

Genetic Engineering of Animals

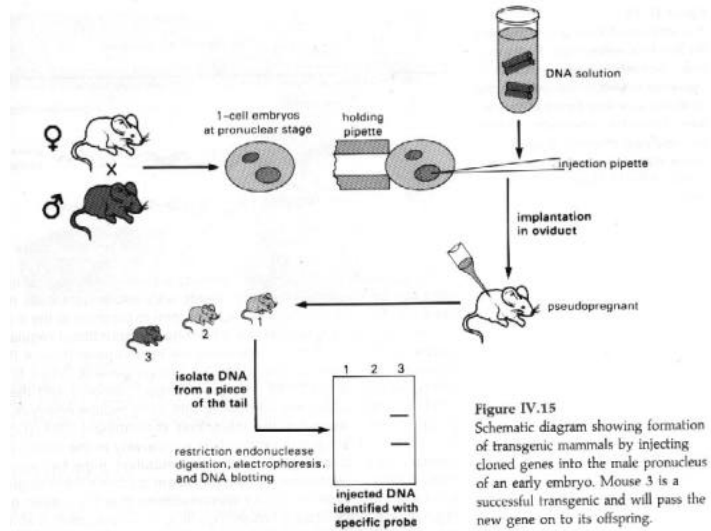
Chem 210

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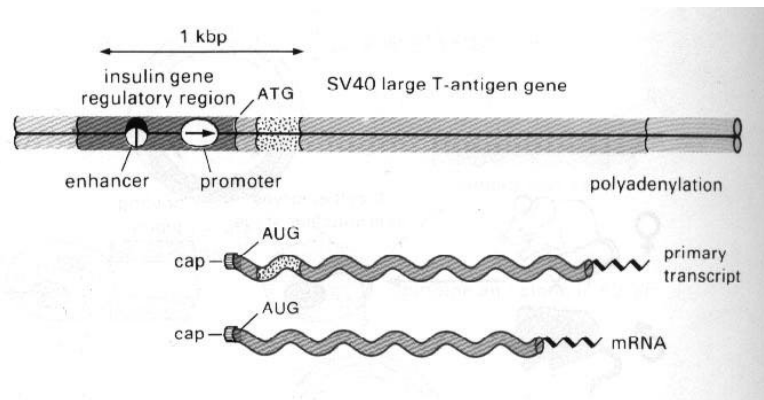
The mouse has been a model system for genetic modification of mammals

- The genetics of mice have been well studied.
- Many specific lines of mice already bred for specific characteristics--historically used as model systems for human diseases
- Small, short gestation period.
- Main research goal: can expression of human genes in mice be used to test the function of human genes? Create models for testing the effect of pharmaceutical therapies?

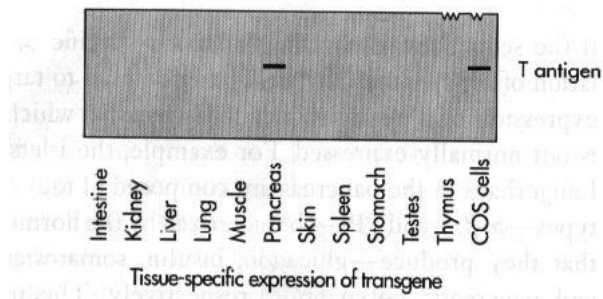
Foreign DNA can be microinjected in freshly fertilized mouse eggs



Genes fused to mouse regulation elements are expressed in specific tissues



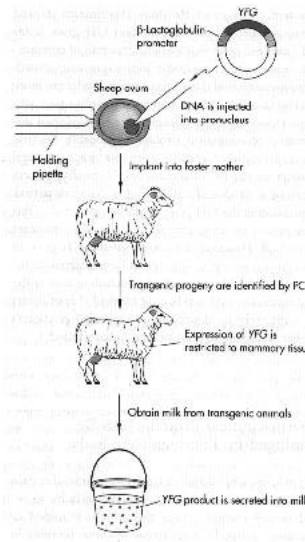
This gene is expressed specifically in the pancreas of the transgenic mouse



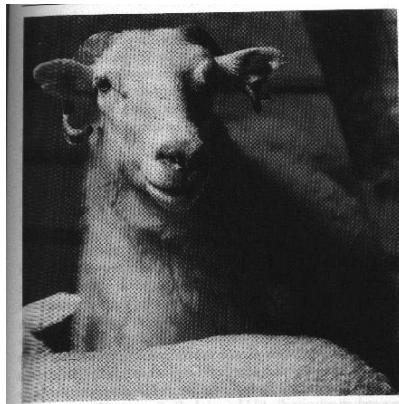
Recombinant proteins can be produced in mammary tissues and secreted in milk

- Use the transgenic animal as a factory for production of the protein.
- An alternative to production of human proteins in bacteria.
 - Prokaryotic cells can do all of the necessary post-transcriptional and post-translational modification of proteins from eukaryotes.
 - For example: many proteins in eukaryotes have carbohydrates (sugars) attached to them--these cannot be added in bacterial expression systems.
- This is increasingly being pursued as a strategy for producing pharmaceutical products.

Foreign genes are fused to lactoglobulin regulatory genes



A drug, α -antitrypsin, is expressed in milk of sheep



- AAT inhibits trypsin, a protease (enzyme which breaks down other proteins).
- Used as a treatment in emphysema.
- Previously obtainable only from human blood (very expensive).
- Can be produced in sheep's milk ~35 g/L.