Study Design for Translational Research Projects

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Center for Clinical Investigation

### Biomedical Research

<table>
<thead>
<tr>
<th>Population-Oriented</th>
<th>Patient-Oriented</th>
<th>Bench-Oriented</th>
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### Biomedical Research Training Activities

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<th>Training Program</th>
<th>Databases</th>
<th>Individuals</th>
<th>Animals, Cells</th>
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<td>Computer Facility</td>
<td>Clinical Trials</td>
<td>Clinical Research Center</td>
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<td>M.P.H.</td>
<td>M.M.Sc: e.g., Scholars in Clinical Science</td>
<td>Ph.D., MSTP</td>
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Scientific Method: Similarities of Approaches

- Formulate a question
- Research the literature
  - Has your question already been answered?
  - Who has addressed questions in this general area?
  - What techniques did they use?
  - What problems did they encounter?
  - What controls are needed?
- Perform preliminary studies to sharpen your question
- Develop a specific, highly focused hypothesis

Where Does the Translational Investigator Obtain Information to Formulate the Question?

- Observational studies
- Animal studies
- Cell based studies
- Previous patient-oriented studies

What Type of Questions Do Translational Investigators Ask?

- Highly focused on mechanisms
  - Human physiology
  - Human pathophysiology
  - Similar to animal studies
- Often assessing environmental interactions
- Often uses genotype to sub-group their study population
Elements of a Translational Research Project

- Nearly always prospective
- Often hypothesis testing not hypothesis generating
- Requires knowledge of the effect of confounders on outcome measures
  - Usual: age, race, BMI, gender
  - Often many others: diet, time of day studied, position, light/dark cycle

Control of Confounders to Minimize Bias in Study Design

- Population research uses statistical approaches to account for confounders
- Pre-clinical research can specifically control confounders by eliminating them in the use of materials—cells, enzymes, genetically engineered animals and cells, caged animals.
- Translational research applies pre-clinical approaches—a human laboratory to control environmental factors—The Clinical Center

Components of Translational Research Study Design

- Established a clearly defined, focused hypothesis
- Identify and control critical confounders
- Address ethical issues
- Partner with a statistician EARLY to establish a statistical plan (including what are primary, secondary and exploratory endpoints) and perform a power assessment.
- Establish early relationships with other technical professionals, e.g. imaging specialist, geneticist, dietary
Components of Translational Research Study Design (con’t)

• Refine hypothesis and prepare a specific protocol
• If the protocol has an intervention component, then use the same approach as in a clinical trial
• *Prepare a consent form
• *Obtain approval from the IRB
• *Identify controlled environment in which study will be conducted---clinical research center.

Implementation of a Translational Research Study

• * Recruit subjects
• * Obtain informed consent
• Conduct study
• Analyze data
• Draw conclusions specifically related to your hypothesis
• Develop new hypothesis based on generated exploratory data and/or failure to prove your primary hypothesis.

Elements Necessary to Conduct a Successful Translational Research Study

• Clear, specific, focused hypothesis
• Identification and control of confounders
• Statistical collaborator
• Technical collaborator(s)
• Human research “laboratory”
• Well designed protocol
• Subjects (patients) as collaborators