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Director, Environmental Health & Safety
16 September 2020

University of Colorado **Anschutz Medical Campus**

TRANSLATIONAL RESEARCH ETHICS

RESPONSIBLE CONDUCT OF RESEARCH
- Cells to Animals to Humans -

Housekeeping

Zoom Etiquette:

- Silence personal devices.
- Stay muted when not talking.
- Set up in a quiet location.
- Remain attentive. Avoid checking email/phone/web.
- Use the Chat function to ask questions or get technical help.
- Use your full name, not an alias.

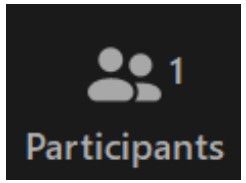
Receiving credit for attendance:

- To satisfy the NIH Requirement for Instruction in the Responsible Conduct of Research, the following are required in order to receive credit for attendance:
  - **Attend the full 90 minutes of the training.** Attending any 8 out of the 9 RCR seminars we offer will satisfy the NIH requirement.
  - **Keep your video camera on throughout the session**. NIH requirements for RCR training specify face-to-face discussion.
  - **Participate interactively throughout the session.** Participate in discussions, respond to polls, and sign the attendance sheet (link will be distributed in the Chat).

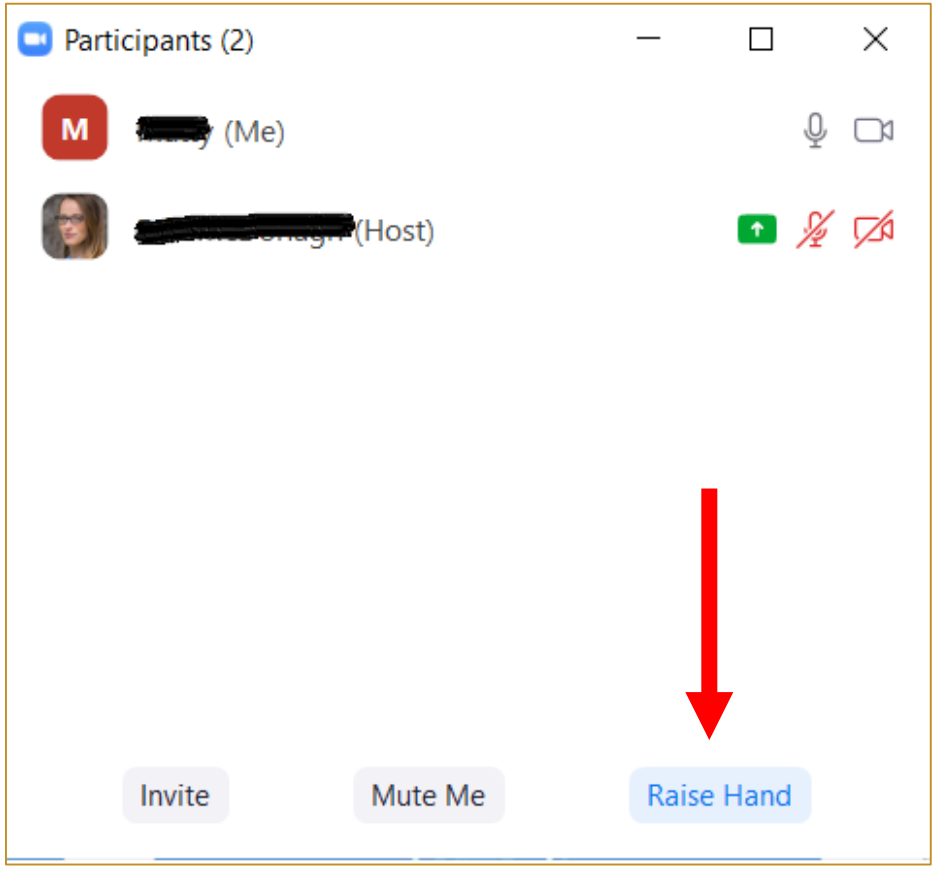
Raise your Hand to participate in discussions

In order to participate in discussions, raise your hand. **Try it now**!

