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The art of crafting metaphors  
in science  
Creativity and intuition



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Home > Research programmes > Epidemiology and public health >

Clinical and Molecular Epidemiology of Cancer  
Scientific documents

- Accumulation of genetic and epigenetic alterations: a key causal process between the environment and the occurrence of cancer
- Integrating lifecourse, environmental, molecular and epigenetic epidemiology
- Environmental toxic substances: exposed individuals and exposed populations
- Between molecules and the environment: keeping patients in the picture

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IMIM Institut de Recerca Biomèdica del Mar  
 Parc de Salut MAR Barcelona  
 PRBB  
 Parc Recerca Biomèdica Barcelona  
 ciberesp Centro de Investigación Biomédica en red Epidemiología y Salud Pública  
 UAB Universitat Autònoma de Barcelona Facultat de Medicina

*It is not possible to do the work of science without using a language that is filled with metaphors.*

In: The Triple Helix (2000) Richard C Lewontin

Metaphors in science are like foghorns and lighthouses: They usually reside in treacherous areas, yet they can also guide research mariners to novel ports.

Avise JC. Science 2001

Evocative metaphors can distill an ocean of information, whet the imagination, and suggest promising channels for navigating uncharted genetic waters.

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Clearly, metaphors vary in utility and can influence research paradigms (3).

Avise JC. Science 2001

The hope for any metaphor in science is that it may bring otherwise unfamiliar subjects to life, make connections not otherwise apparent, and stimulate fruitful inquiry. A danger is that a metaphor can restrict rather than expand research horizons. Many genomic metaphors have elements of truth, and each may have its time and place.

Recent genome-sequencing efforts have confirmed that traditional "good-citizen" genes (those that encode functional RNA and protein molecules of obvious benefit to the organism) constitute only a small fraction of the genomic populace in humans and other multicellular creatures. The rest of the DNA sequence includes an astonishing collection of noncoding regions, regulatory modules, deadbeat pseudogenes, legions of repetitive elements, and hosts of oft-shifty, self-interested nomads, renegades, and immigrants. To help visualize functional operations in such intracellular genomic societies and to better encapsulate the evolutionary origins of complex genomes, new and evocative metaphors may be both entertaining and research-stimulating.



2001 VOL 294 SCIENCE

## Evolving Genomic Metaphors: A New Look at the Language of DNA

John C. Avise

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### The NEW ENGLAND JOURNAL of MEDICINE

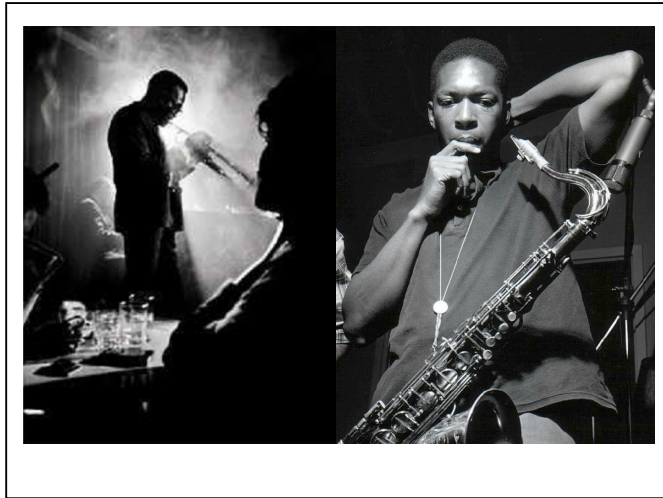
Table 1. Representative List of Organisms with Fully Sequenced Genomes.

Organism	Classification	Genome Size*	Estimated No. of Protein-Coding Genes†
Human ( <i>Homo sapiens</i> )	Placental mammal	3.2 Gb	19,042
Chimpanzee ( <i>Pan troglodytes</i> )	Placental mammal	2.7 Gb	19,000
Mouse ( <i>Mus musculus</i> )	Placental mammal	2.6 Gb	20,210
Dog ( <i>Canis familiaris</i> )	Placental mammal	2.4 Gb	19,300
Platyopus ( <i>Ornithorhynchus anatinus</i> )	Monotreme	2.2 Gb	18,527
Rice ( <i>Oryza sativa</i> )	Plant	389 Mb	37,544
Mosquito ( <i>Anopheles gambiae</i> )	Insect	278 Mb	15,189
<i>Plasmodium falciparum</i> (organism causing malaria)	Protozoa	22.8 Mb	5,300
Yeast ( <i>Saccharomyces cerevisiae</i> )	Fungus	12.1 Mb	6,607
<i>Escherichia coli</i>	Bacterium	4.6 Mb	3,200
Human immunodeficiency virus	Retrovirus	9.1 Kb	9

\* Kb denotes kilobases ( $10^3$ ), Mb megabases ( $10^6$ ), and Gb gigabases ( $10^9$ ).

† Because the process of predicting protein-coding sequences is complex, estimates of gene numbers vary in the literature and change over time.

Feero WG, Guttmacher AE, Collins FS. Genomic medicine  
—an updated primer. NEJM 2010



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~2001 ~past 15 years

Metaphors, images, literary and cultural references used in the announcement of the 'working draft' of the genome & today when daily speaking of genomics made & make reference to


- maps (unexplored territory, discovery)
- books (knowledge, record)
- computers (decoding, deciphering)
- religious themes (book of life, revelation)
- linguistics (nucleotide=letter, gene=word, DNA=language, alphabet, grammar...)


Nerlich B et al. The book of life: how the completion of the Human Genome Project was revealed to the public. *Health* 2002; 6: 445-469.

JUN 1, 2016 @ 06:00 AM 1,268,682

## From \$4.5 Billion To Nothing: Forbes Revises Estimated Net Worth Of Theranos Founder Elizabeth Holmes

*This story appears in the June 21, 2016 issue of Forbes.*

 **Matthew Herper**, FORBES STAFF  
*I cover science and medicine, and believe this is biology's century.*




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JUN 1, 2016 @ 06:00 AM 1,268,682

## From \$4.5 Billion To Nothing: Forbes Revises Estimated Net Worth Of Theranos Founder Elizabeth Holmes

*This story*

 **Matthew Herper**,  
*I cover science and medic.*

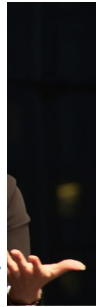
*Elizabeth Holmes speaking at the Forbes Healthcare Summit last December.*

JUN 1, 2016 @ 06:00 AM 1,268,682

Last year, Elizabeth Holmes topped the FORBES list of America's Richest Self-Made Women with a net worth of \$4.5 billion. Today, FORBES is lowering our estimate of her net worth to nothing. Theranos had no comment.

