Graham Walker, Texas Ranger - SOS

3.6.97

SOS

physiological response

SOS response

recA+ lexA+ — DNA Damage →
- induction of λ prophage
- UV induced filamentation (synthesis of septum inhibitor)
- W-reactivation (UV'd λ survive better if host is UV'd)
- W- mutagenesis (need to UV host 1st to get λ mutagenesis)

lexA — recA

- uvrA
- sulA — septum inhibitor
- umuD + umuC — SOS mutagenesis

Uninduced = ~7000 RecAs per cell

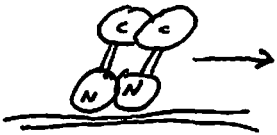
Induced = (single stranded DNA generated by replication after UV)
= RecA forms nucleoprotein filament

Induced

LexA → cleaved at ala-gly

λR → cleaved at ala-gly

Repressor - LexA + λ



→ if cleave, C-C contacts are lost and repressor comes off.

LexA ... other aa in LexA required for cleavage

Mutants

LexA (Ind⁻) = dominant, non-cleavable lexA's (sos⁻)

LexA (def) = recessive, SOS constitutive

RecA (def) = non inducible, recessive

RecA (Cpt^ic) = SOS constitutive

Fine Tuning

1) All LexA repressed genes are expressed at basal level.
(e.g. LexA = 1306/cell)

2) Level of induction varies greatly
- (depends of LexA affinity for SOS box)
- (depends of promoter strength)
- (depends on location)

3) Can achieve intermediate induction

4) LexA weakly represses itself

5) λCI cleaved more slowly than LexA
(phage only wants to bail out if lots of trouble)

1967 - E Witkin
- noticed parallels betw. λ induction of UV and UV induced filamentation

1973 M. Radman

- DNA damage generated signal that led to induction of a set of LexA, RecA regulated genes.

1975 - Jeff Roberts

- λCI cleaved after UV in vivo
- in vitro got λCI cleaved by RecA, ATPγS, ssDNA

1984 J.L. Little

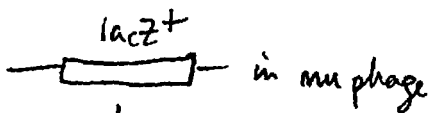
- LexA + λCI autodigest at Ala-Gly at pH 9 or 10 w/o RecA

1990 - Jeff Roberts

Cell needs to try to replicate UVd DNA to generate SOS inducing signal

- dnaC28 (Ts for initiation), uvrB at restrictive T° got no SOS.

C Kenyon 1980



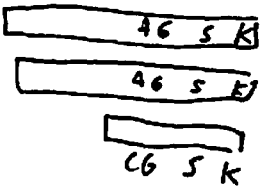
SOS mutagenesis + umuDC

1) W-mutagenesis

2) recA(sos⁻) or lexA(Ind⁻) = non-UV mutable

3) mutational spectra = mutagenesis targeted to lesions
= lesion influenced nature of mutation

4) UV non-mutable E. coli
recA⁻ lexA⁺ umuDC⁻

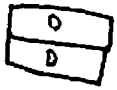


UmuD

cleaved very slowly to active form

Key Players in SOS mutagenesis

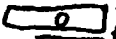
1) umu D' (umuD may be inhibitor)
2) umu C
3) RecA (not just for cleavage) } E. Coli's got bypass in vitro
4) DNA pol III



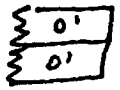
Inactive in SOS mutag.

unuD2

Lect*



} Heterodimers are very stable.



Active in SOS mutag.

unuD'