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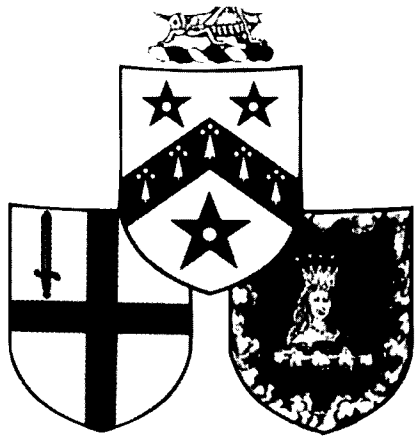

GENES IN THE HEADLINES
PROMISES, PROBLEMS AND PANICS

A Lecture by

PROFESSOR HILARY ROSE & PROFESSOR STEVEN ROSE
Gresham Professors of Physic

4 October 1999

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Gresham Lectures in Physic 1999-2000

Lecture 1, October 4th 1999

Professor Hilary Rose & Professor Steven Rose

Genes and genetics are front page news, and to introduce this series of lectures we want, as respectively a biologist and a sociologist, to discuss some of these headlines, to try to look a little behind them and their implications, and to introduce a number of themes which will inform the later lectures. To do this we see today less as a lecture and more as a performance with our chief props as transparencies. We speak in turns as what we want to do demonstrate the difference between sociolkogists and sociologist of the pair of us whose task is to begin that performance.

Gene talk is everywhere, it can be funny:

Blair cartoon

It can be serious, collecting funds for research to help children and their families carrying severe rare genetic problems. The numbers may be so small that their problems are uninteresting to industry. Then compassion, social solidarity with vulnerable others, and technical skill not investment opportunities come into play.

Jeans for Genes

Gene talk - and even more gene products- can generate immense moral anxiety

Dolly her true story

Or the media and the scientists between them can spin a story on the back of Dolly to generate something akin to moral panic. Here is one such front page news item - in the same issue of the Sunday Times from which the previous transparency came.

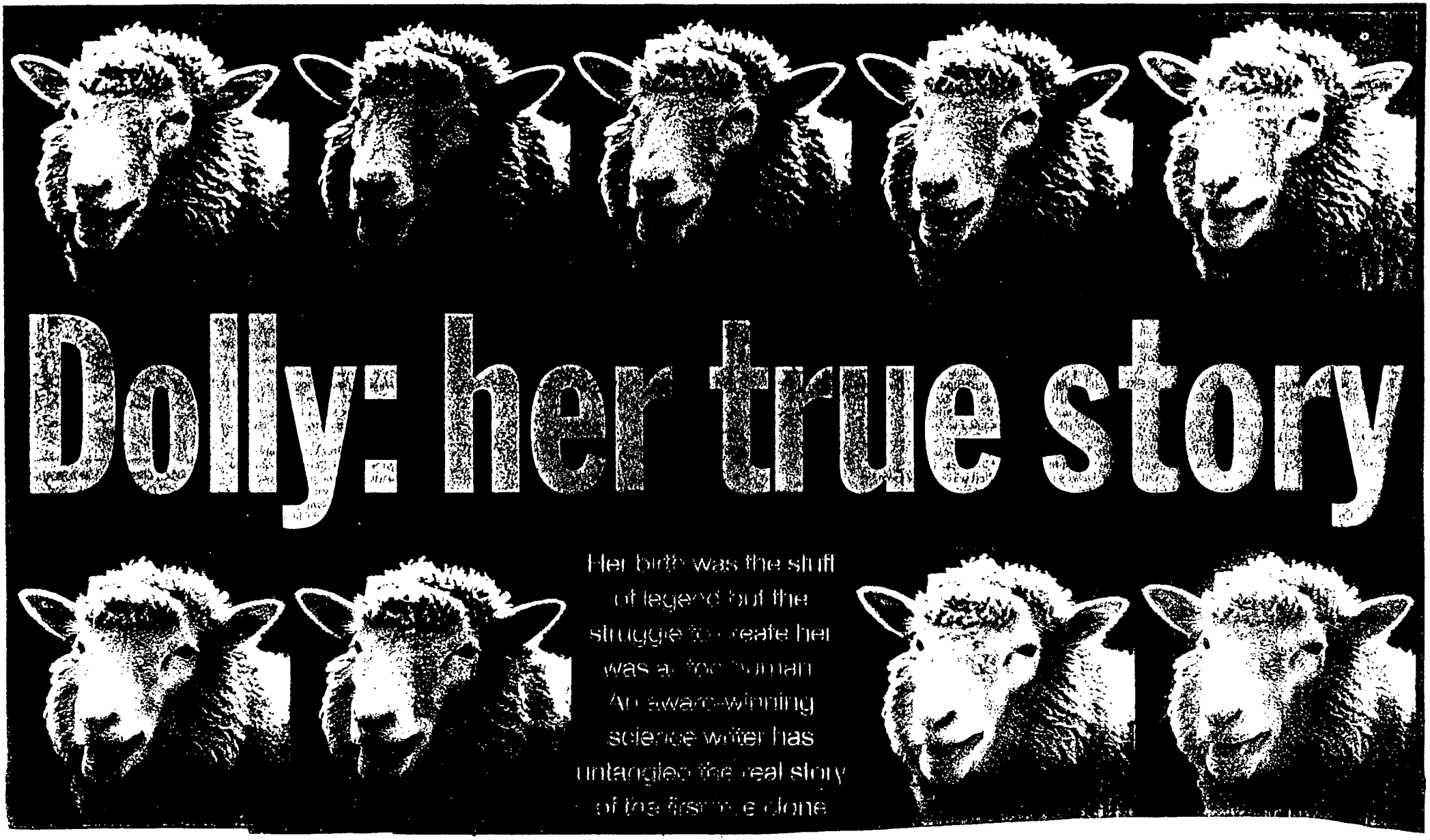
Headless frogs

And while some are made uneasy by the thought of the genetic manipulation of species other than humans, it is as we see with the