Our estimate of Holmes' wealth is based entirely on her 50% stake in Theranos, the blood-testing company she founded in 2003 with plans of revolutionizing the diagnostic test market. Theranos shares are not traded on any stock market; private investors purchased stakes in 2014 at a price that implied a \$9 billion valuation for the company.

Since then, Theranos has been hit with allegations that its tests are inaccurate and is being investigated by an alphabet soup of federal agencies. That, plus new information indicating Theranos' annual revenues are less than \$100 million, has led FORBES to come up with a new, lower estimate of Theranos' value.



Summit last

FEB 17, 2017

## Theranos' \$9 Billion Evaporated: Stanford Expert Whose Questions Ignited The Unicorn's Trouble

Dr. John P. A. Ioannidis, professor of medicine, health research and policy, and statistics at Stanford University, was the first to raise major concerns about the stealth research by Theranos, and its lack of any publications in the literature while preparing to change the entire health system. He asked, "How can the validity of the claims be assessed if the evidence is not within reach of other scientists to evaluate and scrutinize?"

Professor Ioannidis said, "Theranos general counsel reached out to me and suggested a meeting with Holmes to coauthor with her an editorial in some major journal supporting the company view that FDA clearance offered the highest possible level of evidence for any diagnostics blood test technology." They also said, "recant your existing views and writings about these misgivings." Professor Ioannidis declined to write the article or recant his views and never met Holmes.



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FEB 17, 2017

## Theranos' \$9 Billion Evaporated: Stanford Expert Whose Questions Ignited The Unicorn's Trouble



**Roomy Khan**, CONTRIBUTOR

*I give insight into decisions that lead to white-collar crime.*



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### F.D.A. Orders Genetic Testing Firm to Stop Selling DNA Analysis Service



In a crackdown on genetic testing that is offered directly to consumers, the Food and Drug Administration has demanded that 23andMe immediately cease selling and marketing its DNA testing service until it receives clearance from the agency.

In a scathing [warning letter](#) that the agency posted on its website on Monday, it said that 23andMe had failed to provide adequate evidence that its product, Personal Genome Service, provided accurate results.

Photo: Octavia for The NY Times

The personal genome testing company 23andMe is backed by Google and run by Anne Wojcicki, wife of the Google co-founder Sergey Brin.

By ANDREW POLLACK  
Published: November 25, 2013

**The New York Times**

February 3, 2004

**New Cancer Test Stirs Hope and Concern**

metaphors have real effects

August 26, 2008

**Cancer Test for Women Raises Hope, and Concern**

do not fabricate false hopes

By ANDREW POLLACK

A new blood test aimed at detecting ovarian cancer at an early, still treatable stage is stirring hopes among women and their physicians. But the Food and Drug Administration and some experts say the test has not been proved to work.

The test, called **OvaSure**, was developed at Yale and has been offered since late June by LabCorp, one of the nation's largest clinical laboratory companies.

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**The New York Times** **Business**

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**F.D.A. Says Cancer Test Failed to Get Its Approval**

By ANDREW POLLACK  
 Published: October 9, 2008

The Food and Drug Administration has told the Laboratory Corporation of America that it is illegally marketing a blood test to detect ovarian cancer, according to a warning letter posted Wednesday on the F.D.A.'s Web site.

**The New York Times**

October 25, 2008

**Sales of Test for Ovarian Cancer Halted**

By ANDREW POLLACK

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**The New York Times** **Business**

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**F.D.A. Says Cancer Test Failed to Get Its Approval**

By ANDREW POLLACK  
 Published: October 9, 2008

The Food and Drug Administration has told the Laboratory Corporation of America that it is illegally marketing a blood test to detect ovarian cancer, according to a warning letter posted Wednesday on the F.D.A.'s Web site.

The test, introduced in June, has raised hopes among women and their doctors because it promises to detect ovarian cancer at an early stage, when it is still treatable.

But some outside experts, including the Society of Gynecologic Oncologists, have said the test had not been proved accurate and might cause women to have unnecessary surgeries to remove their ovaries. The F.D.A. itself, in a previous letter to LabCorp, said the test "may harm the public health."

And why has the gene revolution failed so spectacularly to deliver anything tangible for patients? Because we have underestimated, even wilfully disregarded, the complexity of disease. Our indifference to physiology—to an understanding of systems in disease—has been a catastrophic loss to medicine.

*The Lancet*  
 Richard Horton Vol 378 November 12, 2011 1688

# Deflating the Genomic Bubble

James P. Evans,<sup>1\*</sup> Eric M. Meslin,<sup>2</sup> Theresa M. Marteau,<sup>3</sup> Timothy Caulfield<sup>4</sup>

Unrealistic expectations and uncritical translation of genetic discoveries may undermine other promising approaches to preventing disease and improving health.

With  
global funding for genomics approaching \$3 billion/year (4)

**Impediments and Hyperbole**



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**QUATERNARY PREVENTION:** procedures and policies that identify individuals and groups at risk of overdiagnosis or overmedication, and that decrease excessive medical and sanitary intervention.<sup>679</sup> Actions that prevent IATROGENESIS and "DISEASE MONGERING."

**"DISEASE MONGERING"** The practice of breaking and widening evidence-based diagnostic and therapeutic boundaries of illnesses and disorders, of inflating frequencies and risks, and of publicly promoting such exaggerated visions in order to expand the markets for those who sell and deliver health-related services and products, which may include segments of some pharmaceutical and biotechnological companies, health professionals, media, and consumer and patient organizations. Part of the process of MEDICALIZATION and GENETIZATION of ordinary life, in which social construction of illness is strongly influenced by corporate interests and DYSREGULATION.<sup>323,337-339</sup> See also IATROGENESIS;

**MEDICALIZATION** The process by which conditions, processes, or emotional states traditionally considered nonmedical are redefined and treated as medical issues. The process of identification and labeling of a personal or social condition as a medical issue subject to medical intervention. The expansion of the influence and authority of the health professions and industries into the domains of everyday existence.<sup>248,292,323,337,338,363,364,470,482,600</sup>

Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).

A DICTIONARY OF  
EPIDEMIOLOGY

**GENETIZATION** The process by which issues considered to be medical but not necessarily genetic become defined as problems with a strong genetic component or as having a genetic cause. The attribution of physiological, pathological, behavioral, or social conditions to genetic causes, often at the expense of clinical, environmental, cultural, economic, or social explanations. The expansion of genetics into the life and health sciences and professions (e.g., the genetization of prenatal medicine, oncology, primary care), and into everyday existence. In genetization processes "genetic" is often considered to be synonymous with inherited, and vice versa, thus neglecting somatic (acquired) genetic alterations and cultural inheritance.<sup>80,187,292,323,361-364,470,481,482</sup>

**metaphors should not contribute to undue genetization**

Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).