- Click "**Participants**" at the bottom of your screen.



- Click "**Raise Hand**" in the popup window.
- Click "**Lower Hand**" to stop raising your hand.



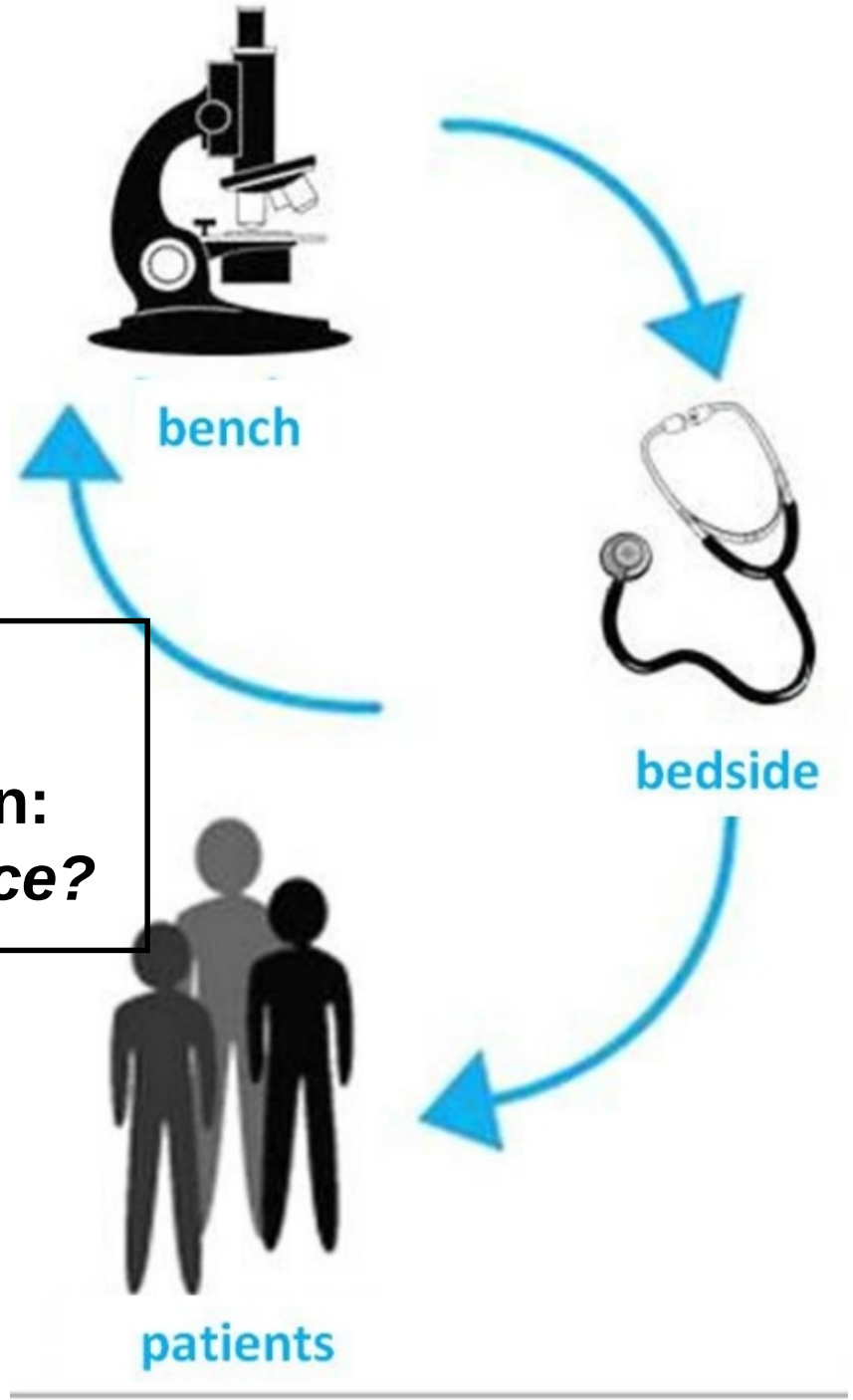
Objectives & Agenda

By default, nearly all research being conducted at the Anschutz Medical Campus is translational.