29.9.99.
Guardian.

THE SUNDAY TIMES

NEWS REVIEW



Dolly: her true story

Her birth was the stuff of legend but the struggle to create her was a [illegible] woman. An award-winning science writer has untangled the real story of the first [illegible] clone

DIEU ET MON DROIT

THE SUNDAY TIMES

No 9,034 19 OCTOBER 1997 Price £1

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ALLERGY ALERT

THE MODERN PLAGUE: SPECIAL ISSUE

Headless frog opens way for human organ factory

SCIENTISTS have created an embryo of a frog without a head, raising the prospect of engineering headless human clones which could be used to grow organs and tissues for transplant surgery.

The headless frog embryos have not been allowed to live longer than a week, but the scientists believe the technique could be adapted to grow human organs such as hearts, kidneys, livers and pancreases in an embryonic sac living in an artificial womb.

If human cloning becomes possible — and many scientists believe it is inevitable following the birth of Dolly, the first adult sheep clone — the two breakthroughs could be combined so that people requiring transplants could have organs grown to order from their own cloned cells.

The advantage of using human clones is that organs could be grown that would perfectly match the patient requiring a transplant and there would be no need for drugs to prevent tissue rejection. It would also solve the increasing shortage of transplant organs.

Growing parts of human embryos to cultivate organs could bypass many legal restrictions and ethical concerns, because without a brain or central nervous system the "organ sacs" may not meet the technical definition of an embryo. The scientists nevertheless accept that many people would still find the research repugnant.

by Steve Connor and Deborah Cadbury

Jonathan Slack, professor of developmental biology at Bath University and a leading embryologist, says he can now create headless frog embryos relatively easily by manipulating certain genes. Using the technique, he has been able to suppress not only development of a tadpole's head, but also its trunk and tail. Under current Home Office rules, they are not considered animals until they are a week old, when they have to be destroyed.

He said the breakthrough could be applied to human embryos because the same genes perform similar functions in both frogs and humans.

Using intact cloned human embryos to grow organs would be out of the question because they would have to be killed and this would be equivalent to murder, Slack said.

"It occurred to me a halfway house could be reached. Instead of growing an intact embryo you could genetically reprogramme the embryo to suppress growth in all the parts of the body except the bits you want, plus a heart and blood circulation," he said.

Neither would it be acceptable to grow parts of a human embryo as an organ sac inside a woman's womb. "More acceptable might be taking a single cell and somehow growing a complete organ in a bottle from it," said Slack.

He nevertheless believes the enormous technical problems can be overcome. It was the cloning of frogs 30 years ago that led to the cloning of Dolly. Scientists at the Roslin Institute near Edinburgh, who created Dolly, said earlier this year that the first human clones could be produced within two years.

continued on back page

Dolly: her story News Review, pages 1-2

metaphor of the organ factory, the possibility of cloning transferred to humans that raises the temperature of moral concern.

How tall would you like your child, sir

Its life but not as we know it

Gene talk fills our newspapers, our television screens and our radio. Genetic science fiction packs the cinema out (Jurassic Park; Gattaca). Nor is gene talk limited to the scientific news items, or the debates over GMOs, it takes over even the advertisements. The master molecule of DNA, that icon of our geneticised times, is recruited to sell cars! For science and scientists this is a historic first.

Steve Jones

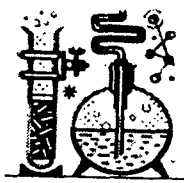
First through the successful Reith Lectures, then the book the scientist becomes a media figure. Then as a media scientist with bankable celebrity status, he is recruited by Renault to sell cars on television. The old gap between science and the market visibly closes.

BMW ads .

Renault's advertising people are not the only one to echoes the DNA evolutionary theme to sell cars. The Beamer series three claims it has "the driving gene" - it has the capacity to evolve into a true "aristocrat". Meanwhile gossip among the geneticists claims, true - false - apocryphal, that the DNA sequences shown as a huge backdrop to the series three Beamer , came from a dinosaur. Even as gossip the geneticists claim is that even while they sold their science they also committed cultural industrial sabotage. The joke however can only be enjoyed by a tiny elite who can read and recognise DNA sequences. It serves to comfort the geneticists that there is still a gap between their science and the commercial world they have so enthusiastically entered.

But just as science and scientists get into everyday culture so everyday culture gets into science, These advertisements for biotech firms and for equipment are taken from Nature and Science - the world's two most prestigious scientific journals.

