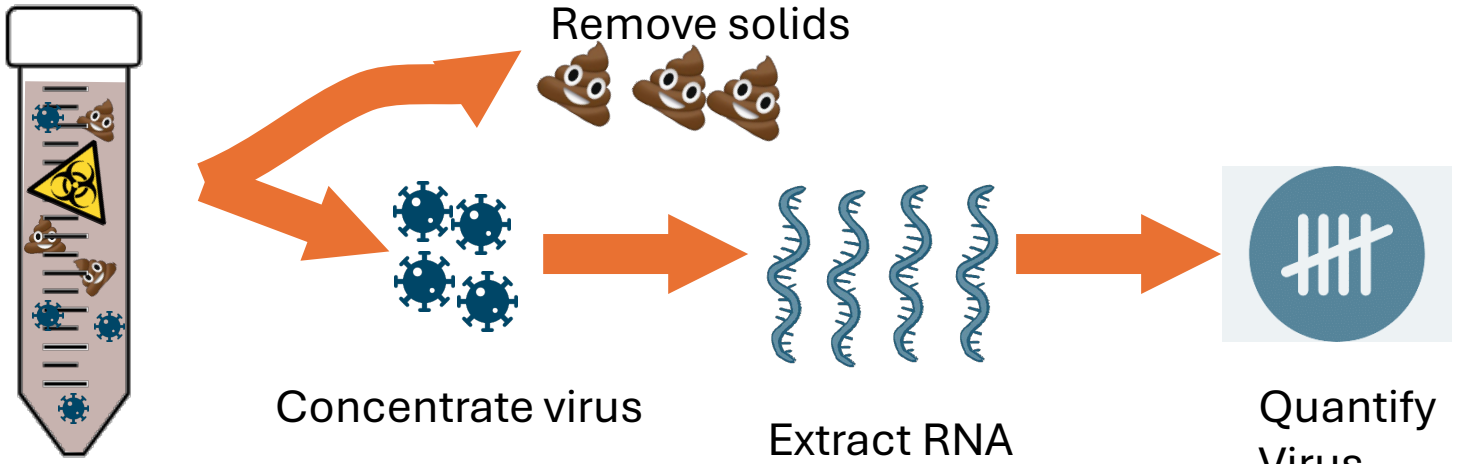
No room for error during COVID

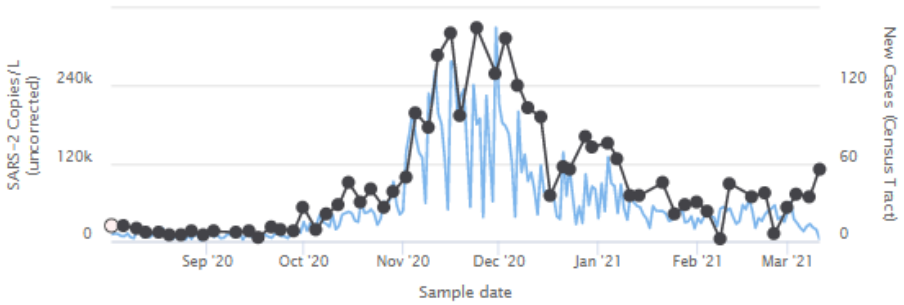
University Dorms

Wastewater Treatment Plants

Grad student and undergrad team working in 8 hr shifts during a pandemic

sample arrival → < 24 hours → publication





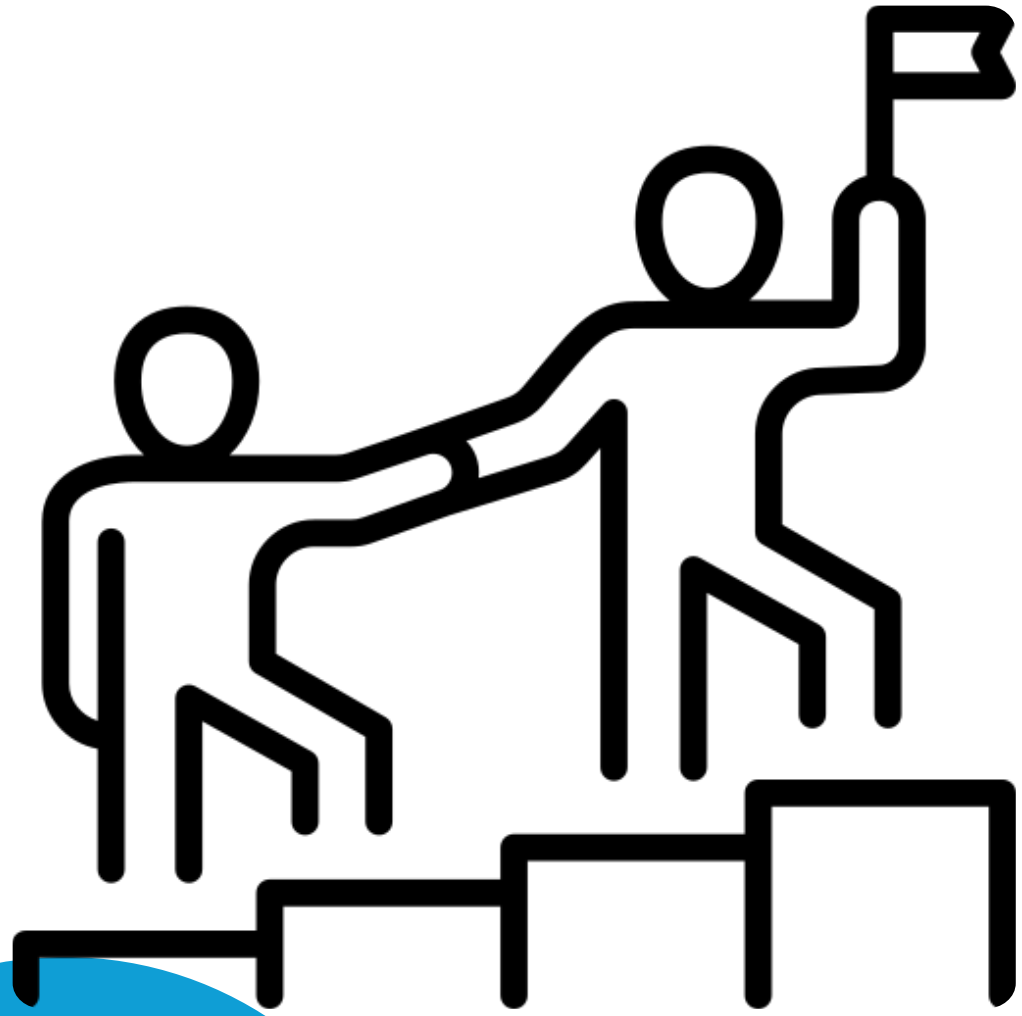
Report SARS CoV2 genome copies/L

Don’t point fingers - ask questions

- Try not to be too scary! Keep an open mind
- Share responsibility – “one fails, we all fail”
- Focus on finding solutions and preventing another error
- See mistakes as learning opportunities
- Consider creating an anonymous reporting system for near misses and risky situations
- Have an SOP for mistakes

Know what you don’t know

- Learn about p-hacking and HARKing (and ways to avoid them)
- Bring in a statistician or a data management expert (and budget for it!)
- Encourage your students to get additional training



Lead by Example

- [x] Learn about the issues contributing to the Reproducibility Crisis
- Take responsibility for training your students in this area
- Own your mistakes
- Be transparent when publishing
- Publish your negative results