A DICTIONARY OF  
EPIDEMIOLOGY

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## Military Metaphors and Their Contribution to the Problems of Overdiagnosis and Overtreatment in the "War" Against Cancer

Heidi Malm, Loyola University Chicago

*The American Journal of Bioethics* 2016

Obesity Metaphors: How Beliefs about the Causes of Obesity Affect Support for Public Policy

COLLEEN L. BARRY, VICTORIA L. BRESROLL, KELLY D. BROWNELL, and MARK SCHLESINGER

The Milbank Quarterly, 2009

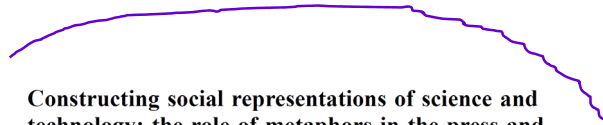
## Metaphors in search of a target: the curious case of epigenetics

*New Genetics and Society*, 2015

Aleksandra Stelmach\* and Brigitte Nerlich

Language is *not* a new metaphor for DNA.

Robert Pollack, *Signs of Life*, 1994: genome = text.



## Constructing social representations of science and technology: the role of metaphors in the press and the popular scientific magazines

Vasilisa Christidou, Kostas Dimopoulos, and Vasilis Koulaidis

Public Understand. Sci. 13 (2004)

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Vista del taller de Joan Miró, construido por Sert, y que se conserva tal como lo dejó el artista.

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The Art of Scientific Investigation (Paperback) by W. I. B. Beveridge

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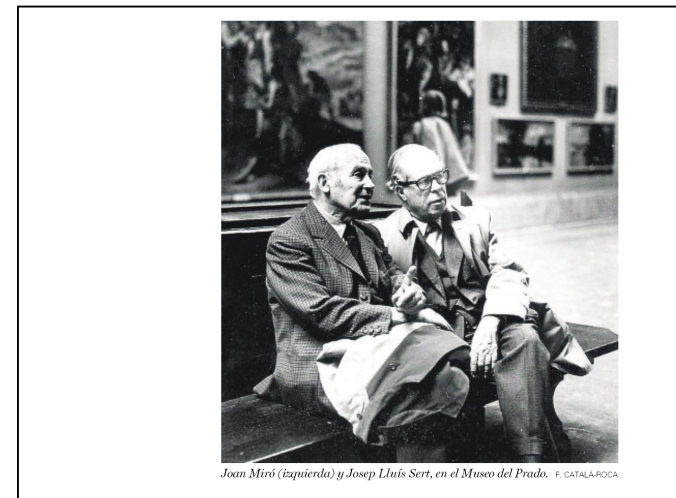
I. PREPARATION  
Study  
Setting about the Problem

II. EXPERIMENTATION  
Biological experiments  
Planning and assessing experiments  
Misleading experiments

III. CHANGE  
Illustrations  
Rôle of chance in discoveries  
Recognising chance opportunities  
Exploiting opportunities

IV. HYPOTHESIS  
Illustrations  
Use of hypothesis in research  
Precautions in the use of hypothesis

V. IMAGINATION  
Productive thinking

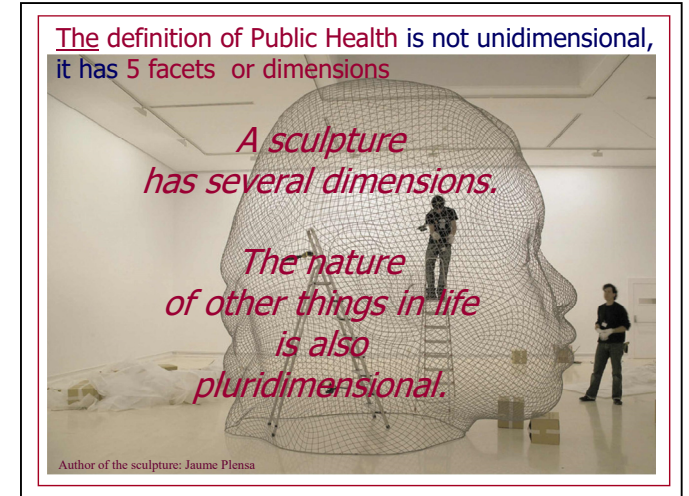


Joan Miró (izquierda) y Josep Lluís Sert, en el Museo del Prado. F. CATALÀ-ROCA



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**PUBLIC HEALTH** Like most sculptures, symphonies, and other works of art, certain important things in life have several dimensions. The definition of public health has four dimensions. Public health is:

1. The health of a whole society. It can be measured and assessed through quantitative and qualitative indicators and analytic processes.
2. The specific policies, services, programs and other essential efforts agreed (ideally, and often, democratically), organized, structured, financed, monitored, and evaluated by society to collectively protect, promote, and restore the people's health and its determinants.
3. The institutions, public and private organizations—including private and public companies—, and other citizens organizations, that plan, develop, fund, and implement such efforts, and which are thus an integral part of local, national, regional, and global public health systems.
4. The scientific disciplines and professions, knowledge, methods, art, and craft essential to positively influence HEALTH DETERMINANTS, and thus prevent disease and disability, prolong life, and promote HEALTH through the organized and collective efforts of society.

Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).



Public health takes care daily of what we breathe, drink, and eat, how we work, move, and live together. Economic, environmental, social, educational, occupational, medical, and other policies intertwined with public health change with changing social values and networks, policies and technologies; yet, the goals—diverse as they are in democratic societies—remain the same: to reduce the amount of health-related suffering, disease, disability, and premature death in the population. Public health is a SYSTEM of professions and scientific disciplines, social organizations and institutions, values, and actions.<sup>1,2,5,6,13,14,17,19,28,33,38-42, 67,72,83,85,96,113-117,123,128,140,150,158,160,161,164,183,186,188,213-215,248-250,254,267,279,285-287,302-320,357-360,366,382,436-439,522-678</sup>

Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).

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Cristina Iglesias en el Museo Lluís, entre las piezas de su obra 'Tres corredores colgantes'.