Molecular ludo



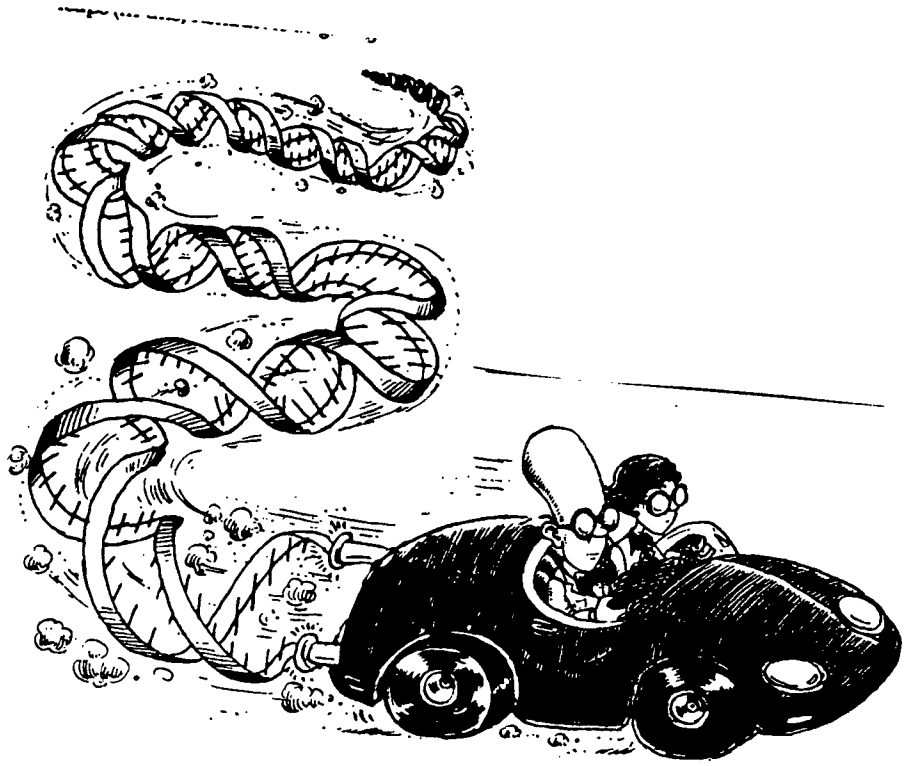
And how tall would you like your child sir?

A quiet revolution is underway. One that will change our lives in ways we can barely imagine. Such is the pace of discovery that most of us will live to see the ageing process slowed, if not reversed, and quite possibly dinosaurs brought back to life. We will be able to 'read' the personality of individuals before they are born and even choose the traits of our children. Yet the elite band of thinkers shaping our destiny remain largely unknown to us. In the first of two unique reports based on in-depth interviews on both sides of the Atlantic, **Henry Porter** offers a revealing portrait of the gene scientists and the way they view the new world they are creating. Today he profiles the (largely) publicly-funded purists; tomorrow the entrepreneurs racing to exploit the cracking of the human code

It's life, but not as we know it

Henry Porter on the scientists who are remaking mankind

FORD



75

Advertising Cars 1998-9 Winter
Steve Jones "evolved" Renault
Laguna.

BMW - DNA sequences.

BMW advertisement -Vanity Fair, November 1998

"Clearly, it's the driving gene."

The new BMW 3 Series...is a car for tomorrow, inheriting characteristics developed across three decades....automotive DNA for a new generation.

The BMW ad continues:

"its technological fingerprint saluted its heritage. BMW's particular strain of DNA was starting to kick in. If you wanted a well-bred car, the 3 series delivered an aristocrat.....[it] inherited the driving traits that had made the previous models so successful....

yacht

The same kind of advertisement puts an emphasis on speed and indicates the extent to which science shares the competitive values of industry.

mouse transit

It also indicates how far biological research has itself been industrialised

research inc.

Sentinel Mol Beacons

And how the new genetics is very much a technoscience - in which technology and science are indissolubly linked - both within the knowledge production process itself and also as its products. We will pick this up later in the lectures with story of sequencing DNA - from Sanger's fifteen year struggle crowned with a Nobel prize to today's robotic sequencer.

