Going past the genome's basic structure — What is turned on, off, and modulated (even between each of monozygotic twins) — is apparently a major part in determining whether disease will strike as a result of having "bad" genes

Published:
8 December 2011 – 15:27

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What we would have predicted, given recent discoveries in epigenetic effects

The nematode (round worm), *Caenorhabditis elegans* — that I wrote about two days ago, regarding extra-chromosomal inheritance of acquired characteristics — is also involved in a new discovery about disease variations between people with essentially identical sequences of DNA codons.

In Spain, a research has been trying to figure out why "bad" genes that are present in each individual of a pair of monozygotic twins will cause illness in one, but not the other:

> Using *Caenorhabditis elegans* as a model system, we identify two compensation mechanisms that vary among individuals and influence mutation outcome.
>
> First, feedback induction of an ancestral gene duplicate differs across individuals, with high expression masking the effects of a mutation.
>
> Second, during normal embryonic development we find that there is substantial variation in the induction of molecular chaperones such as Hsp90 . . . .
>
> Chaperones act as promiscuous buffers of genetic variation, and embryos with stronger induction of Hsp90 are less likely to be affected by an inherited mutation.
>
> [T]he results establish that inter-individual variation in both specific and more general buffering systems combine to determine the outcome inherited mutations in each individual.
>
> © 2011 Alejandro Burga, M. Olivia Casanueva, and Ben Lehner, *Predicting mutation outcome from early stochastic variation in genetic interaction partners*, Nature 480 (7376): 250-253 (08 December 2011) (from the abstract, paragraph split)

« AN IMAGINATION STRETCHER — 2 LARGEST BLACK HOLES WITH MASSES OF 9.7 BILLION SOLAR-SIZED SUNS

MODEL INDICATES THAT DEVIATIONS IN THE ORBITS AND RELATIVE VELOCITIES OF NASA'S TWO GRACE SATELLITES MAY SHOW THAT JAPAN'S 11 MARCH 2011 EARTHQUAKE WAS DEEPER AND SLIGHTLY STRONGER THAN PREVIOUSLY THOUGHT — BUT I'M NOT SURE THAT I'D COUNT ON THE ACCURACY OF THE CALCULATION »

Hsp90 is a heat shock protein. It appears to function in protein folding (and unfolding), signaling, and tumor repression. Wikipedia has an understandable write-up, here.

> *Note — an aside that makes a point about precision in science*
>
> The "90" in Hsp90's name comes from its approximate mass in daltons.
>
> Daltons are units of mass, abbreviated "Da". A dalton is also called a unified "atomic mass unit" (amu).
>
> One atomic mass unit equals approximately the mass of one neutron or one proton. More technically (as Wikipedia puts it), "It is defined as one twelfth of the rest mass of an unbound neutral atom of carbon-12 in its nuclear and electronic ground state."
>
> I add this definition because it illustrates the precision with which good science is done. Defining one's terms and measures is essential.
>
> If you are wondering why proteins are often characterized by their masses, that's an artifact of the history of biology.
>
> Proteins were initially often separated by how far they migrated on an electrified gel (gel electrophoresis) strip. Obviously, the larger molecules/fragments moved more slowly along the strip, given roughly equal charge balances on them.
>
> The distance the different proteins migrated separated them from one another based on their size/mass *or* the ways and amounts in which their electrical charges were distributed along the various molecules.

"Stochastic," as used in the study's title, just means "non-determined" or effectively "random," insofar as we understand what's going on.

> *For what it's worth — using incomprehensible words doesn't do anyone any good*
>
> Using jargon (words like "stochastic") puts up an unnecessary barrier to understanding. "Jargon-ese" is almost certainly the result of people's ego-derived need to flaunt their alleged superiority over one another.
>
> If you read as many abstracts and "professional" articles as I do, you have to laugh at how egotistically dense many of these authors are. Poor communication does neither the profession involved, nor the world, any favors. Incomprehensibility defeats the purpose of even talking to one another.
>
> Jargon is one reason that the American public so distrusts scientists and the "elite."

What the Centre for Genomic Regulation said about the mutations study

The Press Office explained that:

> Since the genetic composition and the environment are insufficient to determine whether or not a mutation will affect an individual, they developed a methodology to measure small differences in gene expression in vivo.
>
> "The challenge was not only to develop a method to quantify these small differences among individuals, but also to predict which genes are relevant for a particular mutation", adds Ben Lehner, coordinator of the study and ICREA Research Professor in the European Molecular Biology Laboratory-Centre for Genomic Regulation Systems Biology Research Unit.
>
> "In both round worms and humans, genes cooperate and help each other to perform functions within the cell.
>
> "A few genes are very "generous" and help hundreds of others to perform many different processes, whereas others only help a few other genes to perform more specific functions.
>
> "The key to predict what will happen in each individual is to measure variation in the expression of both types of gene".
>
> [T]o develop personalised and predictive medicine it will . . . be necessary to consider the varying extent to which genes are turned on or off in each person.
>
> © 2011 Press Office, *Why does the same mutation kill one person but not another?*, Centre for Genomic Regulation (07 December 2011) (paragraphs split)

The moral? — Optimistic predictions about soon-to-be realized benefits from the Human Genome Project were based on a much too simplistic understanding of the way the genome actually works

It is advisable to be highly skeptical of exaggerated claims about making quick steps "forward" in biology and medicine. Or most anything else that deals with complicated systems and their interactions.

Humility is good. We're not as knowledgeable (or as smart) as we often think we are.

Tagged: Alejandro Burga, Ben Lehner, buffer, C. elegans, Caenorhabditis elegans, Centre for Genomic Regulation, chaperones, codons, disease, DNA, epigenetic, gene, heat shock protein, Hsp90, Human Genome Project, M. Olivia Casanueva, monzygotic, mutation, stochastic, twins