

## Lecture 10: Animal biotechnology application

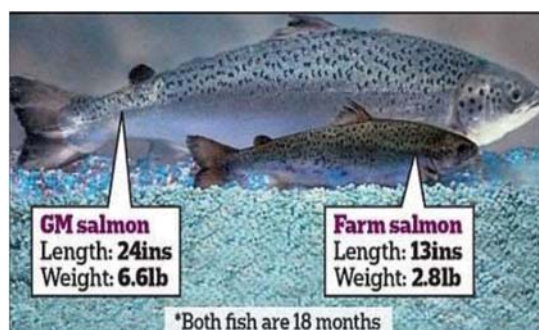
### Glo fish :

GloFish is a type of transgenic zebrafish (*Danio rerio*) that have been obtained via insertion of a green fluorescent protein (GFP) gene.



### Super fish

Growth hormone gene inserted into fertilized egg. The transgenic salmon were larger and grew faster than the nontransgenic controls.

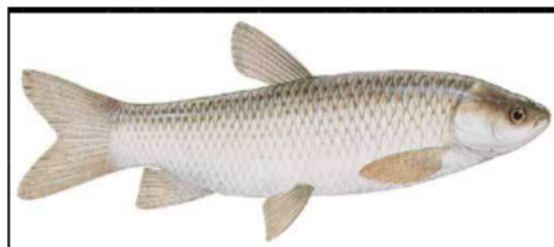


### Transgenic rainbow trout (*Oncorhynchus mykiss*)

to study muscle development.  
source of Protamine



### Transgenic Grass carp (*Ctenopharyngodon idella*) – production of human lactoferrin



(GloFish, medaka, transgenic angel fish, lionhead fish etc)



### **Alzheimer's mouse**

In the brain of Alzheimer's patients, dead nerve cells are entangled in a protein called amyloid. Mouse made by introducing amyloid precursor gene into fertilized egg of mice.



### **ANDI Monkey**

“ANDI” was the first transgenic monkey, born in 2000. ANDI proves that transgenic primates can be created and can express a foreign gene delivered into their genome.



### **Transgenic rabbits**

1st transgenic rabbit – 1985 by Pronuclear microinjection to use it for CVD, AIDS & cancer research, RPs – produced large scale, - cost lower  
Eg. Human  $\alpha$  glucosidase, human erythropoietin, human AAT etc



## **Transgenic cow**

1990: World's 1st transgenic cow – “Herman” the bull (Netherlands)

Herman carried the human lactoferrin gene (pronuclear microinjection)

Cow's milk & artificial formula do not naturally contain lactoferrin, Other RPs in transgenic cow's milk – lysozyme, human lactalbumin, rA TIII, Factors VIII & IX etc

Scientists in both China and Argentina have genetically engineered cows to produce milk similar in composition to that made by humans.

After modifying embryos, an Argentinian cow – Rosita Isa – was born that expressed milk containing proteins present in human milk but lacking in cow milk.

However, there are a number of scientific, safety and taste issues that would have to be overcome before this replaces “mother's milk” for infants.

1. A **genetically-altered growth hormone** that could be then injected into dairy cows to produce more milk.

The consumption of **milk** from cows injected **rbGH** leads to an increase in **IGF-I** in humans cause increased rates in colon, breast, and prostate cancer.

2. GM products have been developed with resistance to **herbicides** are commonly carcinogens.



### **GM Goats**

- BioSteel is a trademark name for a high-strength based fiber material made of the recombinant spider silk-like protein extracted from the milk of transgenic goats, made by Nexia Biotechnologies.
- The company has successfully generated distinct lines of goats that produce in their milk recombinant versions of either the MaSpI or MaSpII dragline silk proteins, respectively.
- Nexia Biotechnologies, however, went bankrupt and is no longer company.

### **GM chickens**

The Roslin Institute is working on GM chickens that contain an extra gene that interrupts the transmission of avian flu. Unlike a vaccination, the modification still protects the bird if the virus mutates. However, some farmers argue it is better to enforce good farming practices than create disease-free animals.