MJ RESEARCH

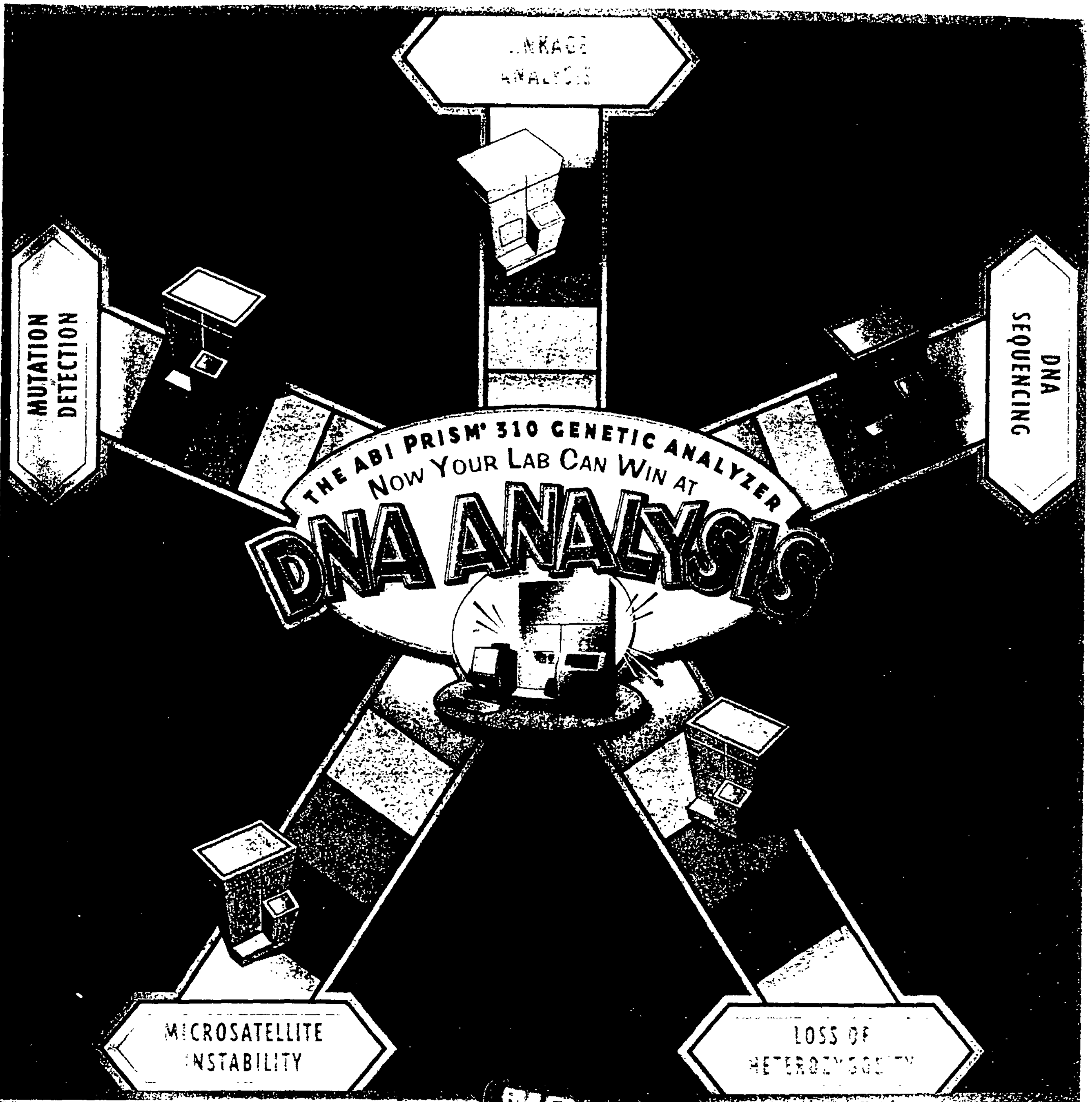
Elite molecular biologists and geneticists tend to own, have shares in or be well paid consultants to biotech industry. While this closing of the gap between science and industry may well aid innovation it carries with it problems about the 'independence' of scientists and their advice.

Clontec and Quiagen

Gene talk as we began is also about jokes. The joke is used in many ways not least as a marker of unease - a socially acceptable way of expressing criticism even hostility. Today we use gene talk to mock ourselves, and explain away everyday frailties: a moment of clumsiness, a sudden passion to eat chocolate, the impulse to succumb to another glass of wine. 'I must have a gene for it' we say. These are the everyday signs that we live in a geneticised culture.

<u>But we are not cultural dopes</u>. We don't simply absorb media or even scientific messages like sponges. Reading, as Gresham's professor of rhetoric would surely insist is an active not a passive business. We bring our histories, our knowledge, our experience of the everyday world to our reading.

Kennedy alcohol gene story .