Agenda

- Definitions
- Framing the problem
- Case studies
- Decision Trees
- Institutional Resources

First Polling Question:
Who is in the audience?



Translational research poses ethical dilemmas

"I am the principal investigator for a clinical trial and would like to recruit subjects for this study from my practice. What precautions need to be taken to address potential conflicts of interest?"

"What are the potential ethical issues associated with putting a human neuronal stem cell into the brain of a developing mouse embryo?"

"I have completed a study looking at genetic variants associated with coronary artery disease. These variants are not routinely evaluated by cardiologists but may impact the health of volunteers in my study. Should I share these findings with my research subjects and, if so, what's the best way to contact them?"

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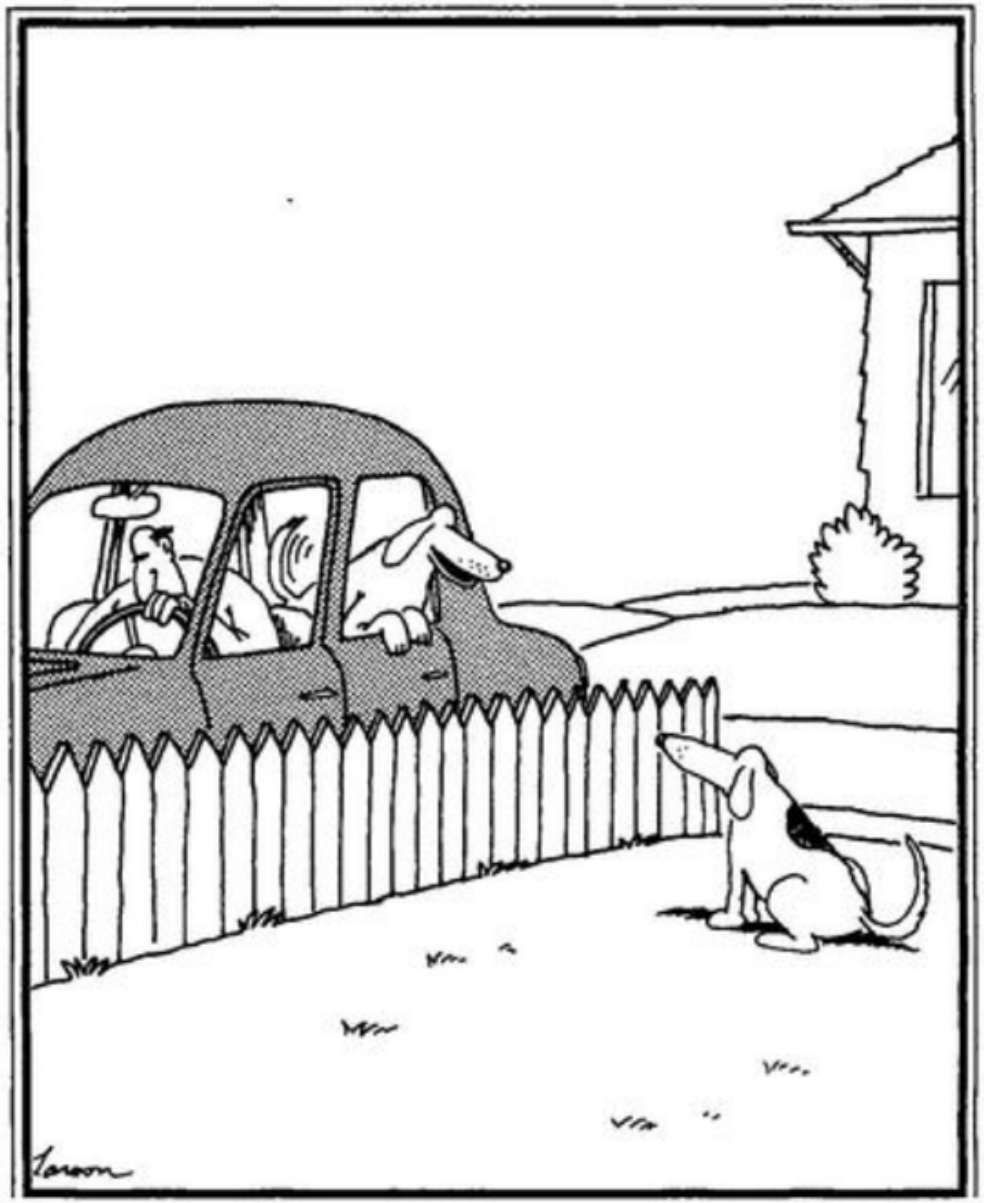
Know the ground rules,
Know what you are getting into