### **GM sheep**

Genome editing technology is being used at The Roslin Institute to increase the productivity of sheep bred for the meat industry.

Naturally-occurring mutations that stop a gene called myostatin from functioning have shown that animals with these mutations have up to 20% more muscle mass compared to animals without the mutations.

Animals with myostatin mutations convert feed to muscle more efficiently, reducing the amount of resources needed to produce meat.

The meat from these animals is also of a higher quality and is healthier, containing less fat.

- The sad part of Dolly the Sheep was she died on February 14th, 2003, nearly six years after her birth progressive lung disease was caused because her cells were already old she also had premature arthritis.



### **Larger Mice**

- 1982: somatotropin gene of rats was cloned and inserted into fertilized mouse eggs, Genetically engineered mice were larger
- Recombinant human somatotropin (rHST) Used to treat hormone deficient type of dwarf
- Genetically engineered mice: Marathon Mouse, Mighty Mouse, Fierce Mouse, Smart Mouse, K14-Noggin

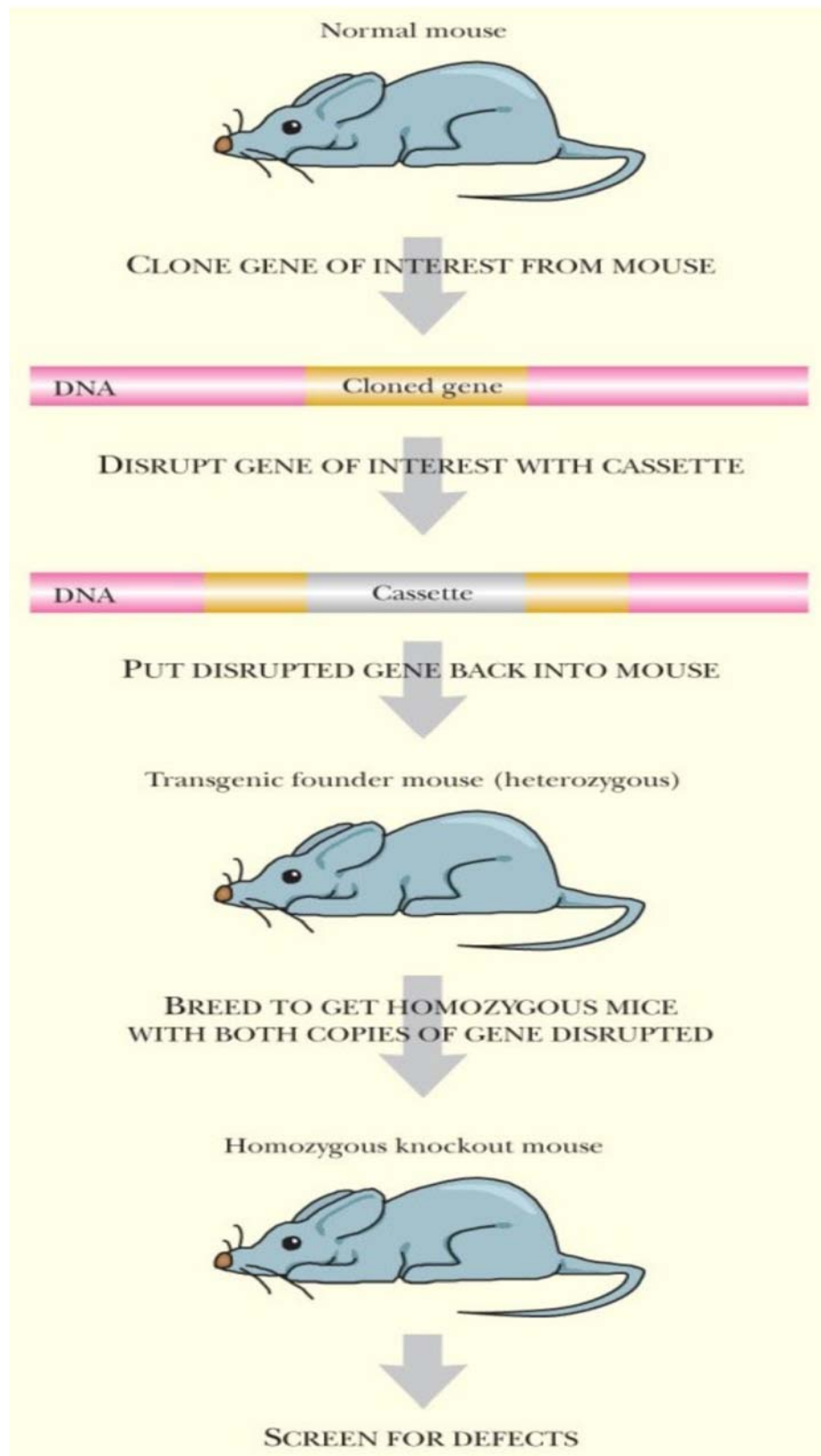
### **Knockout Mice**

Widely used in medical research to investigate gene function, They have selected inactivated genes, Used for genetic analysis of inherited diseases and cancer

Knock out gene of interest to study the defects it causes, Target gene is cloned  