- Adjust your expectations when reviewing papers and grants
  - Be more accepting of negative results and replication studies
  - Hold authors and journals to a high standard with respect to transparency and reporting

Take Home Messages

Lead by example

Make the right way easier than the wrong way

Create a blame-free environment

Make training in R & R **explicit**

Know what you don’t know – ask an expert

Thank you!

Happy to share resources and engage in further discussions!

August 2020-July 2023

9 students trained

CDC Antimicrobial Resistance Fellow

Alexa Doyle

Fertility Lab Tech Washington Univ.

Luke Hampton

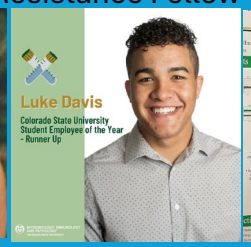
Associate Scientist Biogen

James Montavon

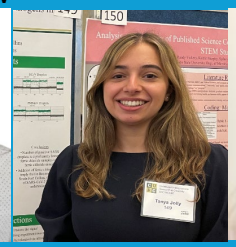
Communicable Disease Training Specialist at CDPHE

Parrish Van Ausdall

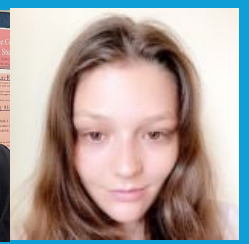
Halley Pucker



Luke Davis



Tanya Jolly



Nicole Albert

>200L WWTP wastewater

>5000 WWTP samples

Shared protocols and expertise with

8 Universities & Colleges

5 County & State Public Health Authorities

7 Companies

National Public Radio

Denver 9 News

~60% of Colorado Population tested twice a week