With respect to translational research…….

It is important to understand what you are getting into



What is Translational Research?

The purpose of translational research is to test, in humans, novel therapeutics strategies developed through basic research and experimentation

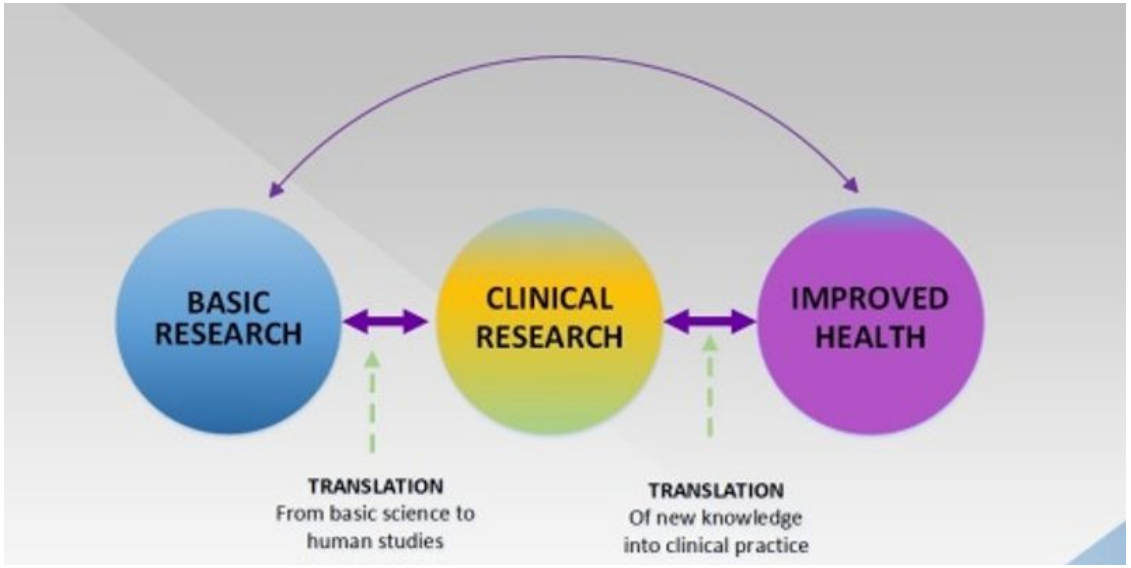
Translational Research

- This is the foundation of the NIH's Bench-to-Bedside Awards which encourage the collaboration between clinicians and basic scientists.
- NIH launched the Clinical and Translational Science Award (CTSA) Consortium in 2006.
- Our institution has been a CTSA awardee since 2008.
- Translational research can occur in these formal, structured environments or in informal collaborations

