

A

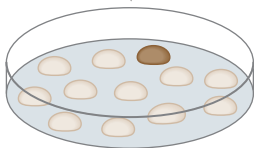
ES cells growing
in tissue culture



Altered version of
target gene
constructed by
genetic engineering

Introduce a DNA
fragment containing
altered gene into
many cells

Let each cell grow to
form a colony



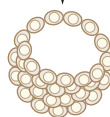
Test for the rare
colony in which the
DNA fragment has
replaced one copy of
the normal gene



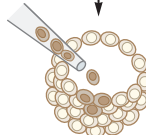
ES cells with one copy of target
gene replaced by mutant gene

B

Remove early embryo
from pregnant mouse



Inject ES cells
into early
embryo



Implant embryo formed
partly with ES cells
into foster mother



Birth



Test somatic cells of offspring
for presence of altered gene
and breed selected mice to test
for gene in germ-line cells



Transgenic mouse with
one copy of target gene
replaced by altered gene
in germ line