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The Praxitype and Genetic Arithmetic

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The cover of the October 9, 2006, issue of Time Magazine melodramatically introduced the story inside about the 99% identity of the genetic code in humans and chimpanzees. We were supposed to accept that the genotype of both species is almost identical while our physiological senses and published facts present us with two overwhelmingly different phenotypes, that is, the consequences and manifestations of the respective genotypes. Whatever the exact degree of identity, it seemed a bit of a stretch that virtually identical genotypes could account for such disparate phenotypes. Since then, over and over we have been led to believe that knowing the genotype allows one to know, to predict the phenotype. And when the phenotype is, for example, a specific protein, a genotype change can be appreciated as a change in one or more of the amino acids that makes up the protein. Changing the genotype changes the phenotype. Conversely, similar genotypes account for similar phenotypes. So, how can two genotypes 99% identical account for phenotypes as different as humans and chimpanzees?

The key to the answer is our not having carefully considered how the genotype is literally "put into practice." Indeed, just what are the operational stages between the genotype and the phenotype? There are some hints about the complexity implicit in there being two distinct phases, transcription and translation: both of which actually involve literal translation, one from DNA to RNA and the other from RNA to amino acids. And the general nature of cellular organelles and specific biochemical structures to facilitate these processes has been realized for some time. And, increasingly, there is acknowledgement of portions of the genotype not directly translated to amino acid sequences, for example, long non-coding RNA (lncRNA) and micro-RNA (miRNA). But, overall, these and other (potentially) contributory elements have have not been organized or synthesized into a specific strategy or mechanism, into a praxitype. It's as though there are merely the genotype and the phenotype such that the details of the relationship are not generalizable beyond the notion that there are some non-specific coded or uncoded genetic influences, broadly referred to as "epigenetic" factors or mechanisms. It's like recognizing there are delivery "issues," without identifying the specific delivery services. Consider how, in the late 1960s, Federal Express forever changed the notion and facts of the practice of package delivery by establishing a scenario and mechanism for reliable overnight package delivery. They literally put sophisticated, organized package delivery into practice.

I have suggested earlier that varied circumstances, such as the Time Magazine cover story considered above, are virtually "begging for recognition – even formulation – of the necessity to acknowledge and formulate how the genotype is put into practice to manifest predictably the expected phenotype. But, up to now, the numbers seemed not to add up! The arithmetic just didn't seem compelling. That would-be acknowledgement and formulation are, however, engendered by the word and notion, "praxitype." Etymologically consistent with the terms, genotype and phenotype, the praxitype is putting into practice the genotype so that it predictably leads to the phenotype encoded in either the wildtype or mutant allele for each gene locus. Of course, the praxitype can/must be vastly different for wildtype versus mutant alleles and obviously even very different from one "normal variant" to another. The praxitype must be formulated independently for each deviation from the consensus wildtype.

The purpose of this brief introduction to and overview of the praxitype is akin merely to turning on a light in a dark room. Except for some extraordinary considerations (beyond the scope of this review), what is to be found in the room is independent of the light or its switch. I merely want you to know that that there is a light. There is a mechanism to understand, or a paradigm to explain the relationship between genotype and phenotype more cogently and more productively. Start by demanding (e.g., of yourself) to know how the genotype is put into practice, given both what you know about the genotype already and what is there to be gleaned – now that the light as been turned on. It is already happening for the autosomal dominant genetic disorder, Neurofibromatosis Type 1 (NF1).

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