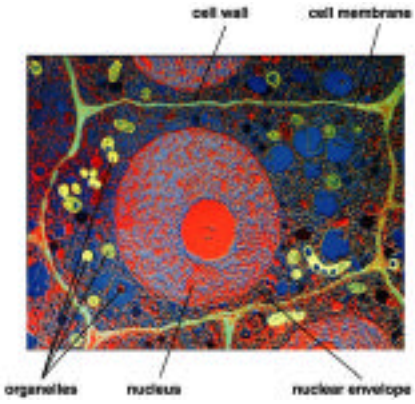
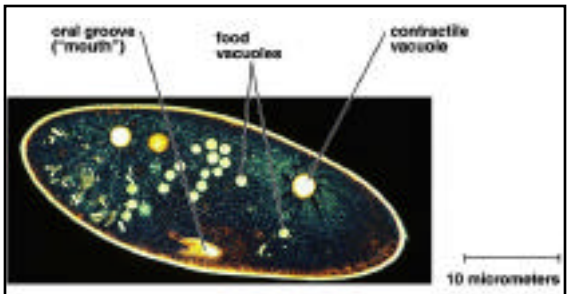
Chapter 1

The Unity and Diversity of Life

Characteristics of Life

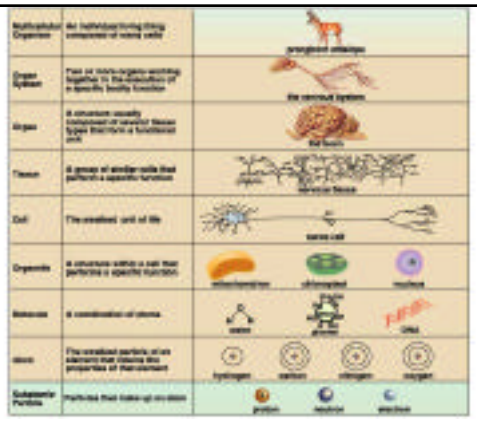
- Complex organized structure
  - Atom, molecules, organelles, cells, tissues, etc.
- Sensitivity
  - Respond to stimuli
- Homeostasis
  - Constant internal environment
- Respire - acquire and use material and energy
- Growth, development and reproduction
  - Crystals? viruses?
- Blueprint called DNA
- Evolve or change

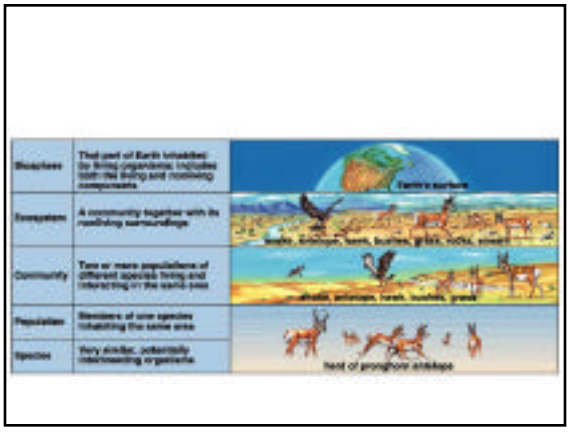




The kingdom Protista (domain Eukarya). This light micrograph of a Paramecium illustrates the complexity of these large, normally single, eukaryotic cells. Some protists photosynthesize, but others ingest or absorb their food. Many, including Paramecium, are mobile, moving with cilia or flagella.

DNA

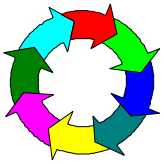




Complex organizaton of life

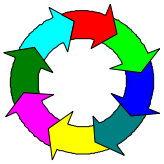
The Scientific Method

- Observation
- Formulate a hypothesis
- Experimentation
- Drawing conclusions



The Scientific Method

- Observation
- Establishing a model
- Formulate a hypothesis
- Experimentation
- Collecting and evaluating results
- Drawing conclusions
- Reporting what has been found



Observations

- Looking
- Hearing
- Smelling
- Touching
- Measuring
- Reading about previous studies
- Serendipity

Models

- A simplified view of how the components of a system operate.
  - Must be consistent with previous scientific knowledge.
  - Must offer new insight.
- May compare a process that is not understood to one that is understood