PATRICIA SEVILLA GORDIA

“Mis esculturas son lugares para pensar”



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## CONSTRUCTIVE CONVERSATIONS ABOUT HEALTH policy and values

Edited by Marshall Marinker

Chapter 13

### Creativity

Miquel Porta

#### Contents

● Health policy and the constructive conversationalist ● The value of values ● Health and wellbeing ● Equity and justice ● Choice ● Democracy ● Stewardship ● Evidence ● Efficiency ● Synergy ● Sustainability  
● Interdependence ● Creativity ● Ethical considerations in health systems ● Justice and the allocation of health care  
● Health values and the politician ● The future

#### Contributors

● Marc Danzon ● Ilona Kickbusch ● Jennifer Prah Ruger ● Giovanni Moro ● Per Carlsson ● Peter Garpendy  
● Constantino Sakellariades ● Derek Yach ● David Hunter ● Morton Warner ● Mihaly Kokeny ● Graham Lister  
● Miquel Porta ● Julio Frenk ● Suzanne Rameix ● Isabelle Durand-Zaleski ● Hans Stein ● Josep Figueras ●



Radcliffe Publishing

**DYSREGULATION** Relative or complete failure to regulate (check, control, enforce, adjust, lead) an organization, system, area, or process to preserve its nature, balance, aims, or functions (such as homeostasis, immunity, metabolism, health, validity, accountability, cohesion, freedom, equity, efficiency, wealth). Examples include many types of physiological, mental, emotional, economic, political, technological, and genetic dysregulation, leading to responses and effects that are poorly modulated, disruptive, costly, inefficient, unjust, corrupt, unsustainable, unhealthy or pathological.<sup>1,3,5,9,24-26,39-42,58,85,128,202,270,279</sup> See also EPIGENETICS; EPIGENOME; GLOBALIZATION; MULTISTAGE MODELS.



Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).

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**CREATIVITY**

1. The ability to produce ideas, knowledge, policies, and objects (including scientific knowledge and “knowledge objects”) that are both novel or original and worthwhile or appropriate (i.e., useful, attractive, meaningful, relevant, and valid).<sup>237</sup>
2. In EPIDEMIOLOGICAL RESEARCH, the capacity of a set of studies to harmonize relevance, validity, meaning, innovation, feasibility, and precision—ideally, beauty and simplicity as well. An epidemiological study reflects creativity to the extent that it generates knowledge that is relevant, new, valid, practical, and precise. Complexity may be a plus; it need not clash with simplicity and elegance. Relevance may be social, environmental, sanitary, clinical, biological, methodological, ethical, technological, intellectual.... Studies may blend, weave, knit, or weld such qualities in extraordinarily different ways.
3. A public health policy or program shows creativity when it is relevant, meaningful, useful, and attractive for populations, persons, companies, and institutions... when it is innovative, imaginative, simple... if effective and efficient in abating harmful determinants of health and significantly improving important health indicators. It may be morally and socially relevant if it increases freedom, justice, education, equity, or social cohesion. It needs to be culturally, environmentally, and economically sustainable. Creativity is an important value for epidemiology and the other health, life, and social sciences.<sup>26,38,58,202,290,462</sup>

**EPIDEMIOLOGICAL RESEARCH** Scientific research among human populations and defined groups of individuals into the frequency of occurrence, distribution and causes of phenomena of public health, clinical, social, or biological RELEVANCE, with valid selection of subjects and measurements, and formal CAUSAL INFERENCES on the DETERMINANTS of such phenomena.<sup>1,3,5,9,24-26,39-42,58,85,128,202,270,279</sup> See also CREATIVITY; INTEGRATIVE RESEARCH.

**INTEGRATIVE RESEARCH** Research that integrates knowledge, data, methods, techniques, reasoning, and other scientific and cultural referents from multiple disciplines, approaches, and levels of analysis to generate knowledge that no discipline alone could achieve. For instance, research that integrates cultural, economic, and other “macro-level” or contextual factors with individual factors, as in MULTILEVEL ANALYSIS; analyses of the relationships among gene structure, expression, and function; research on the relationships among molecular pathways, PATHOPHYSIOLOGY, and clinical phenotypes, as in clinical pharmacology and clinical genetics; research that integrates interactions among environmental, genetic, and epigenetic processes.<sup>1,13,26,33,80,146,202,323,339,411,548,799</sup> Epidemiology is an inherently integrative discipline, and so are many of its subspecialties, and approaches, like CLINICAL and MOLECULAR EPIDEMIOLOGY, SOCIAL EPIDEMIOLOGY OF ENVIRONMENTAL EPIDEMIOLOGY; DEVELOPMENTAL AND LIFE COURSE EPIDEMIOLOGY, for instance, attempts to integrate biological and social risk processes.<sup>23,25</sup> See also CLINICAL STUDY; HEALTH IMPACT ASSESSMENT; TRANSDISCIPLINARITY; REDUCTIONISM.

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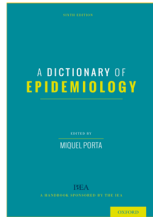
**INTEGRATION**

1. The action or process of integrating. To integrate: to make a new whole; to combine parts into a new system and get them to interact so that the system expresses functions unavailable to the parts. The organizing of elements to form a coherent whole or system. Integration of knowledge from different scientific disciplines yields knowledge that no discipline alone may achieve.
  2. In HEALTH PROMOTION and disease PREVENTION, strategies that target several risk factors, use multiple STRATEGIES at various levels of influence, and require INTERSECTORAL ACTION.<sup>123</sup> Integration entails multiplicity (more than one RISK FACTOR, level, sector, agent), and synergy resulting from multiplicity.<sup>17</sup>
- Integration is no less crucial to science than to the functioning of postmodern societies. Examples: quality public transportation favors integration of disabled individuals and disadvantaged groups into society; integration of racial and ethnic minorities into the educational system; integration of preventive services into clinical care.<sup>25,33,426,548</sup> Synonyms, analogies, and METAPHORS are here useful as well; integration involves and refers to interaction, dialogue, complicity, performance, symbiosis, sharing, pooling, porousness, amalgamation, merging, coalescing, fusing, welding, blending, weaving.

Source: Porta M, ed. A dictionary of epidemiology. 6th. edition (2014).

## RELEVANCE

1. **The importance for existing ideas or practices.** The degree to which a study, program, policy, or organization should theoretically change or can actually influence knowledge, beliefs, ideas, attitudes, decisions, actions, policies, structures, procedures, techniques, or processes of all sorts (social, cultural, political, organizational, individual, medical, biological, etc.).
2. In epidemiology, a relevant study or program may be one that makes a practical or a theoretical contribution to the identification, characterization, understanding, or solution of a public health, environmental, social, clinical, biological, or technological problem. EPIDEMIOLOGICAL RESEARCH usually aims at having social, environmental, or public health relevance; epidemiological studies often also have clinical, biological, methodological, or technological relevance.
3. In clinical and epidemiological research, *relevance* is commonly used as a synonym of importance and of SIGNIFICANCE. Statistical significance must be distinguished from clinical and public health significance. A statistically significant effect may be found in a study with a large number of participants and yet lack clinical or public health significance (because the magnitude of the effect is small, for instance). Hence, statistical significance should never be assumed to equal *significance*, and *significance* encompasses more than statistical significance. Clinical studies usually aim at being clinically significant, important, or relevant for the care of patients. Sometimes, epidemiological and clinical studies are also mechanistically relevant; e.g., they produce knowledge on mechanisms of disease.<sup>1,3,5,9,23,26,28,31,101,202,227</sup> See also MECHANISTIC EPIDEMIOLOGY; MINIMALLY IMPORTANT DIFFERENCE; SIGNIFICANCE, CLINICAL.