CTSA Objectives

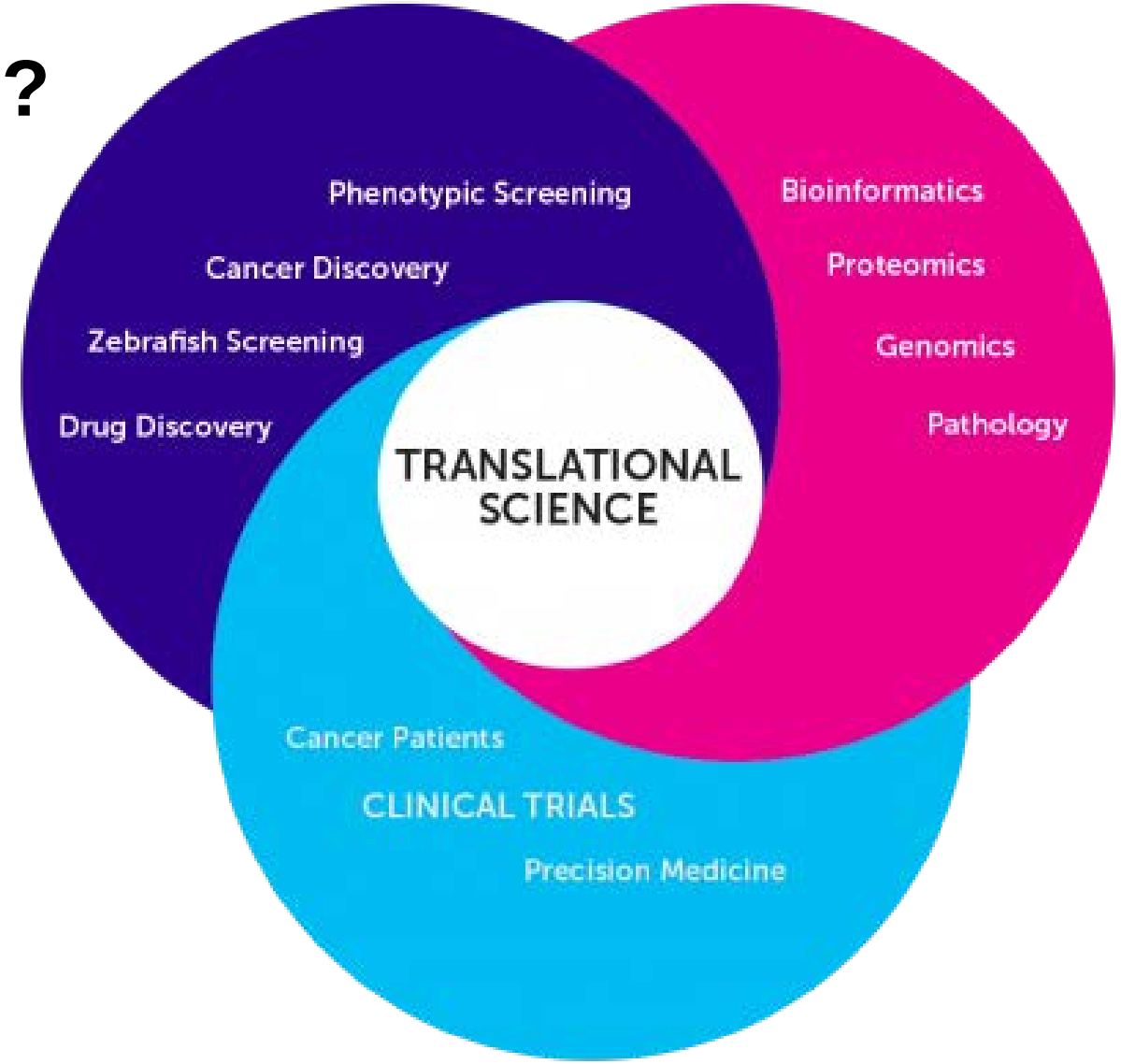
“Speed discoveries to improved patient care..”