Hypothesis

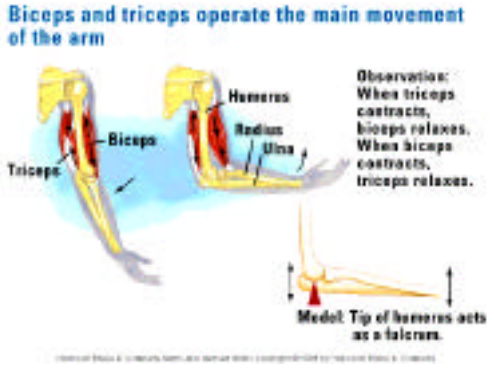
- Is NOT an educated guess.
- Someone can devise an experiment to disprove the hypothesis if it were incorrect.
  - Can you truly prove an hypothesis correct??
- A hypothesis is valuable only if it is testable.

Two forms of hypothesis

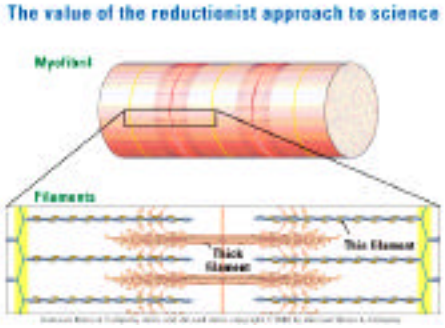
- Null hypothesis (H_o)
  - States that what is observed or measured is not unusual from what is usually observed, or from what is seen in the control experiment.
- Alternative hypothesis (H_a)
  - States that what is observed or measured is unusual from what is usually observed.

Experiments

- Procedures carried out under conditions controlled by the scientist.
- Experiments include controls and treatment variables designed and implemented to prove the hypothesis false if possible
  - Controls?
  - Treatment variables



Reductionism: understanding the whole in terms of parts



Collecting and Evaluating Results

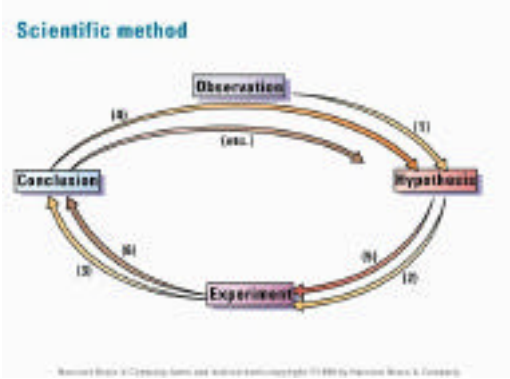
- Collect experimental data.
- Computer and statistical analysis.

Conclusions

- Evaluate the results.
  - Statistics -- collecting and analyzing numerical data
- Refine hypothesis or test alternative hypothesis.

Reporting

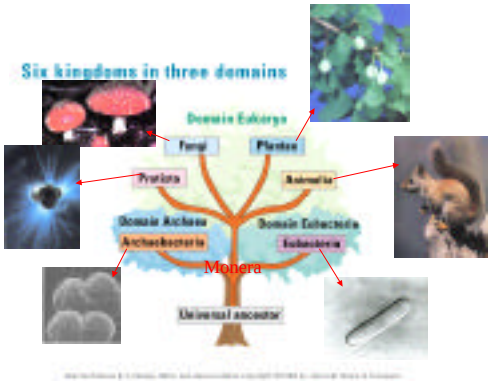
- Inform other scientists.
- Permits scrutiny of scientific community.
- Informs the public.



Theory

- A set of related hypotheses that consistently resists scientists efforts to disprove them.

How do organisms differ from each other?



Observations

- IFNγ favors Th-1 responses
- IFNγ activates NO producing cells -- peripheral macrophages, microglia, and astrocytes
- IFNγ activates oxygen metabolite producing cells -- neutrophils, monocytes
- Therapy for certain intracellular infections
- Enhances in vitro effector-cell antifungal activity against *Coccidioides immitis*

Model

Hypotheses?

Objective

- Determine the therapeutic efficacy of IFNγ alone and in combination with fluconazole for the treatment of experimental coccidioidal meningitis.