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VIEWPOINT

Viewpoint

THE LANCET • Vol 357 • March 3, 2001

### Misconceptions about the use of genetic tests in populations

Paolo Vineis, Paul Schulte, Anthony J McMichael

#### False metaphors for DNA

The emphasis on genetic testing (which has a clear commercial motivation) is based on false metaphors of the role of DNA and genes. One common metaphor compares the gene to a computer program—ie, the gene is a set of instructions to reach a certain goal. However, a computer program merely executes the instructions, without changing them on the basis of context. In fact the relations between genotype and phenotype are much more complex than usually depicted in popular accounts.

GuardianUnlimited

## Clinton and Blair hail gene 'triumph'

"Today we are learning the language in which God created life," Mr Clinton said.

Bill Clinton today congratulated scientists on a "stunning and humbling achievement" in a joint announcement with Tony Blair called to mark the decoding of the human genome.

Speaking from the White House, Mr Clinton said: "Our children's children will only know cancer as a constellation of stars" and hailed the completion of the project after a 10-year race that cost billions.

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Britain's Prime Minister Tony Blair smiles during

### False metaphors for DNA

The emphasis on genetic testing (which has a clear commercial motivation) is based on false metaphors of the role of DNA and genes. One common metaphor compares the gene to a computer program—ie, the gene is a set of instructions to reach a certain goal. However, a computer program merely executes the instructions, without changing them on the basis of context. In fact the relations between genotype and phenotype are much more complex than usually depicted in popular accounts. Jeffrey Lewis has proposed a much better metaphor: “if the genome can be seen as a text or a script, then its phenotypic expression can be seen as a performance of that script, bringing the text to vibrant and unique life just as actors on a stage bring life to the words on a page”.<sup>1</sup>

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**organism = a performance of the genomic text.**

#### *The Metaphor Itself*

I would like to add an additional dimension to this metaphor to expand its scope in order to incorporate the phenotype. Pollack's metaphor is ultimately a metaphor of the genome and has little to say about the organism itself. Building upon the idea of the genome as a text, I suggest that an organism should be viewed as a performance of that text. With this metaphor, I hope to create a concise way to express the complexity of biological development while simultaneously acknowledging the validity of the strategy of reductionism.

Lewis J. The performance of a lifetime: a metaphor for the phenotype.  
*Perspectives in Biology & Medicine* 1999.

**organism = a performance of the genomic text.**

**We need to reshape the guiding metaphors used to interpret the genome's causal significance.**

**The metaphors that molecular biologists have used to present their work have failed to convey the complex relationship between genotype and phenotype.**

Once the complexities of DNA's context-dependence are taken into account, pure genetic upward causation is an insufficient explanation.

Contexts: Genomic  
Cellular  
Organismic  
Pathophysiological  
Environmental

Lewis J. The performance of a lifetime: a metaphor for the phenotype.  
*Perspectives in Biology & Medicine* 1999.

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The metaphor offers a number of useful entailments. When viewed in this way, the biochemical apparatus that manipulate DNA and enable its expression are actors performing on a cellular stage. They are responsible for reading the script, interpreting it, and physically expressing it in a meaningful way. (Throughout this paper I will be referring to performance in this sense, and not in the sense of improvisational or unscripted theater.) The physical and biochemical laws that set the parameters within which the cellular apparatus expresses the text are the lighting and scenery. They determine the immediate environment, mood, and atmosphere, and physically constrain the performance. In addition, this metaphor sees performance as a process dependent upon both environmental constraints and historical contingencies. The extent to which performances of the same text can vary should inform our judgment concerning the relationship between our bodies and our genes. Finally, seeing biology in light of performance can allow us to reassess our roles as scientists and physicians, and suggests that there are many, equally valid strategies for evaluating and improving the human condition.

Lewis J. The performance of a lifetime: a metaphor for the phenotype.  
*Perspectives in Biology & Medicine* 1999.

**Beveridge:**

The important thing to realize is that the conjuring up of the idea is not a deliberate, voluntary act. It is something that happens to us rather than something we do.

It is not possible deliberately to create ideas or to control their creation. When a difficulty stimulates the mind, suggested solutions just automatically spring into the consciousness. The variety and quality of the suggestions are functions of how well prepared our mind is by past experience and education pertinent to the particular problem.

It happened in class. (The idea for the genome / jazz metaphor). I was explaining Lewis' metaphor.

Lewis J. The performance of a lifetime: a metaphor for the phenotype. *Perspectives in Biology & Medicine* 1999.

## The genome sequence is a jazz score

Miquel Porta

The main purpose of this paper is to suggest a metaphor—among many possibly valid and evocative—for the role of genes in complex chronic diseases. It is based on the inherent role of host-environmental interactions on the expression of low-penetrant genes. The relationship between an individual's genetic makeup and its phenotypic expression can be likened to the relationship between a jazz score and the performed music.

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The screenshot shows a Kindle book interface. On the left, there is a sidebar with the book title 'The Art of Scientific Investigation (Paperback) by W. I. B. Beveridge', a star rating of 4.5 (18 reviews), and a price of \$12.00. Below this, there are promotional messages about one-day shipping and a free app. The main content area on the right displays the book's table of contents with five sections: I. PREPARATION (Study, Setting about the Problem), II. EXPERIMENTATION (Biological experiments, Planning and assessing experiments, Misleading experiments), III. CHANGE (Illustrations, Role of chance in discoveries, Recognising chance opportunities, Exploiting opportunities), IV. HYPOTHESIS (Illustrations, Use of hypothesis in research, Precautions in the use of hypothesis), and V. IMAGINATION (Productive thinking). At the bottom, there are two search bars: one for 'metaphor' and one for 'jazz', both showing '0 results for [term]'. Purple arrows point to the search bars and the book title.

*The genome is thus like the innumerable scores that a jazz aficionado would play during all her life, some with great fidelity to the original musical text, many just—but deeply—inspired by it, still many others almost totally invented, whether improvised or consciously crafted. Surely the music that she expresses stems from the scores (through a marvellously complex process); but well beyond technique and script, every instant the unique music expresses what the musician knows, feels, and wishes to play. (Once, the origin of the music is a scent she smelled in infancy; once, a recent love loss; often the 'source code' is unknown.) And the music grows and evolves: with time—and, much more, with the people and places where it swells and flows. Stemming from the score. Sensitive to the other musicians with whom she plays. Delicately responsive to the audiences to whom and with whom she feels, every time of her lifetime.*



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*International Journal of Epidemiology* 2003

### Metaphors and jazz and genetics: three words of caution

**1: There are many ways to understand the nature, attributes and functions of metaphors; I here use just one.**

**2: No single metaphor could grasp the multiple realities, meanings and implications that the human genome sequence holds; I here emphasise just a couple.**

**3: Jazz is so diverse...!**

The style of a jazz musician is unique.  
Why is it unique? Noy easy to tell...