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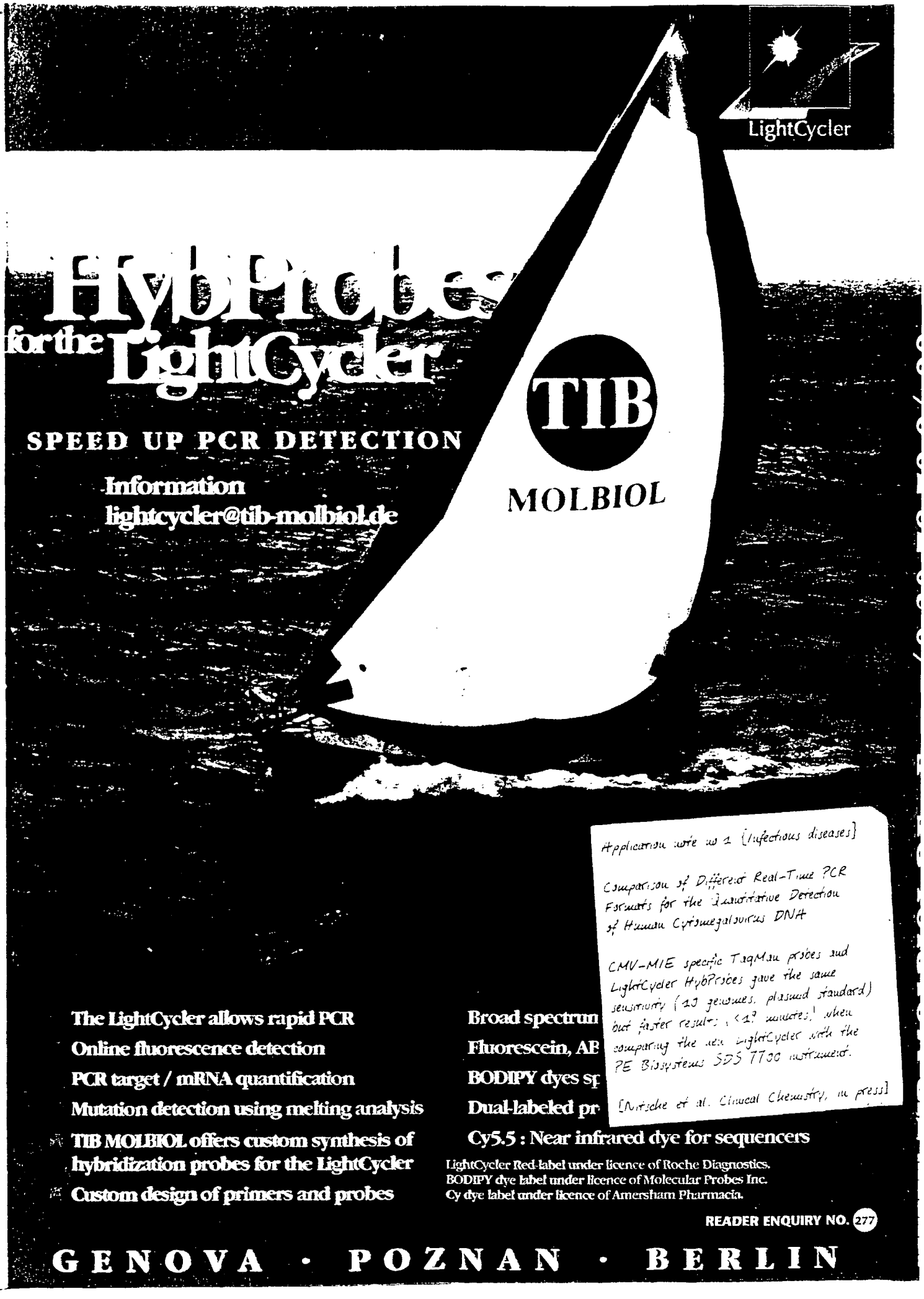
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Comparison of Different Real-Time PCR Formats for the Quantitative Detection of Human Cytomegalovirus DNA
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[Nitsche et al. Clinical Chemistry, in press]
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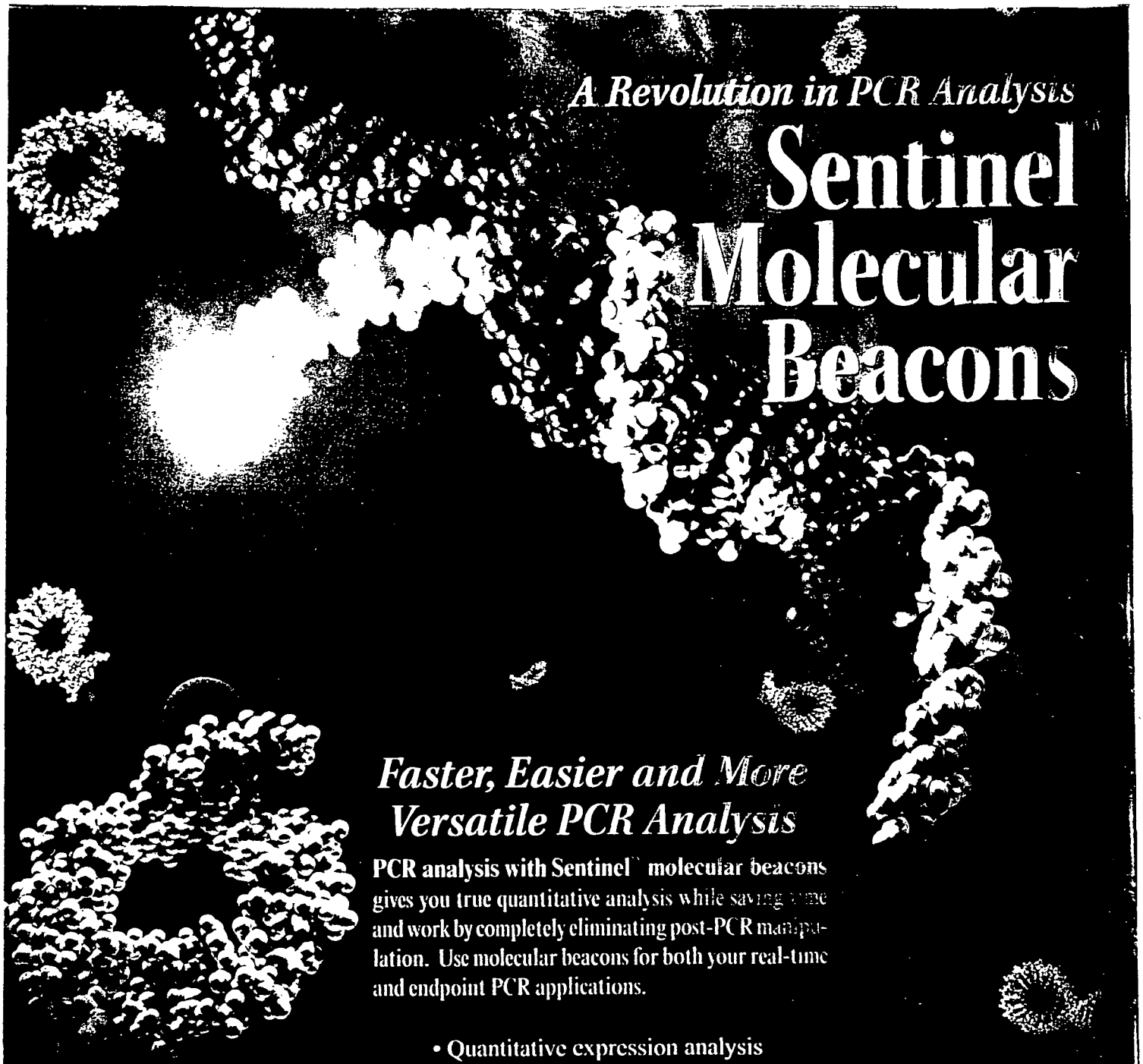