Methods

- NZW Rabbits, 3-4 kg, male
- Hydrocortisone acetate, I.M. Days -1, 0, 1, 2, 3
- *Coccidioides immitis* challenge, 4.4 x 10^4 & 6.0 x 10^4 arthroconidia, intracisternally, day 0
- Treatment - 21 days starting on day 5
  - PEG-200 orally Q.D. & Saline SQ Q.O.D. (control)
  - PEG-200 orally Q.D. & IFNγ (1 x 10^6 U/kg) SQ Q.O.D.
  - FCZ (40 mg/kg/day) orally Q.D. & Saline SQ Q.O.D.
  - FCZ (40 mg/kg/day) orally Q.D. & IFNγ (1 x 10^6 U/kg) SQ Q.O.D.
  - Uninfected animals - PEG-200 orally Q.D. & IFNγ (1 x 10^6 U/kg) SQ Q.O.D.

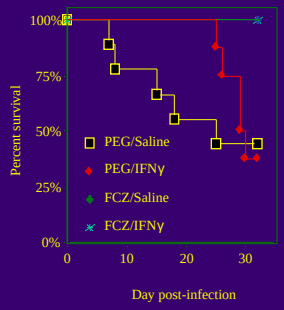
Methods

- Daily clinical evaluation
- CSF and serum sampled every 7 to 12 days
- Buprenorphine was given as needed to alleviate pain and discomfort
- Moribund animals were euthanized
- Euthanize surviving animals 7 or 8 days after last treatment

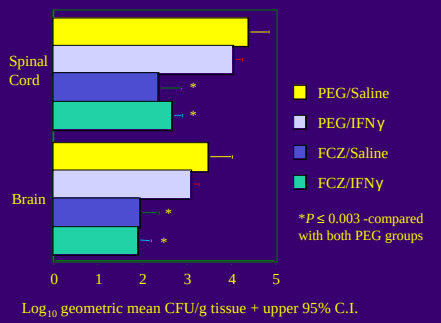
Time to Euthanasia

Treatment	n	Mean time to euthanasia (days)
PEG/Saline	9	22.3
PEG/IFNγ	8	29.4
FCZ/Saline	8	32.0*
FCZ/IFNγ	8	32.0*

*$P \leq 0.02$



Recovery of *C. immitis* from Spinal Cord and Brain



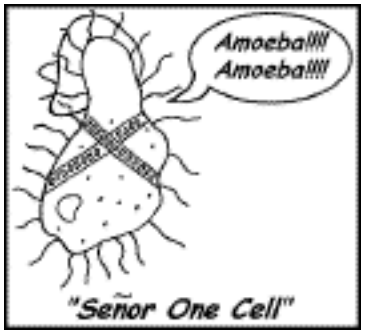
*$P \leq 0.003$ -compared with both PEG groups

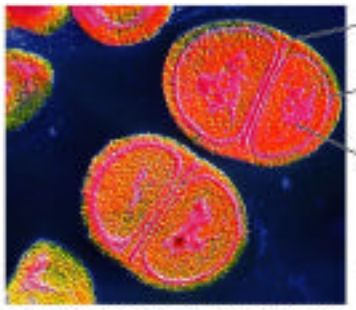
Log_{10} geometric mean CFU/g tissue + upper 95% C.I.

Conclusions

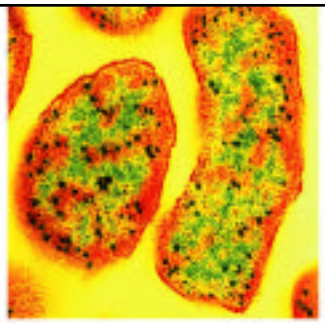
- IFNγ appeared to have a modest effect on survival and tissue CFU reduction, however, it was not significant.
- Fluconazole was effective at controlling coccidioidal meningitis and reducing *C. immitis* in the CSF and tissues.
- At the dosages tested, it is not clear if IFNγ-FCZ combination therapy has an advantage over fluconazole alone.

End





The domain Bacteria. A color-enhanced electron micrograph of a dividing bacterium. Bacteria are unicellular and prokaryotic; most are surrounded by a thick cell wall. Some bacteria photosynthesize, but most absorb food from their surroundings.



The domain Archaea. A color-enhanced electron micrograph of an archaean. The cell wall appears red, and DNA is scattered inside. Many archaeans can survive extreme conditions. This Antarctic species lives at temperatures as low as –2.5°C.