LEARNING AND MEMORY IN ANIMALS: LEARNING MUTANTS, FORWARD GENETICS

Reading: p.189-198

NATURE VS NURTURE

NATURE
Biological - usually called "genetic", but actually more complicated, ill-defined. Component of intelligence that is inherited.

NURTURE
Social - usually considered family background, education, socio-economic influences, ill-defined

IMPLICATIONS
Social programs
Head Start
School curricula
Child-rearing practices

"FORWARD" GENETICS
(mutational analysis, functional analysis)

FUNCTION (learning) → mutation → GENE (loss-of-function) → clone → PROTEIN (stupidity)

LEARNING TEST MUTANT SCREEN → IDENTIFY MUTANT MUTANT STRAIN → MAP GENE CLONE GENE (positional cloning) → PROTEIN SEQUENCE

MAKING AND CHARACTERIZING MUTANTS
(overview)

MUTAGENESIS → damage DNA of one gene (single gene mutation) (germline - pass on to progeny) (somatic - cancer)

SCREEN → identify mutants with learning test or screen (dominant mutations, recessive mutations)

NUMBER OF GENES?
complementation tests

FUNCTIONAL PATHWAYS?
double mutant analysis

"Genetic model" organisms
bacteria, yeast, Drosophila, C. elegans, zebrafish, Arabidopsis, mouse, human

LEARNING THAT ODOR MEANS ELECTRIC SHOCK
(classical conditioning)

ODOR + SHOCK → training → association → AVOID ODOR ALONE

Psychology
Shock = unconditioned stimulus (US)
Odor = conditioned stimulus (CS)

Odor "symbolizes" electric shock

DROSOPHILA LEARNING APPARATUS

Psychology
Learning occurs between two stimuli:
Shock = unconditioned stimulus (US)
Odor = conditioned stimulus (CS)

Odor "symbolizes" electric shock.
RESULTS OF LEARNING TESTS

Learning in normal flies 
dunce flies: no learning

MUTATIONS

MUTATIONS (radiation)

IONIZING RADIATION

Ultraviolet
X-rays
Gamma rays

DELETION

TRANSLOCATION

PATHWAYS DEFINED

BY DROSOPHILA

LEARNING GENES

AVOID ODOR

INITIAL LEARNING

dance rutabaga

SHORT-TERM MEMORY

AMNESIA

MEDIUM-TERM MEMORY

ANESTHESIA-RESISTANT MEMORY

radish dCREB2

LONG-TERM MEMORY

1st (X) 2nd 3rd 4th

MUTATIONS chemical

Mutagen/Carcinogen
ethylmethanesulfonate
ethylnitrosourea
(demethylation drugs)

AMINO ACID SUBSTITUTION

STOP CODON SUBSTITUTION

G → A

G → TAG

gly

ser

trp

stop

G → GT

A → GT

discoverer of white mutant; most mutants
polytene chromosome maps; free love

DROSOPHILA CHROMOSOME MAPS

3 major chromosomes (1, 2, 3)
1 minor chromosome (4th)
180 Mb
13,600 genes

2000

April

1892

1917

Dr. Mark A. Tanouye

Columbia University
which chromosome is the dnc mutation on?

Possibilities for two mutations (genes)

- Independent assortment (common)
- Recombination (rare, "closely-linked")
- No linkage (different chromosomes)

Look for missing class of animals for linkage

dnc

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GENETIC MAPPING

(Recombination mapping - distance)

<table>
<thead>
<tr>
<th>dnc</th>
<th>w</th>
</tr>
</thead>
<tbody>
<tr>
<td>(female)</td>
<td>(male)</td>
</tr>
</tbody>
</table>

RECOMBINANTS

+ dnc

= stupid (exptl) w = white eyes (marker) (phenotype?)

distances (eg. 2% = 2 map units)

THREE FACTOR CROSS

w-dnc 2 map units
dnc-cv 3 map units
cv-w 5 map units

(fw w & cv are known, unique solution)

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POSITIONAL CLONING

| w | dnc | cv |

1. clone entire map interval
2. identify all genes (transcription units)
3. transgene rescue (final identification)

DROSOPHILA LEARNING MUTANTS

- dnc = cAMP phosphodiesterase named after John Duns Scotus, 13thC opponent of classical learning
- rutabaga = unknown radish = unknown
cabbage = unknown

The vegetable series: because they're as dumb as vegetables

- amnesiac = neuropeptide similar to mammalian pituitary adenyl cyclase activating peptide (PACAP)
- latheo = unknown Greek for "forgetful" related to the Lethe River of Hades, a drink and you forget your former life

- CaMKII = Ca/calmodulin-dependent protein kinase II
- dCREB2 = cAMP response element binding protein (transcription factor)