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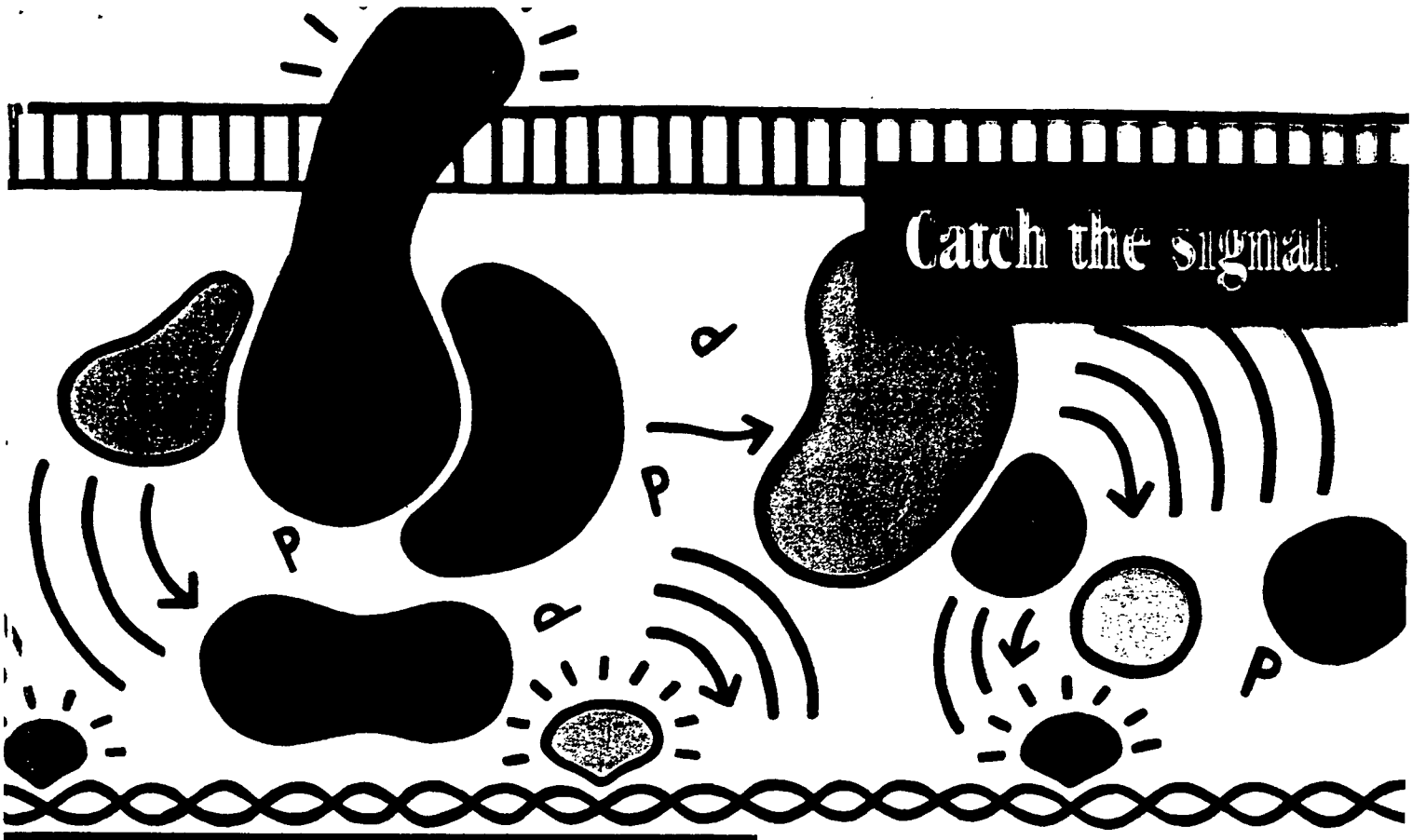

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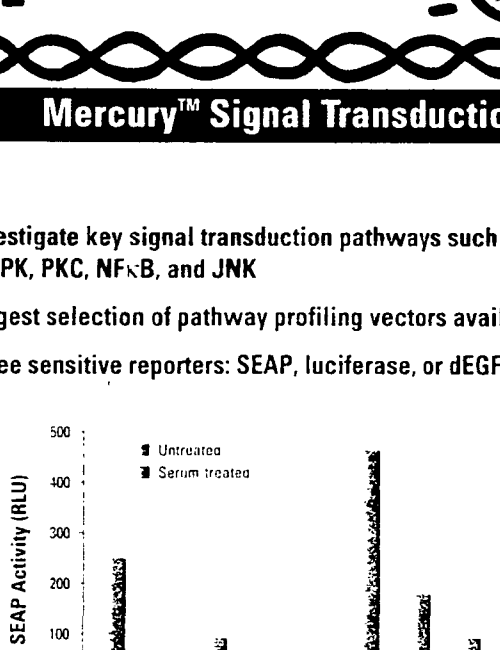