Gene is disrupted by inserting a DNA cassette into its coding sequence, Inserted DNA segment prevents correct protein synthesis, Inactive gene copy is reinserted into animal, Founder mice are breed together with both copies to produce knockout mice

### **Human ear on a mouse**





### Alzheimer's mouse

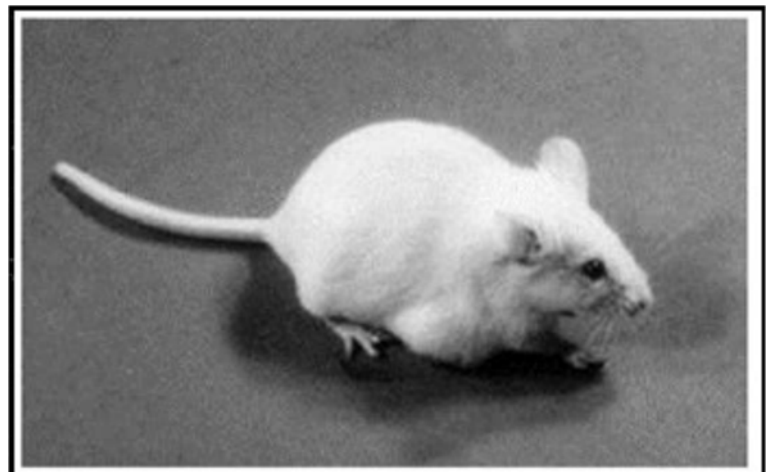
AD is a neurodegenerative brain disorder, Amyloid plaques – amyloid  $\beta$  peptide ( $A\beta$ ), fragment of  $\beta$ -amyloid precursor protein (APP)

- World's 1st Alzheimer's mouse incorporated an APP mutation (PDGF- $\beta$  promoter) - neurotoxic  $A\beta$  appeared in the same parts of Alzheimer's mouse brain as it did in human brains.



### Oncomouse

1<sup>st</sup> patented transgenic animal created by Philip Leder and Timothy Stewart (Harvard University in 1984). To study cancer formation and to screen anti-tumor drugs, 13 different strains were engineered to contain a human oncogene that causes tumor formation.





## Transgenic models for Diabetes

For studying the genes, & their role in peripheral insulin action. Models of insulin secretion – Glucokinase, hepatic glucose production in T2 diabetes

Others –  $\beta$  receptor knockout mouse, Uncoupling protein (UCP1) knockout mouse, Acute & chronic models for antidiabetic agents.



## Smart mouse

- Superior learning and memory.

## Youth mouse

- eat ~20% less and live ~20% longer than the wild type
- Exhibit a young look even at old ages.
- Useful biological model – study of developmental processes & aging (especially in relation to diet).

