

Gatell *et al.* that carries out the complete reduction to ethene has a similarly restricted diet, and the same question can be posed on its behalf.

Equally fascinating is the rapidly growing number of microorganisms now identified that are capable of the partial halo-respiration of PCE and TCE to *cis*-DCE (3). Most are not as restrictive in their diets as *D. restrictus* and Strain 195, but can obtain energy for growth from many other electron donors and acceptors. Indeed, Strain MS-1, which can reduce PCE to *cis*-DCE while using acetate as an electron donor, can grow fermentatively on a wide variety of organic compounds and can even use oxygen or nitrates as electron acceptors in energy metabolism (9). These it uses first if available because of the much greater energy generation. But when they

are not available or become depleted, PCE can then be used.

Several laboratories have been attempting to isolate strains that can completely dehalogenate *cis*-DCE or VC to ethene. Strain 195 is the first isolated, but undoubtedly many others with this ability exist. Whether these others will be similarly restrictive in diet remains to be seen, but it seems likely they will not, judging from the broad capability of organisms recently identified that convert PCE to *cis*-DCE. We have much to learn about how these microorganisms obtain energy through halo-respiration, whether they all use similar biochemical pathways, and how the process is regulated. Some electron donors may provide a better competitive advantage for halo-respiring organisms, and we need to understand why. The significant step taken by

Maymó-Gatell *et al.* should help answer many of these questions about halo-respiration of chlorinated solvents.

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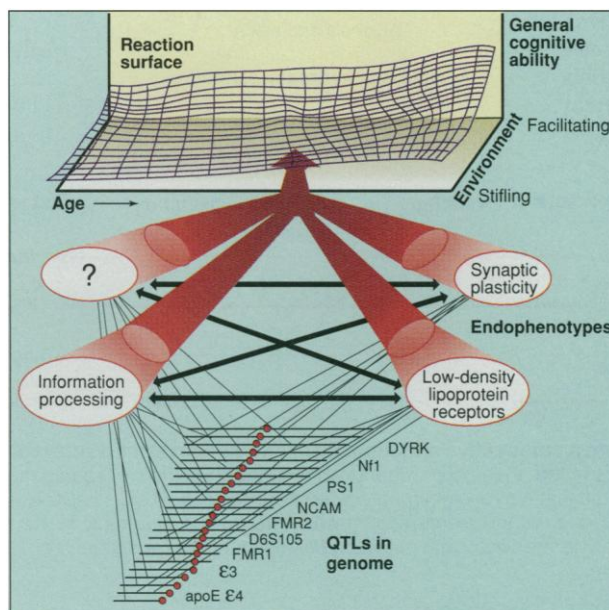
HUMAN GENETICS

Twins: En Route to QTLs for Cognition

Irving I. Gottesman

Suppose you want to measure the contribution of genes to cognitive ability. So you suggest an experiment that requires cloning human beings in order to guarantee that one of your tested groups is 100% genetically similar. Many eyebrows would surely be raised. But if truth be told, such experiments of Nature have been conducted routinely since the days of Sir Francis Galton (1875) (1) on identical (monozygotic) and fraternal (dizygotic) twins to study both diseases and quantitative traits [traits such as blood pressure or intelligence quotient (IQ) that vary continuously, rather than in an all-or-none manner]. Since Galton's time, the journey of behavioral geneticists from their reputation as determinists (genes determine behaviors) to the one they now strive for as probabilists (genes determine the likelihood of behaviors) has been an uphill struggle. Now, a landmark study on page 1560 of this issue marks an achievement in this struggle and reports the counterintuitive result that the genetic contribution to cognitive ability is remarkably constant throughout life (2).

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Influence of genes, environment, chance, and time on general cognitive ability. [Adapted from Sing *et al.* (7)]

The U.S.-U.K.-Swedish team of researchers analyzed the cognitive abilities of an extensive sample of Swedish octogenarian twins using the classical method (that is, determination of the genetic contribution to cognition at a single time point). For these 240 intact pairs of twins, the heritability (proportion of trait variance attributable to genetic agents) of general cognitive

ability is 62%, a value remarkably consistent with the value of this parameter in adolescence and onward (3). These data fill a gap in theories about the epigenesis of intellect over the course of life; previously it was supposed that with accumulated experience the contribution of one's genetic makeup to intellectual functioning declined; now it seems that in fact it remains rather stable.

Such cross-sectional samples of twins at single time points and their allegedly simplistic statistics have technical flaws, but nevertheless have yielded well-cited data (1, 4). The flaws in this approach can be captured in the words of the physicist P. Hansma (5, p. 1882), who was contrasting electron microscope images of RNA with the dynamic creation of enzymes: [Heritabilities are] "like snapshots of a ballerina. They won't tell you about the ballet." As a consequence of this shortcoming, current practitioners, including the authors of the new study, have already moved from this classical approach to multitime point, longitudinal designs and to the hunt for QTLs (quantitative trait loci), both of which are required to complement the classical strategies for understanding complex traits (6).