A specific performance depends on:

- (a) the original themes, the scripts he uses;
- (b) his personal story, the music he has listened to, the musicians he has played with, daily training & practice;
- (c) his personal talent, something innate;
- (d) the mood of the moment;
- (e) the interactions with the environment, the dialogue with the audience...

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**What is crucial in DNA functioning is the double ability**

- **to preserve the message through generations (stability), and**
- **to adapt to a changing environment** through an array of different functions:
  - DNA repair, or apoptosis in case of serious damage
  - hypermutability in bacteria to overcome environmental stress
  - mutations and selection to provide better adaptation to changing environments

**Therefore, in DNA we have a balance between conservation, improvisation, and reuse of old structures for different purposes.**

## Why the metaphor of jazz?

The script of a ballad, the original text (e.g., *Let's get lost*), is frequently used for "adaptation" and interpretation,

like, in the case of DNA, the original sequence is "reinterpreted" depending on the context based on mechanisms as

- Methylation of promoters
- Alternative splicing

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- Methylation of promoters, i.e., change in the expression of genes, which are transcribed or not into RNA (and translated into proteins) depending on need.

- Alternative splicing: the old equation "one gene - one protein" is no longer true, each gene can be used to produce different proteins, even combining sequences with adjacent genes.

The original DNA sequence is "interpreted" depending on the context based on such mechanisms.

- Methylation of promoters, i.e., change in the expression of genes, which are transcribed or not into RNA (and translated into proteins) depending on need.

- Alternative splicing.

yet, when I crafted the genome / jazz metaphor I did not have in mind many specific mechanisms

The original DNA sequence is "interpreted" depending on the context based on such mechanisms.

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## The NEW ENGLAND JOURNAL of MEDICINE

Table 1. Representative List of Organisms with Fully Sequenced Genomes.

Organism	Classification	Genome Size*	Estimated No. of Protein-Coding Genes†
Human ( <i>Homo sapiens</i> )	Placental mammal	3.2 Gb	19,042
Chimpanzee ( <i>Pan troglodytes</i> )	Placental mammal	2.7 Gb	19,000
Mouse ( <i>Mus musculus</i> )	Placental mammal	2.6 Gb	20,210
Dog ( <i>Canis familiaris</i> )	Placental mammal	2.4 Gb	19,300
Platypus ( <i>Ornithorhynchus anatinus</i> )	Monotreme	2.2 Gb	18,527
Rice ( <i>Oryza sativa</i> )	Plant	389 Mb	37,544
Mosquito ( <i>Anopheles gambiae</i> )	Insect	278 Mb	15,189
<i>Plasmodium falciparum</i> (organism causing malaria)	Protozoa	22.8 Mb	5,300
Yeast ( <i>Saccharomyces cerevisiae</i> )	Fungus	12.1 Mb	6,607
<i>Escherichia coli</i>	Bacterium	4.6 Mb	3,200
Human immunodeficiency virus	Retrovirus	9.1 Kb	9

\* Kb denotes kilobases ( $10^3$ ), Mb megabases ( $10^6$ ), and Gb gigabases ( $10^9$ ).

† Because the process of predicting protein-coding sequences is complex, estimates of gene numbers vary in the literature and change over time.

Feero WG, Guttmacher AE, Collins FS. Genomic medicine —an updated primer. NEJM 2010



Joan Miró (izquierda) y Josep Lluís Sert, en el Museo del Prado. F. CATALA-ROCA

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## La fama

Haber visto crecer a Buenos Aires, crecer y declinar.  
Recordar el patio de tierra y la parra, el zaguán y el aljibe.  
Haber heredado el inglés, haber interrogado el sajón.  
Profesar el amor del alemán y la nostalgia del latín.  
Haber conversado en Palermo con un viejo asesino.  
Agradecer el ajedrez y el jazmín, los tigres y el hexámetro.  
Leer a Macedonio Fernández con la voz que fue suya.  
Conocer las ilustres incertidumbres que son la metafísica.  
Haber honrado espadas y querer razonablemente la paz.  
No ser codicioso de islas.  
No haber salido de mi biblioteca.  
Ser Alonso Quijano y no atreverme a ser don Quijote.  
Haber enseñado lo que no sé a quienes sabrán más que yo.  
Agradecer las dones de la luna y de Paul Verlaine. [...]

[...] Haber urdido algún endecasílabo.  
Haber vuelto a contar antiguas historias.  
Haber ordenado en el dialecto de nuestro tiempo  
las cinco o seis metáforas.  
Haber eludido sobornos.  
Ser ciudadano de Ginebra, de Montevideo, de Austin y  
(como todos los hombres) de Roma.  
Ser devoto de Conrad.  
Ser esa cosa que nadie puede definir: argentino.  
Ser ciego.  
Ninguna de esas cosas es rara y su conjunto me depara  
una fama que no acabo de comprender.

Jorge Luis Borges, La fama.

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... it may thus be warranted to remember the radical  
warning –the fascinating suspicion– of Borges:

**“[...] *es quizá un error suponer que puedan inventarse metáforas. Las verdaderas, las que formulan íntimas conexiones entre una imagen y otra, han existido siempre; las que aún podemos inventar son las falsas, las que no vale la pena inventar.*”**

J.L. Borges. Nathaniel Hawthorne.  
In: Otras inquisiciones.



... it may thus be warranted to remember the radical warning –the fascinating suspicion– of Borges:

***“[...] it is perhaps an error to assume that metaphors can be invented. The true metaphors, those that formulate intimate connections between an image & another, they have always existed; the metaphors we can still invent are the false metaphors, those that it is not worth inventing.”***

J.L. Borges. Nathaniel Hawthorne.  
In: Otras inquisiciones.

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*It is not possible to do the work of science without using a language that is filled with metaphors.*

Richard C Lewontin

***“[...] it is perhaps an error to assume that metaphors can be invented. The true metaphors, those that formulate intimate connections between an image & another, they have always existed; the metaphors we can still invent are the false metaphors, those that it is not worth inventing.”***

J.L. Borges. Nathaniel Hawthorne.  
In: Otras inquisiciones.