- Develop a distinct discipline for clinical and translational science at institutions
- Provide opportunities and resources for original research on novel methods
- Develop translational technologies and a knowledge base for the full spectrum of clinical and translational science
- Synergize partnerships with industry, foundations, and community physicians
- Train the interdisciplinary teams who will conduct the clinical and translational research of the future

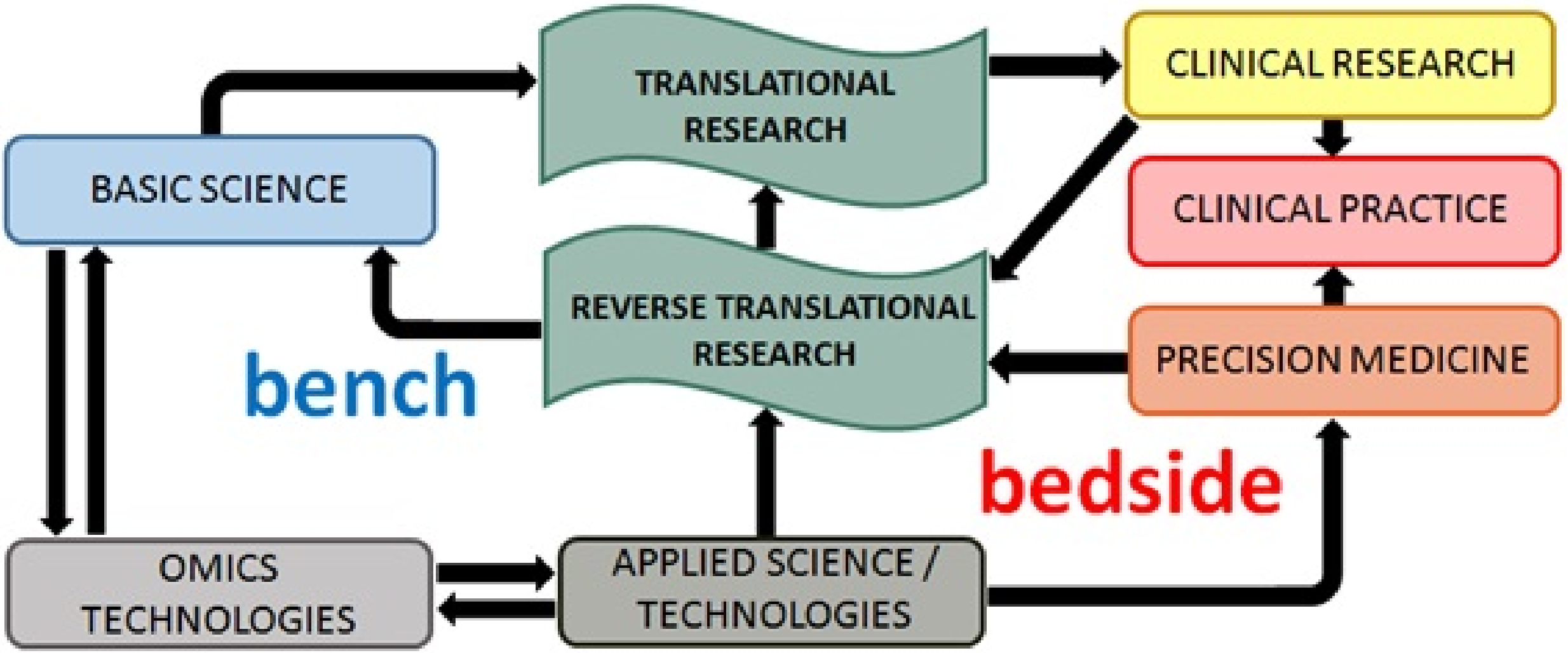


Why Conduct Translational Research?