The new data complement existing evidence for the strength of genetic influences on cognition. The correlational similarity of various indicators of general cognitive ability, sometimes referred to as *g*, has been assessed for pairs of relatives ranging from 0 to 100% gene overlap and from 0 to 100% environmental overlap. An overview of these data (3) indicates that genetic agents ac-

count for 0.50 of the variance in general cognitive ability, shared environmental agents account for 0.33, nonshared environmental agents 0.17, and error of measurement 0.10. Thus, genetic agents are indeed important in the determination of intellect and its closely related traits (such as working memory and spatial skills), but environmental and experiential agents are also critical.

Such a conclusion about the contributions of genetics to intellectual function validates and empowers the search for QTLs that underlie the genetic agents for complex traits (7). The figure is an adaptation of a cartoon from the work of Charlie Sing that originally described the contributions of genes to the differences among individuals in developing coronary artery disease (7). It substitutes a different end point—intellect—for coronary artery disease and shows the general relation among genes, the environment, and the passage of time in determining human traits. An article was published in 1996 with the title "Molecular genetic research on IQ: Can it be done? Should it be done?" (8). The answer to both questions was yes, and the authors went on to start the study with an association strategy, fully aware of the odds against finding genes that underlie IQ. But rapid improvements in the numbers of identified genes and markers permit a dense map of the human genome, a minimum requirement for identifying any gene that by itself may account for as little as 1% of the phenotypic variance, as is the case for the genetic determinants of variation in intellect. A stringent statistical conscience must be in place for such expeditions into the causes of complex diseases and traits (9) so as to avoid false promises and disappointments; statistical allowances must be made for genomewide scans, whether conducted or only implied.

What do we know so far about the specific genes? The genes in the cartoon, depicted as contributing to cognition, are from a larger set, all implicated by linkage or association strategies in humans, mouse, or *Drosophila* in some aspect of brain functioning relevant to cognitive abilities. Some appear to have a role both in single major locus conditions as well as be potential QTLs for IQ or cognitive decline (10). Various hypothetical "endophenotypes" are shown that mediate the impact of gene products on emergent systems and set the stage for being expressed on the "reaction surface" (11). Each person and each confirmed facet of cognitive ability will require its own such blueprint, but the constancy of heritability for *g* after adolescence reflected in the new information about octogenarian twins suggests that in this case we may not need to concern ourselves with marked age-dependent effects (12) that would frustrate QTL searching. Data from twin studies for complex traits can be used to screen for "candidate traits" that can become the focus for connecting to candidate genes. The high

heritabilities of traits such as general cognitive abilities and diseases such as schizophrenia tell us where to invest our efforts first.

Galton is credited with the enduring alliterative phrase "nature versus nurture," likely inspired by *The Tempest*, wherein Prospero says of Caliban (13): "A devil, a born devil, on whose nature nurture can never stick, on whom my pains, humanely taken, all, all lost, quite lost" (4.1.187–190). The true genetic nature of humans has still not been defined, but if you are looking for a place to invest your intellectual capital and have a high tolerance for risk, then the search for QTLs for complex behavioral traits and diseases can be recommended as a long-term buy—but beware of the near-term volatile oscillations in your investment.

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13. W. Shakespeare, *The Tempest*, 4.1.187–190. Caliban's mother was a witch, his father a devil, making the latter a dominant gene character in the Bard's view.



Polymers and liquid crystals

<http://plc.cwru.edu/>

Two of world's most important human-made materials—polymers and liquid crystals—are featured in this Web site at Case Western Reserve University. With a rich assortment of graphics, animations, and hypertext, the PLC Virtual Textbook guides the user through explanations of polymer properties. The material is available in both low- and high-bandwidth versions for users with a range of computing power and is supplemented by an excellent bibliography and well-designed downloadable simulations.

Swiss sequences

<http://expasy.hcuge.ch/>

Molecular biology is a field of such breadth that it would be nearly impossible for any one Web site to do it justice. The ExpASy site hosted by the Geneva University Hospital fulfills an important part of this aim where protein and nucleic acid sequence data are concerned. Included are access points to numerous sequence databases, structural images, and software tools. ExpASy also features an electronic version of the well-known "Biochemical Pathways" index of Boehringer Mannheim Corp., a impressively detailed map of metabolic pathways and enzyme biochemistry.

Space science site

<http://ispec.ucsd.edu/intro.html>

Space physics is the study of how charged particles behave in the dynamic electrical and magnetic environment outside Earth's atmosphere. The International Space Physics Educational Consortium is a group of researchers at institutions involved in space science research. Their Web page collects a range of resources under one electronic roof, including a Virtual Learning Center with a clickable map of the solar system leading to related Web links.

Edited by David Voss

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