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FOR YOUR ATTENTION**

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IMIM Institut de Recerca Hospital del Mar Parc de Salut MAR Barcelona **PRBB** Parc Recerca Biomèdica Barcelona **ciberesp** Centro de Investigación Biomédica en red Epidemiología y Salud Pública **UAB** Universitat Autònoma de Barcelona Facultat de Medicina

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**EPINOR**  
NASJONAL FORSKERSKOLE I POPULASJONSBASERT EPIDEMIOLOGI

# Las quiero a morir

*Este elogio del goce y el gozo masivo de la música cuestiona si sabemos apreciar, sin remilgos ni beatitudes digitales, los beneficios humanos que las nuevas tecnologías pueden estar haciendo realidad.*

[https://www.geyseco.es/epi2014/documentos/2012\\_CLAVES-beyondSpotify.pdf](https://www.geyseco.es/epi2014/documentos/2012_CLAVES-beyondSpotify.pdf)

Claves de razón práctica  
enero-febrero 2013

MIQUEL PORTA SERRA

De repente me alarma descubrir que llevo semanas escuchando pasmado una versión de Jarabe de Palo de una romántica canción (no diré cuál, pero en menos de 10 segundos muchos lectores lo verán: haciendo clic donde ellos saben). Y lo que es peor, Pau Donés la canta junto a Alejandro Sanz... Como no creo en la bioquímica del amor ni en la neurociencia de las emociones, en mi tablero de a bordo se encienden ciertas *leds* de horror. Porque, a mayor abundamiento, la canción la escucho también docenas de veces en una versión francesa, en una de Muchachito Bombo Infierno y hasta en una muy estimable de Shakira. ¡Diablos!



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# CLAVES

Directores: Javier Padilla / Fernando Santer. Diciembre 2007. Precio Br. Nº 158

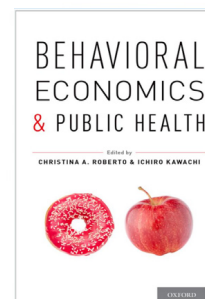
GENÉTICA

## LA SECUENCIA DEL GENOMA ES UNA PARTITURA DE JAZZ

MIQUEL PORTA SERRA

“Más allá de esta metáfora algo importante está en juego: el papel de la cultura, de la salud pública y de las otras ciencias sociales, de la salud y de la vida en la construcción social de riesgos y metáforas relacionadas con la genética y la salud.”

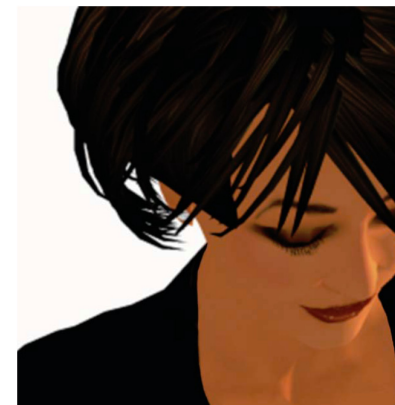
“the powerful notion of causal base rates...”  
“the neglect of base-rate information is a cognitive flaw...”



“denominator neglect, duration neglect, availability cascades, substitution, insensitivity to the quality of information, risk aversion, intuitive judgments under uncertainty, framing, priming, anchoring...”

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World Health Organization

<http://www.who.int/reproductive-health/artforhealth/gallery.htm>

www.thelancet.com Vol 368 December 16, 2006

[www.elisabettafarina.com](http://www.elisabettafarina.com)

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sculptor Anish Kapoor. /PHILLIPE CHANCEL

Anish Kapoor

Proc. R. Soc. Lond. B 205, 581-598 (1979) 581  
Printed in Great Britain

The spandrels of San Marco and the Panglossian paradigm:  
a critique of the adaptationist programme

By S. J. GOULD AND R. C. LEWONTIN  
Museum of Comparative Zoology, Harvard University,  
Cambridge, Massachusetts 02138, U.S.A.

An adaptationist programme has dominated evolutionary thought in England and the United States during the past 40 years. It is based on faith in the power of natural selection as an optimizing agent. It proceeds by breaking an organism into unitary 'traits' and proposing an adaptive story for each considered separately. Trade-offs among competing selective demands exert the only brake upon perfection; non-optimality is thereby rendered as a result of adaptation as well. We criticize this approach and attempt to reassert a competing notion (long popular in continental Europe) that organisms must be analysed as integrated wholes, with *Baupläne* so constrained by phyletic heritage, pathways of development and general architecture that the constraints themselves become more interesting and more important in delimiting pathways of change than the selective force that may mediate change when it occurs. We fault the adaptationist programme for its failure to distinguish current utility from reasons for origin (male tyrannosaurs may have used their diminutive front legs to titillate female partners, but this will not explain *why* they got so small); for its unwillingness to consider alternatives to adaptive stories; for its reliance upon plausibility alone as a criterion for accepting speculative tales; and for its failure to consider adequately such competing themes as random fixation of alleles, production of non-adaptive structures by developmental correlation with selected features (allometry, pleiotropy, material compensation, mechanically forced correlation), the separability of adaptation and selection, multiple adaptive peaks, and current utility as an epiphenomenon of non-adaptive structures. We support Darwin's own pluralistic approach to identifying the agents of evolutionary change.

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Epidemiology • Volume 15, Number 1, January 2004

## Genetic Testing for Sale

Paolo Vineis\* and David C. Christiani†

### SCIONA /BODY SHOP

More expansive claims appear in advertisements for Sciona found in the European Body Shop stores: "Find out how your body copes with the following and what you need to eat to improve your body's efficiency: Detoxifying—Is your body as efficient as it could be at removing toxins? Antioxidant Capacity—Does your body cope with free radicals as well as it should? Tissue Repair—Do you need to boost your vitamin intake to ensure effective tissue repair? Alcohol Metabolism—Can your body cope with alcohol consumption?"

Ad: "Order your genetic test kit today"  
"Preventive health profile" • \$50 • 19 genes  
"...You have a favorable profile  
that helps fight oxidative stress..."

### U.S. Government Accountability Office (GAO)

Nutrigenetic testing

"...That industry represents a fraudulent mutation  
of the genetics industry..."

<sup>1</sup>GAO, *Nutrigenetic Testing: Tests Purchased from Four Web Sites Mislead Consumers*, GAO-06-977T (Washington D.C.: July 27, 2006).

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## DIRECT-TO-CONSUMER GENETIC TESTS

### Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices



GAO-10-847T

## What GAO Found

GAO's fictitious consumers received test results that are misleading and of little or no practical use. For example, GAO's donors often received disease risk predictions that varied across the four companies, indicating that identical DNA samples yield contradictory results. As shown below, one donor was told that he was at below-average, average, and above-average risk for prostate cancer and hypertension.

### Contradictory Risk Predictions for Prostate Cancer and Hypertension

Gender	Age	Condition	Company 1	Company 2	Company 3	Company 4
Male	48	Prostate cancer	Average	Average	Below average	Above average
		Hypertension	Average	Below average	Above average	Not tested

Figure 1: Selected Contradictory Risk Predictions for Donor 1

Gender	Age	Condition	Company 1	Company 2	Company 3	Company 4
Female	37	Leukemia	Above average	Below average	Average	Not tested
		Breast cancer	Average	Above average	Average	Above average

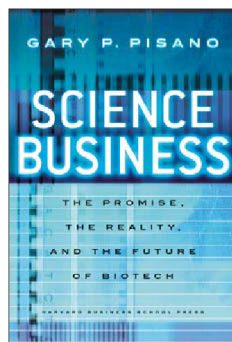
GAO-10-847T

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## Science Business: the Promise, the Reality, and the Future of Biotech

Gary P Pisano. Harvard Business School Press, 2006. Pp 237.  
US\$29.95. ISBN 1-591-39840-1.

