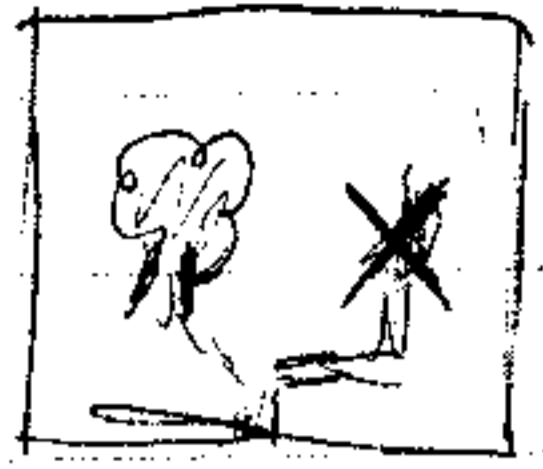


Rick Myers : Towards a Genetic Understanding of Humans



Using Genetics to Study Humans

- ① structural & f(x) conservation
- ② advances in technology
- ③ common diseases are genetic - heart, autoimmune, psychiatric, cancer
- ④ interesting & important phenotypes

Human Genome Project

- 1998 ① 100 Kb resolution physical map (markers that recognize region uniquely)
- 1994 ② 2cM meiotic map
- 2005 ③ identify all human genes
- ④ sequence of entire genomes
E. coli - 1995
S. cere - 1996

Why 100 Kb map?

- ① targeted cloning of disease genes
- ② isolation of chromosomal break points
- ③ identify genes
- ④ reqd. for sequencing

How 100 Kb map?

- ① 30,000 markers if evenly spaced
- ② determine order & distance betw. markers
 - in-situ
 - meiotic linkage
 - YAC STS-content
 - radiation hybrid

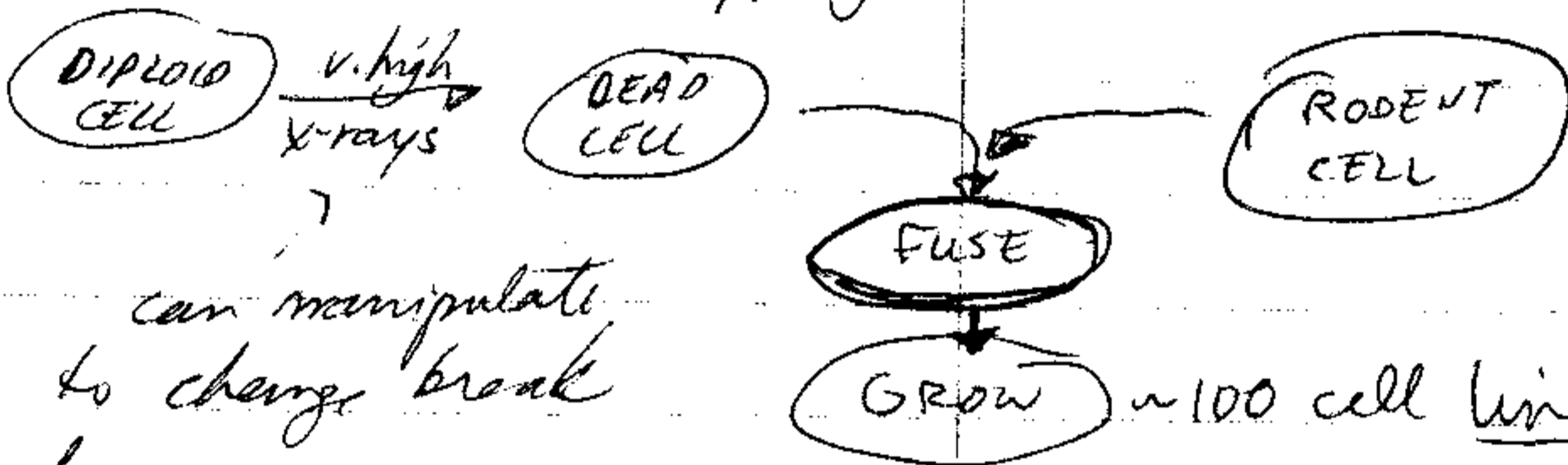
YAC-STS Content mapping

- ① take YAC library
- ② find which YAC a marker lies on
- ③ build clones into overlapping configs