1. **Complexity**. Basic mechanisms of disease must be studied in more simple forms – cells and animals.
2. **Expertise**. No one person or research group possesses all of the skills required.
3. **Safety**. Novel modalities must be tested safely before being used in humans.
4. **Efficiency**. Well-coordinated translational research can conserve resources and speed the delivery of treatments and cures to human disease.



A TRANSLATIONAL SCENARIO



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Why is translational research an RCR topic?

The foundation of translational research is to foster and promote multi-investigator and multi-institutional collaboration and sharing.

Multiple methods and technologies are used.

Numerous federal regulations, institutional policies and best practices govern cell, animal, and human research.

- Federal regulations – CFRs
- FDA regulations
- HHS privacy (HIPAA)
- Export controls & shipping
- Conflict of Interest (COI)
- NIH Grants Policy
- Inter-entity material transfer agreement
- Institutional oversight cmte's
- Industry agreements

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2nd Polling Question: ***Translational research concerns***

Translational Research & Compliance

Institutional Oversight of Translational Research

1. Colorado Multi-Institutional Review Board (COMIRB) – reviews all human subjects research
2. Radiological Safety Committees – review all research using radiological materials
3. Institutional Animal Care and Use Committee (IACUC) – reviews all research using animals
4. Institutional Biosafety Committee – reviews all research using rDNA, Select Agents, Dual-use Research and infectious material
5. Department of Environmental Health and Safety
6. Office of Regulatory Compliance – oversees DURC, EC, COI and HIPAA compliance; Clinical Research Support Center (CRSC)
7. Clinical Research Administration Office (CRAO)– oversees the protection of intellectual property and material transfer agreements (MTAs)
8. Colorado Clinical & Translational Sciences Institute (CCTSI) – has a Regulatory Knowledge & Support Core (RKSC)

Translational Research & Compliance

Review of several scenarios and hypothetical case studies that represent commonly occurring situations in translational research

Reminder: To participate in discussions, raise your hand.

- Click “Participants” at the bottom of your screen.
- Click “Raise Hand” (click “Lower Hand” when done).

Sign the Attendance Sheet now by clicking the link in the Chat.

Scenario #1

3rd Polling Question:
Diagnostic Testing

You are conducting SARS-CoV-2 / COVID-19 diagnostic testing on symptomatic people using the nasal pharyngeal swab (NPS) collection method. A colleague has been working on a C-19 detection method using saliva and asks you if you can have the patients spit into a collection cup during their testing so that she can determine if she can detect a viral load and compare it to your NPS sample results.

What, if anything, needs to be done for you add this collection method to your test?

Scenario #1 - Discussion

A revised informed consent may be required.

It is possible that this extra collection can be readily done under the auspices of Quality Improvement (QI)

It is likely that the saliva method is not FDA approved for the detection of SARS-CoV-2 and diagnosis of COVID-19, therefore the results from the saliva test can not be shared with the patient or published.

Scenario #2

4th Polling Question:
Patient sample sharing

A colleague at the Anschutz Medical Campus is in the middle of a clinical study collecting liver biopsy samples from subjects to study liver enzyme function in alcoholics (40 out of 60 subjects enrolled). Your lab is interested in exploring liver function during bipolar disorder. You would like to use both the stored 40 samples and upcoming 20 samples to be collected.

What, if anything, needs to be done for you to access these samples?

Scenario #2 - Discussion

If the samples are de-identified, with PI approval you can access the stored biopsy samples. The PI must ensure you do not have access to the key.

For the future samples, the informed consent must be modified and COMIRB notified that you will be looking at aspects beyond the initial scope of approval.

Question to ask: Can an identifiable group be stigmatized by new research?

Scenario #3

A colleague at University of Iowa developed a novel monoclonal antibody and has agreed to share this with you. You want to use this antibody to evaluate protein expression and localization in macrophages you have collected from bronchiol-alveolar lavage fluid from patients.

