

## **PRISONERS OF GENES**

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The discovery of our meagre gene numbers - by two major groups of international scientists - reveals that environmental influences are vastly more powerful in shaping the way humans act. Their analysis of the first human genetic map - known as the genome - shows that we have as few as 30,000 genes, the blueprints for brain and body cells. This is a far lower total than expected, and dramatically undermines claims that human beings are prisoners of their genes."

Most readers of this list have doubtless been groaning at these headlines that Ian has been posting since, of course, had we been endowed with the previously estimated 100,000 genes, the nature-nurture issues would have been the same. I append below a few paragraphs that I posted on a non-scientist-serving list I frequent, and post them here in hopes that they will serve as helpful "talking points" for others in the months ahead.

Reporters are concluding from our unexpectedly small number of genes that it's really nurture over nature after all. I'm all for the importance of nurture -- all biologists are -- but this particular spin on the genome results is at best misleading. Fact is that even if we had the expected number of genes -- the old number was an estimated 100,000 rather than the current tabulation of ~30,000 -- that wouldn't have begun to be enough to account for things on a one-gene one-trait basis. It has been clear for several decades that complexity is wrought in many other ways, of which I will lift up three.

1) A given gene can encode more than one protein. A botched-up explanation of this in a Washington-Post account states that proteins get chopped up and the pieces are used, but what in fact happens is that the messenger RNA gene transcripts are edited in different ways ("alternative splicing") to produce instructions for different kinds of proteins.

2) Proteins rarely generate a phenotype on their own; instead, they combine with other proteins, and the resultant protein complex interacts with other protein complexes, and so on. A given gene is often expressed in different cell types at different stages of development/differentiation. In each instance, the protein product of that gene finds itself in a unique context, with a novel set of "partner proteins" due to the differential expression of other genes in that cell or its precursor cells. That is, the process is deeply combinatorial and, as we know, combinatorial systems can generate large numbers of variants with a small number of initial units. Moreover, the system is designed to keep the combinatorial process going: certain novel protein complexes have the necessary configuration to switch on the next set of genes whose protein products then make the next set of protein-partner choices.

3) The human phenotype that we're most interested in, our sentient brain, has for some time been known to develop in an "epigenetic" fashion. That is, during brain development, key genes are expressed ab initio and key genes are expressed along the way, but much of what happens is the consequence of cell-cell interactions and cell-hormone interactions that depend directly on protein-protein interactions. Genes set

all this up, and in this way they are essential -- no genes, no brain -- but they don't directly participate in most of the "decisions" made as the brain develops. Faulty versions of key genes compromise the project, often early in neurogenesis, but we left behind some time ago the notion that there's a gene "for" this neuronal connection or that one. Given the trillions of neural connections in the brain at birth, not to mention those that form as a consequence of experience, 100,000 genes were no more up to the task than 30,000.