Functional Genomics

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Introduction

- **Functional genomics** is a field of molecular biology that attempts to make use of the vast wealth of data produced by genomic projects (such as genome sequencing projects) to describe gene (and protein!) functions and interactions.
- It deals with the dynamic aspects such as gene transcription, translation, and protein-protein interactions, as opposed to the static aspects of the genomic information such as DNA sequence or structures.

Introduction

- *The ultimate goal of functional genomics is the improved understanding of cell organisation at different levels, from individual genes to groups of bio molecules and complete genomes.*

- It is the understanding of gene function and the subsequent application of this new information that will ultimately yield benefits.
- Consequently, a shift of emphasis is now occurring from genome mapping and sequencing to determination and interpretation of genome function.
- This is the challenge for the post-genomic period which we are now entering and is the area known as *functional genomics*.

Areas Of functional genomics

- Functional genomics includes function-related aspects of the genome itself such as mutation and polymorphism (such as SNP) analysis, as well as measurement of molecular activities.
- The latter comprise a number of "-omics" such as:
  - Transcriptomics (gene expression),
  - Proteomics (protein expression),
  - Metabolomics.
- Together these measurement quantifies the various biological processes and powers the understanding of gene and protein functions and their interactions.

Technology Used for Functional Genomics

- Developments in large-scale, high throughput technologies and robotics now allow researchers to simultaneously profile vast numbers of different genes or proteins in parallel.
- The technologies, which used to study genes include:
  - DNA and protein micro arrays (chips)
  - Large scale 2-dimensional gel electrophoresis.
  - Mass spectrometry (proteomics)

Methodology

- Genome sequences are used first to predict the set of possible proteins, which are compared with all known sequences in central databases.
- In many instances, for approximately half of the proteins, there is a reasonable match to a previously sequenced protein from another organism.
- Because the function of many proteins already has been determined in some organism, and similarity in sequence generally reflects similarity in function.

Methodology

- These database comparisons can at least partially interpret a substantial fraction of the genome.
- But how can the function of the many uncharacterized genes be addressed on a genome wide basis?

C. elegans as a Model Organism

- The function of a protein often can be determined through the use of simple experimental organisms.
- These organisms have rapid doubling times and are amenable to uncomplicated genetic analyses yet they undergo complex cellular processes common to mammals.

C. elegans

- *C. elegans* consists of only about 1,000 somatic cells, but it has the basic body plan of an animal, including muscle, digestive organs, nervous system, epidermis, etc.
- Moreover, the body is transparent, which allowed the entire pattern of cell divisions from the fertilized egg to the adult, termed the cell lineage, to be described

Why use C. elegans

- Additionally, this transparency permits the analysis of gene expression at the level of individual cells throughout development.
- The targeted knockout or inhibition of gene function can be readily accomplished by injection of double-stranded RNA.
- But importantly, about half of the genes so far implicated in human disease have a homologue in the worm.

Why use C. elegans

- A striking example of the significance of this conservation was the ability of a human gene implicated in Alzheimer's disease to complement a worm mutation
- The subsequent analysis of mutant human genes through assay of their activities in the worm.

Life cycle of C. elegans

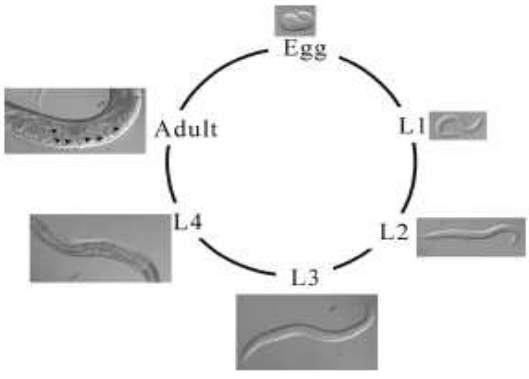

Fig. 1. *C. elegans* as a model organism. The lifecycle of the nematode *C. elegans* is shown. *C. elegans* undergoes four larval stages to become an adult. An adult hermaphrodite animal, as shown in the figure, is anatomically a female animal that temporarily produces a limited number of sperm as well as eggs. Arrowheads indicate some of the eggs inside the hermaphrodite adult.

RNAi

- RNA interference is a phenomenon discovered in *C. elegans*, and now used as a favorite method of knocking down a gene function in various species.
- In *C.elegans,* there are three ways to perform RNAi experiments.
- One can inject RNA into the intestine, the hypodermis see the RNAi effects.

RNAi

- A second method involves the feeding of a bacteria that produce dsRNA of interest.
- The third way of delivering dsRNA into the nematode is to soak the worms in the RNA solution without injection, nor feeding.

Micro array approach