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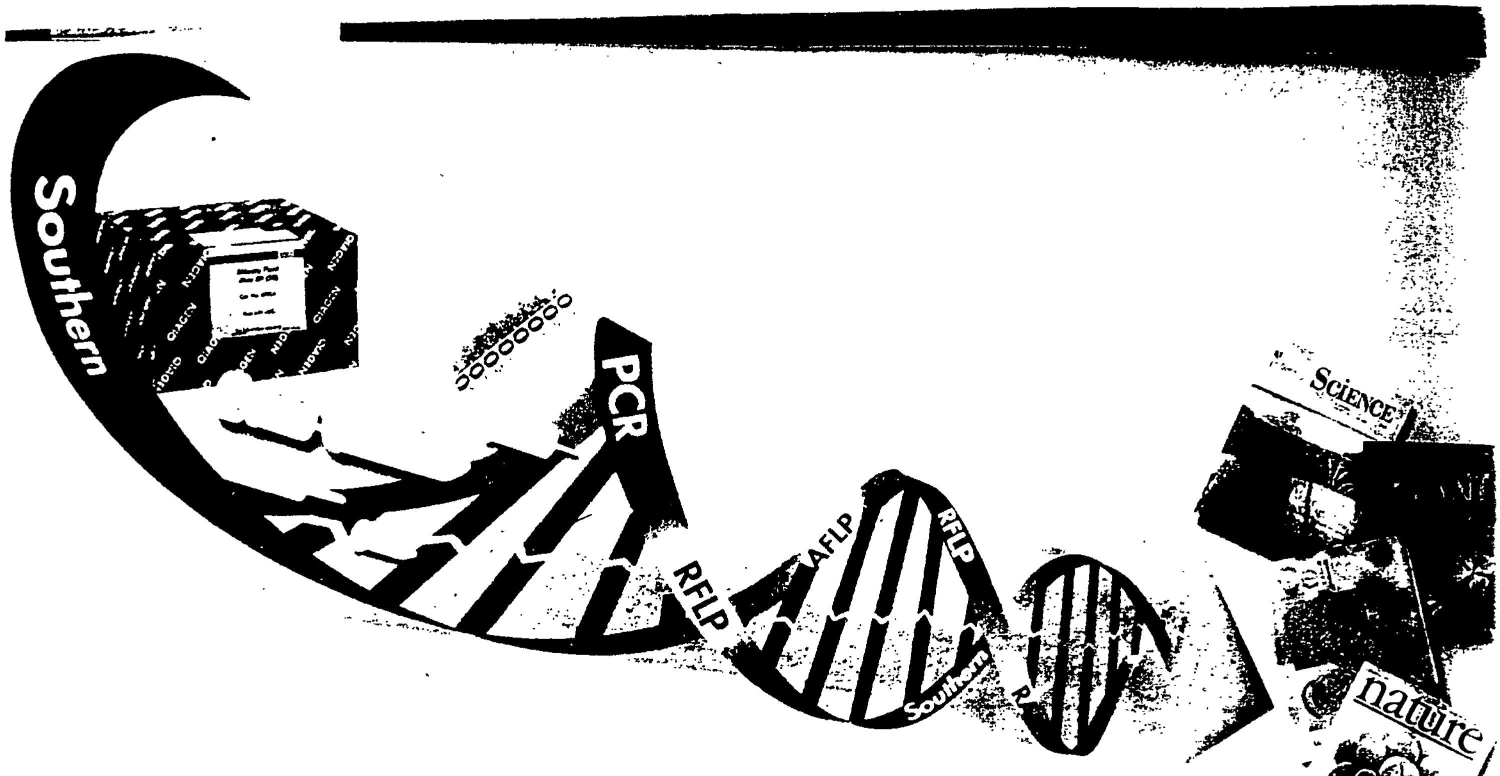

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Kennedy's 'alcohol genes'

ROBERT Kennedy Jr, son of the senator murdered in 1968, has said that alcohol problems are "in the genes" of the Kennedy political dynasty. In an interview to be broadcast on CBS television tomorrow, Mr Kennedy also says that he feels that he was "born alcoholic" and that "it wasn't something I became".

Several members of the Kennedy clan, which made a fortune out of bootlegging during Prohibition in the 1920s, have admitted to drink and drug problems over several years. Mr Kennedy, a New York environmental campaigner, was convicted of heroin possession 13 years ago. — *Martin Kettle, Washington.*

Guardian 16/9/97

But sometimes the joke that cartoonists make speaks to our unease at the claims of genetics

Genes for homosexuality cartoon

So what type of scientific claim is this joke based on?

It stems from a scientific paper, published in 1993 with a massive set of press releases and as a result huge media attention.

The paper's title was modest

Hamer transparency

but the researchers and their sponsors were not slow to spell out its potential implications

Born to be gay transparency

Critique of the scientific claims - Hamer looked for genetic markers in gay and straight brothers and found gay sibs were concordant for a gene marker on the X-chromosome - that is, inherited from their mothers. Later studies have failed to replicate, and this clearly cannot 'explain' homosexuality. Also note that it speaks only of male homosexuality. Nonetheless Hamer claims in debate that he proposes to go on to try to identify the gene and patent it - 'to prevent others from abusing it.'

This example can be multiplied many times. Take for instance the following paper:-

Brunner transparency

published with an accompanying press release claiming that the team had identified a gene for aggression - a claim specifically rejected by Brunner himself, though not his American colleagues, The MAOA gene - associated with a particular neurotransmitter in the brain which is also the target for much pharmaceutical research - began to be studied in animals too. One of the new genetic techniques - which we will be discussing in more detail in later lectures - makes it possible to delete - 'knockout' is the technical term specific genes from mice. What happens if this gene is indeed knocked out?