but - problems w/ YACs

Radiation Hybrid Mapping

- ① rediscovered w/ David Cox
- ② like meiotic mapping

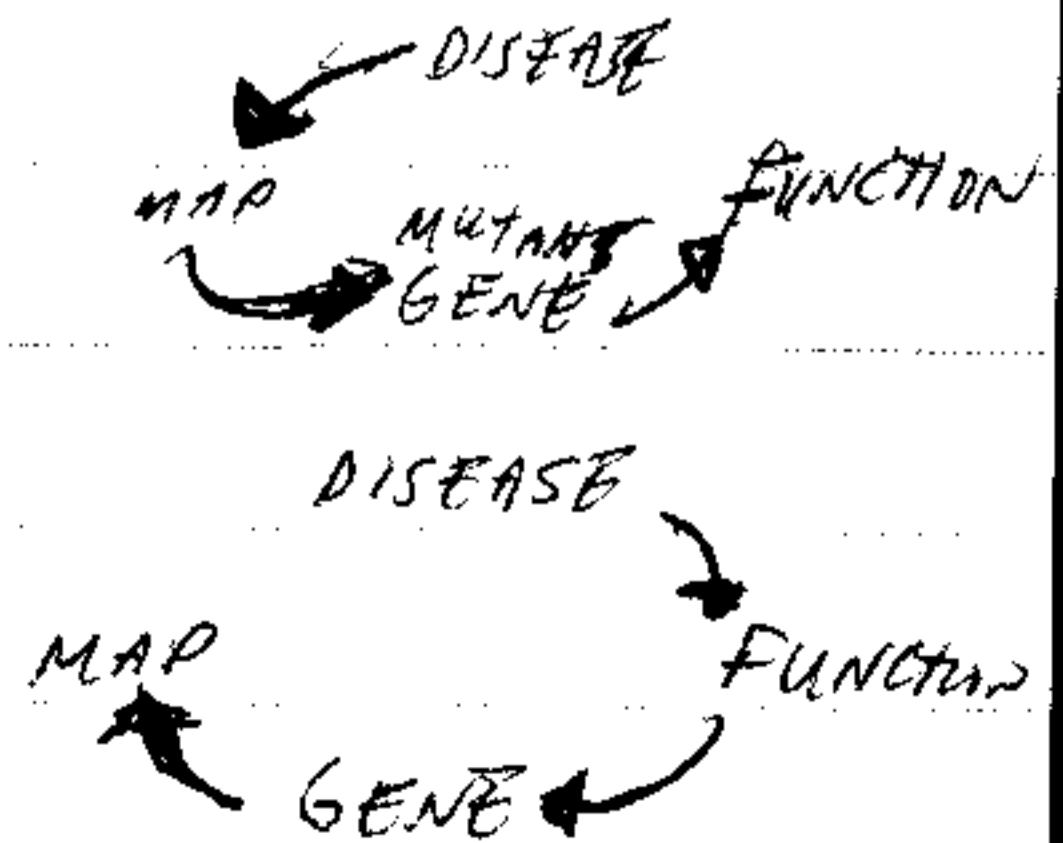


can manipulate to change break frequency

- each retains ~15% of human genome
- score for +/- for markers
- if two markers are close they should be more likely to be in same clone

Use of Maps

- ① positional cloning... (Sturtevant)
- ② functional cloning...



APOPTOSIS

Identity by Descent

- two individuals which have same phenotype & phenotype likely comes from genotype identical by descent
- can detect by ID: regions identical between two individuals even w/o pedigree

Huntington's Disease

- chorea
- psychiatric problems
- auto. dominant
- complete penetrance

1st EXON -
- CAG stretch (poly-Glutamine)

- 10-35 copies in unaffected
- 37-121 in affected

Why 37-121 have phenotype?

Why only certain cell types?

① maybe those more unstable?

Mouse -

① KO?

② model mutation?

CAG's

Huntington
SBMA
Spinocerebral ataxia
Haw river
Machado-Joseph
Dentato-rubral

GAG

Fragile X-A
Fragile X-E

CTG

myotonia