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Systematic RNAi in *C. elegans*

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Abstract

Caenorhabditis elegans populations in which each gene on chromosome I is blocked in turn by RNAi have been grown and phenotypically screened.

Significance and context

When classical geneticists are interested in a particular organ or biological function in a model organism, they often use mutagenic screens to search for the genes involved.A large population of the organism is first exposed to agents that cause mutations at random over the entire genome. The geneticist then searches for individuals with defects in the organ or function of interest. In such candidates, the mutations causing the defect must then be identified by positional cloning, and the gene product confirmed, which may take months or years. Fraser *et al*. have pioneered a new genetic strategy for finding biochemical players without the need for positional cloning. The technique, called systematic RNA interference (RNAi), temporarily blocks the function of each mRNA in an organism. When an individual lacking a known mRNA is screened and shown to exhibit a phenotype of interest, that message is implicated directly in the phenotype without an extra cloning step. The authors have used RNAi in *C. elegans* to screen the genes on chromosome I for embryonic lethality or, in viable animals, for effects on body morphology, movement and reproduction.

Key results

The authors screened 87% of the genes on chromosome I and assigned phenotypes to 14% of them. Some positive control genes are known from previous work to be both present on chromosome I and identifiable by a screen similar to that used here. Fraser *et al*. detected 90% of such positive controls known to be embryonic lethal, and 45% of other positive controls. Their screens enriched for conserved proteins: genes assigned an RNAi phenotype are more likely than the average *C. elegans* gene to have homologs in other species.

Methodological innovations

Fraser *et al*. made a library of bacterial strains, each producing a double-stranded RNA (dsRNA) corresponding to one gene on *C. elegans* chromosome I. Worms were fed the bacteria and incorporated the dsRNA, which hybridizes to expressed mRNA *in vivo* and blocks its function. The behavior of the treated adults and their progeny was then observed and scored.

Links

A closely related paper by Gonczy *et al*. on the use of RNAi to analyze cell division in *C. elegans* appears in the same issue of *Nature*, and is available to subscribers.

Conclusions

The authors conclude that systematic RNAi can be a useful way to assign function to unknown genes in a high-throughput manner.

Reporter's comments

The most important results here are the gene phenotype classifications themselves. Given the reasonable track record for identifying positive controls, the rest of the data remain hypotheses to be tested by further biochemical work.

Table of links

Nature

References

1. Fraser AG, Kamath RS, Zipperlen P, Martinez-Campos M, Sohrmann M, Ahringer J: Functional genomic analysis of *C. elegans* chromosome I by systematic RNA interference. Nature. 2000, 408: 325-330. 0028-0836