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Introduction to Biomedical Research

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What is Scientific Research?

Scientific research is limited to studying only the problems of the natural world that can be understood by using the processes of science.

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Scientific Research

- Scientists deal with natural phenomena (events) which can be;
  - observed
  - measured
  - tested

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So What is a Scientist?

A scientist uses his/her senses to observe (directly and/or indirectly) and evaluate data

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If a scientist is an observer we must assume….

- Natural world is
  - Orderly
  - Reasonable
  - Testable

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The characterisitics of science

- Consistent
- Observable
- Natural
- Predicatble
- Testable
- Tentative

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Consistency

The results of repeated observations and/or experiments concerning a naturally occurring event are reasonably the same when performed and repeated by competent investigators.

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Observability

The event under study can be observed and explained. The observations are limited to the basic human senses or to extensions of the senses by instrumentation.

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Natural

A natural mechanism must be used to explain why or how the naturally occurring event happens.

- No Supernatural explainations

- Scientists cannot conduct controlled experiments in which they have designed the intervention of a supreme being into the test.

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Predictability

The mechanism of the naturally occurring event can be used to make specific predictions. Each prediction can be tested to determine if the prediction is true of false.

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Testability

The mechanism of the naturally occurring event must be testable through the processes of science, controlled experimentation being essential.

Reference to supernatural events or causes are not relevant tests.

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Tentativeness

- Scientific theories are subject to revision and correction, even to the point of the theory being proven wrong. Scientific theories have been modified and will continue to be modified to consistently explain observations of naturally occurring events.

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So a scientist can…..

Observe, predict and test a reasonably consistent natural phenomenom that may or may not be right

- Without the intervention of a supreme being!!

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What is not Science?

If CONPTT defines what science is we can assemble a hit-list of non-science

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Non-Science

An area of knowledge which does not meet the criteria of science (CONPTT).

Non-science topic areas may be very logical and based on good reasoning, but simply do not fall within the realm of science.

religious beliefs
philosophy
personal opinions
attitudes

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False Science

Non-science which is portrayed and advertised as a legitimate science by its followers and supporters

e.g

- astrology
- creation science

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The Scientific Method

How do we "Do" Science & Scientific Research?

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The Scientific Method

- Pick a problem
- Understand the problem
- Hypothesise
- Design an experiment
- Test your hypothesis
- Analyse your data
- Draw conclusions

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Choosing a Problem

- What are you interested in?
  - In line with your career
  - Is there expertise existing
- Ask a question?
  - Why does this problem occur
  - Note; The question must be testable
    - No supreme beings, ghosts , aliens etc.
- Do you have the skills / resources needed to answer the question
  - Laboratory
  - Technical skills
  - Computational skills etc

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Steps of the Scientific Method

1. Choose a problem.

State the problem as a question.

2. Research your problem.

Read, get advice, and make observations.

3. Develop a hypothesis.

Make a prediction about what will happen.

4. Design an experiment.

Plan how you will test your hypothesis.

5. Test your hypothesis.

Conduct the experiment and record the data.

6. Organize your data.

Create a chart or graph of your data.

7. Draw conclusions.

Analyze your data and summarize your findings.

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Choosing a Problem

- Research theme should ideally be
  - Relevant to you
    - » Clinicians should study disease, not why a duck can't hear it's own quack!
  - For the greater good
    - » The output of your work should be useful to mankind
    - » Researching biological weapons is science, but is hardly in the common good
  - Not be driven by financial pressures
    - » Research agenda should be independent from financial interest
  - Ethical
    - » Should not impinge on the dignity and rights of others

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Research the Problem

Whats known already?

- State of the art

Is it feasible to research?

- Expertise
- laboratory space
- laboratory equipment

Do You have skills?

- Is the research feasible

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Research The Problem

- Obtaining information
  - Supervisor
  - Local Expertise
  - PubMed
  - The Library
  - Google!
  - Other people in this room

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Develop a hypothesis

- Prediciting what will happen in your system
- Goal of the expt. Is to test your prediction
- E.g
  - If we silence gene x the cells will stop proliferating

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Hypotheses & Research

- Hypothesis testing experiments
- Hypothesis generating experiments

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How to develop a hypothesis

Two Approaches

Analytical Approach

Collect all the available data and try to make a sensible prediction of what will happen in your experiments

Argumentative approach

Persuasive

Data are gathered to suport the initial hypothesis.

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Analytical Approach

- Hypothesis is always a question
- Inductive Reasoning
  - Specific Point ➔ General Point
  - This type of approach is characterised by
    - Inquisitive nature
      - Always start with a question but…
        - » May not find an answer

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Argumentative Approach

- Hypothesis is always a statement
- Deductive Reasoning
  - General Case ➔ Specific evidence

Data is collected to support the initial hypothesis

Always a statement

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Design The Experiment

- How will you test the hypothesis that you have generated?
- What experiments do you need to do to test the hypothesis?
- Will the experiments that you have designed give you the data needed?

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Experimental Design

- Consider
  - Are the experiments feasible
  - Do you have the skills
  - Is the laboratory infrastructure available
  - Do you have the funding
  - Will the experiments produce significant data
  - Can you analyse the data

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Experimental Design

- Dependent on the question you are asking
- E.g Microarray Expt
  - Biological Question
    - Cellular response to exogenous agent
  - Experimental Approach
    - Time course of expression in response to agent
  - Results
    - Discern temoral responses of the cell to the agent

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Experimental Design

- Dependent on the question you are asking
- E.g Microarray Expt
  - Biological Question
    - Effect of mutant gene
  - Experimental Approach
    - Pair-wise comparisons of wild type and mutant cells
  - Results
    - Discern genes whose expression depends on function of altered gene

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Test the Hypothesis

- Perform the designed experiment to test your hypothesis
- Data generation phase
- Key issues
  - Controls
    - Positive and negative
  - Error
    - Reduce to minimum (but will always be there)
  - Significance

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Sources of Error

- E.g Microarray Expt.
  - RNA preparation
  - Non-linear amplification
  - Human error (pipetting, measurement)
  - Non-linearity of array response vs. concentration
  - Non-uniform hybridisation kinetics
  - Improper probe sequences
  - Cross-hybridisation
  - It’s a noisy world out there!!!

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Data Analysis

- What analysis must you do to answer the question?
- Do you know how to do the analysis?
- Significance / statistics!!!

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Analysis employed is dependent on initial information
e.g Microarray Expt

No Idea:

Utilise subjective Methodologies

Data clustering

- hierarchical
- Non-hierarchical

Pattern Matching

- fluctuations in data
- Principal components

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Analysis employed is dependent on initial information
e.g Microarray Expt

Some Idea:
Utilise Objective Methodologies

Data clustering
- Include functional annotations
- Weight genes dependent on function
- Overlay data with pathway information
- Incorporate clinical data

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Draw conclusions

- Summarise Your findings
- What does the data mean
- Have you supported / refuted original hypothesis

- Write the paper

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Practicalities of the Scientific Method