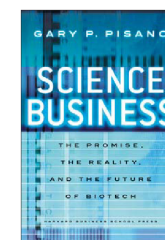


Book

www.thelancet.com Vol 369 June 2, 2007

What happened to the biotechnology revolution?

Pisano argues that “monetization of IP” has been a powerful shaping force in biotech. The idea behind monetization of IP is that you do not need to actually develop a product; you can just develop a piece of IP, and then capture financial returns through licensing or other market arrangements. This has worked wonderfully in semiconductors and software; but monetization of IP only works there because of some very specific conditions. You need to have a very modular knowledge base; that is, you need to be able to break up a “big puzzle” into its relatively independent pieces so that a particular piece can be valued independently. So, we have been breaking up the pieces of the puzzle into independent pieces when what matters is the way we integrate the pieces. Integration matters a lot.



<sup>1</sup> Excerpts of an interview by Sean Silverthorne, editor of the Harvard Business School newsletter “Working knowledge,” to Gary Pisano, author of *Science Business: The Promise, the Reality, and the Future of Biotech* (Harvard Business School Press, 2006). Published 13 November 2006 [12].

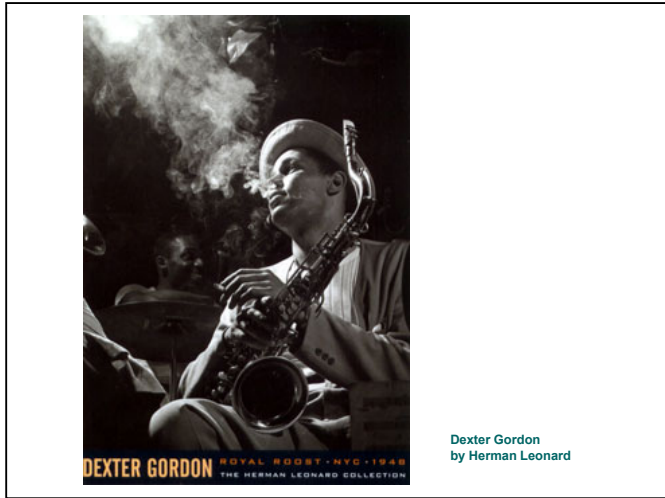
Journal of Clinical Epidemiology 60 (2007)

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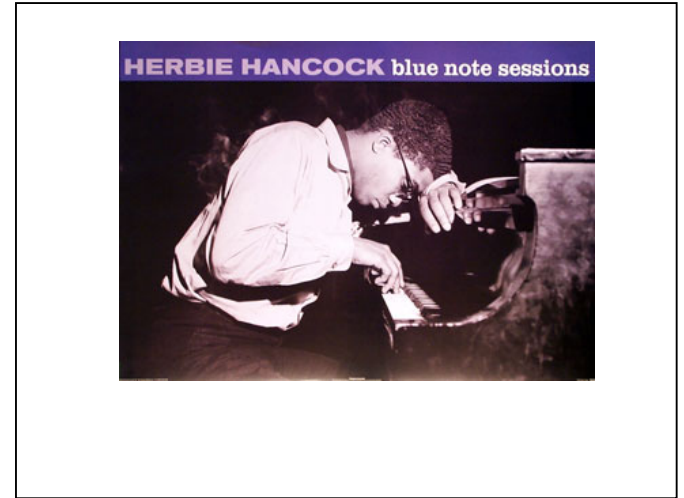
- According to Arthur D. Levinson, Chief Executive Officer of Genentech, “Since 1976, when our company was founded, the biotech industry has lost \$90 billion in aggregate. I think it’s the biggest money-losing industry of all time. It is hemorrhaging. There are some exceptions: We are doing well, and Amgen is doing well, But for most of the 1,300 to 1,400 companies -300 or 400 of them public- this is a money-losing enterprise.”<sup>2</sup>

<sup>2</sup> Chase M. How Genentech wins at blockbuster drugs. CEO to critics of prices: “Give me a break”. The Wall Street Journal; 5 June 2007; page B1  
Journal of Clinical Epidemiology 60 (2007)



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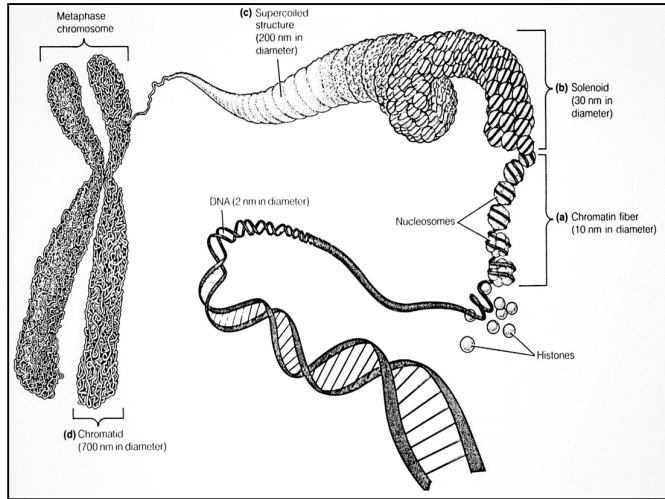
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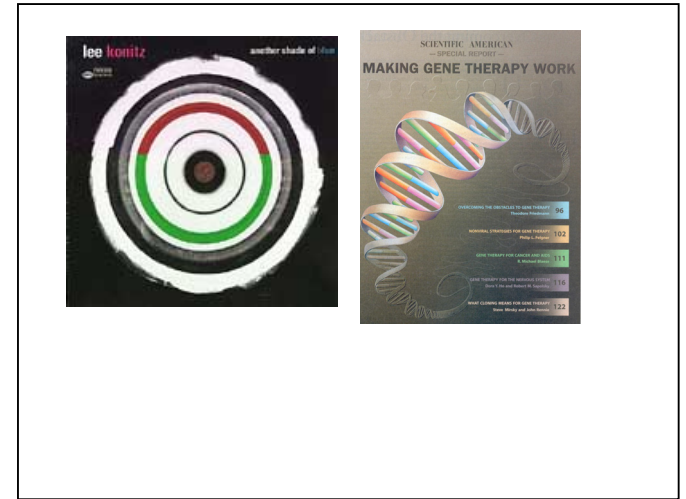
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