What, if anything, needs to be done for you to receive this probe and use it in your studies?

5th Polling Question:
Patient sample sharing

Scenario #3 - Discussion

Because the antibody is the intellectual property of the University of Iowa investigator, a Material Transfer Agreement (MTA) will need to be executed between the two institutions.

If the gene and protein of interest in the macrophages was previously covered in the informed consent with COMIRB, no additional action is needed. If not, COMIRB should be contacted.

In general, our institutional policy is that an MTA must be executed for the exchange of ALL scientific material with external entities.

Scenario #4

You have an approved IACUC protocol to investigate cardiovascular function in aging rats. Five drugs were approved for use in this protocol.

A clinical colleague, who has had very interesting observations in some of her patients using a different FDA-approved drug, approaches you about treating your rats with what she has used.

What, if anything, needs to be done for you to treat your rats with this drug and give your colleague the hearts and aortas from these rats?

Scenario #4 - Discussion

If the goals of the colleague's work are the same as your own, you must file an IACUC amendment requesting to add this additional drug to your protocol. No work can begin until this protocol is approved.

If the colleague's goals are distinctly different, she will have to submit her own protocol for review. No work can begin until this protocol is approved.

What if your colleague just needs the untreated tissue for controls?

Scenario #5

You have purchased a stock of kidney (MDCK) cells from American Type Cell Culture (ATCC). In addition to experiments on untransfected cells, you will also be transfecting these cells with various sodium channel constructs.

Your colleague across the bench would like a couple of plates of these cells to conduct their own, unrelated research.

What, if anything, needs to be done for you to give him several plates of cells?

Scenario #5 - Discussion

Per our Institutional Materials Transfer Agreement (MTA) with ATCC, material purchased from ATCC may only be used by the purchaser.

Exception: Transfer of material is authorized if the collaborator is doing work directly tied to the original purchaser's project.

Scenario #6

You are interested in studying the pathogenicity of the influenza and SARS-CoV-2 viruses, to include exploring the mechanisms that could enhance human to human transmission.

Published work from University of Florida and Beijing University indicate possible collaborators on this project. You have secured space in our BSL-3 lab for this work.

What, if anything, should be your considerations for this work?

Scenario #6 - Discussion

Research involving the manipulation or enhancement of the pathogenicity of infectious agents may fall under federal “Dual Use Research of Concern” (DURC). DURC regulations include a variety of other areas, as well.

In addition to DURC, shipping material such as high path influenza also falls under new federal regulations pertaining to “Export Controls”.

Finally, if biological materials will be shipped between collaborating institutions FAA/IATA shipping training must be taken by the shipper.

RCR Decision Trees

Several decision trees will be placed on the RCR website

1. Overall Translational Research
2. Cellular Research
3. Animal Research
4. Human Subjects Research
5. Bio-Banking

https://research.cuanschutz.edu/EHS

Summary

- Translational research can be a formal or informal process.
- Translational research is complicated with a multitude of compliance decision points.
- Numerous institutional resources exist to facilitate the research and collaboration.

Institutional Resources

Office of the Vice Chancellor for Research

Office of Regulatory Compliance
AVC Alison Lakin, PhD

Environmental Health & Safety
Ethan Carter, PhD, Director

Office of Research Committee Support (ORCS)
IACUC, IBC, Radiation Safety
Mark Douse, PhD, Director

Office of Laboratory Animal Resources (OLAR)
AVC Jori Leszczynski, DVM, Institutional veterinarian

Colorado Multi-Institution Review Board (COMIRB)
John Heldens, Director

Dual Use Research of Concern and Export Controls
Christine Ahearn, JD

Office of Grants & Contracts
AVC Amy Gannon

Other Departments/Resources

1. **Clinical Research Administration Office**
   crao_contracts@ucdenver.edu
   303-724-1111

2. **CCTSI**
   https://cctsi.cuanschutz.edu/

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