Cases paper transparency

These poor mice, which could barely survive beyond infancy, showed a scarcely surprising tendency to bite the experimenter when handled. Of all

"If homosexuality is inherited, shouldn't it have died out by now?"

Drawing by Booth; © 1993/The New Yorker Magazine, Inc.

Hamer, Dean H, Hu, S, Magnuson, VL, Hu, NN and Pattatucci, AML

"A linkage between DNA markers on the X-chromosome and male sexual orientation."

Science, v 261, pp321-327, 1993

The doubts that followed hard on the heels of the gay gene discovery in 1993 have only intensified the search for the origins of homosexuality, says *Vittoria D'Alessio*

Born to be GAY?

SOME parents cannot stomach the news that their son has embraced a gay lifestyle. But when Roger Gorski tells them that their sons have inherited "an immutable, behaviourally expressed, bimodal trait" rather like left-handedness, homosexuality assumes a whole new mantle of respectability.

"I recently spoke at a seminar for Mormon parents of gay children in Salt Lake City and it was amazing," says Gorski. "I felt like I was talking in a vacuum, with every word sucked up. It was the parents who were coming out."

Such meetings are all in a day's work for the neurobiologist from the University of California in Los Angeles. He welcomes the chance to tell angst-ridden parents a few biological facts: that homosexuality is a normal genetic variant, that it is not a lifestyle choice, a disease, or a mental illness, and that in all probability it was passed down from the person's mother.

Vindicated

Everyone leaves these cosy assemblies smiling—Gorski has dispensed some soothing news, gay men feel vindicated, parents can go back to loving their homosexual sons unconditionally. And Dean Hamer, the molecular geneticist from the National Institutes of Health near Washington DC, who, in 1993, discovered where in the genome the gay gene nestles, can pat himself on the back for fostering goodwill on earth.

Gorski has also contributed to the idea that gayness is biological in origin. In 1992, he showed that the anterior commissure, a bundle of nerves that connects a small region of the right and left sides of the brain's cortex, is larger in gay men than in straight. All the same, Gorski is the first to acknowledge that in the name of community spirit, the scientific fellowship is quietly blending fact with biological theory. For in reality, today's scientists are about as baffled by homosexuality as they have ever been.

In the intervening three years, Hamer's spectacular finding has started to look shaky. Some geneticists have poked holes in his original methodology, and others have failed to confirm the existence of the gay gene with their own studies.

But those disappointments have done nothing to dull the intense scientific and public interest in what triggers gayness. And if human genetics has drawn a blank in the past few years, new studies of fruit fly courtship are reinforcing the idea that, in the end, homosexuality will come down to the difference of a gene or two. Meanwhile, one Cornell psychologist has introduced a fresh twist to the ancient argument that homosexuality is an acquired rather than innate behaviour—with his controversial "exotic to erotic" theory of sexual orientation.

That gayness is at least partly genetic is just about indisputable. A man with a gay identical twin brother—that is a brother who to all intents and purposes shares all his genes—has a 52 per cent chance of being gay, and a man with a gay non-identical twin only a 22 per cent chance, according to a 1991 study from psychologist J. Michael Bailey at Northwestern University in Chicago.

'Parents can go back to loving their gay sons unconditionally'

X-rated

In their study, Hamer's team showed that specific genetic markers on a region of the X chromosome called Xq28 were shared by 33 of 40 pairs of gay brothers. Chance dictates that the brothers inherit either of their mother's X chromosomes at the same rate, that is that only 20 pairs of brothers should have shared the markers. Hamer concluded that within a region of 4 million DNA base pairs on the tip of the long arm of the X chromosome, lies a locus related to sexual orientation. He calls this locus GAY-1.

Harvard biologist Evan Balaban loathes the over-simplification of the gay gene topic by both scientists and journalists that accompanied Hamer's original identification of GAY-1. "I wish that some of the work was done a bit more carefully and presented more conservatively," said Balaban. "It can only lead to misunderstanding and disappointment."

Certainly, with the air still ringing from the trumpets and cymbals that accompanied the release of Hamer's original research paper, it comes as a great anticlimax that other scientists

"Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase A"

Brunner et al (1993) *Science* 262, 578-80

Eight men

'living in different parts of the country at different times'

across three generations showed

'an abnormal behavioral phenotype'

including

'aggressive outbursts, arson, attempted rape and exhibitionism.'

"Aggressive behavior and altered amounts of brain serotonin and norepinephrine in mice lacking MAOA"

Cases et al (1995)*Science* 268, 1763-8

the mouse pups show 'trembling, difficulty in righting and fearfulness...frantic running and falling over...[disturbed] sleep...propensity to bite the experimenter...hunched posture'

but nevertheless, these results support

'the idea that the particularly aggressive behavior of the few known human males lacking MAOA...is a more direct consequence of MAO deficiency.'

the deficits listed, Cases and his colleagues chose to highlight 'aggression' and the story was taken to confirm the Brunner results. There were indeed genes 'for aggression.'

From which followed a rush of books, newspaper articles and TV presentations

Genetics of antisocial behaviour

Mind to crime

Crime and damaged brains

Of course we need to be very careful about what we mean by 'aggression' - aggressive surgery, aggressive businessmen, aggressive soldiers... etc. All nuances are forgotten, and we end up with murderers in the US claiming diminished responsibility because they possess 'aggressive genes. ' research programmes aimed at explaining inner city violence as the result of genetic disorders in US youth, and drive-by shootings in Los Angeles explained by reference to knock-out mice!

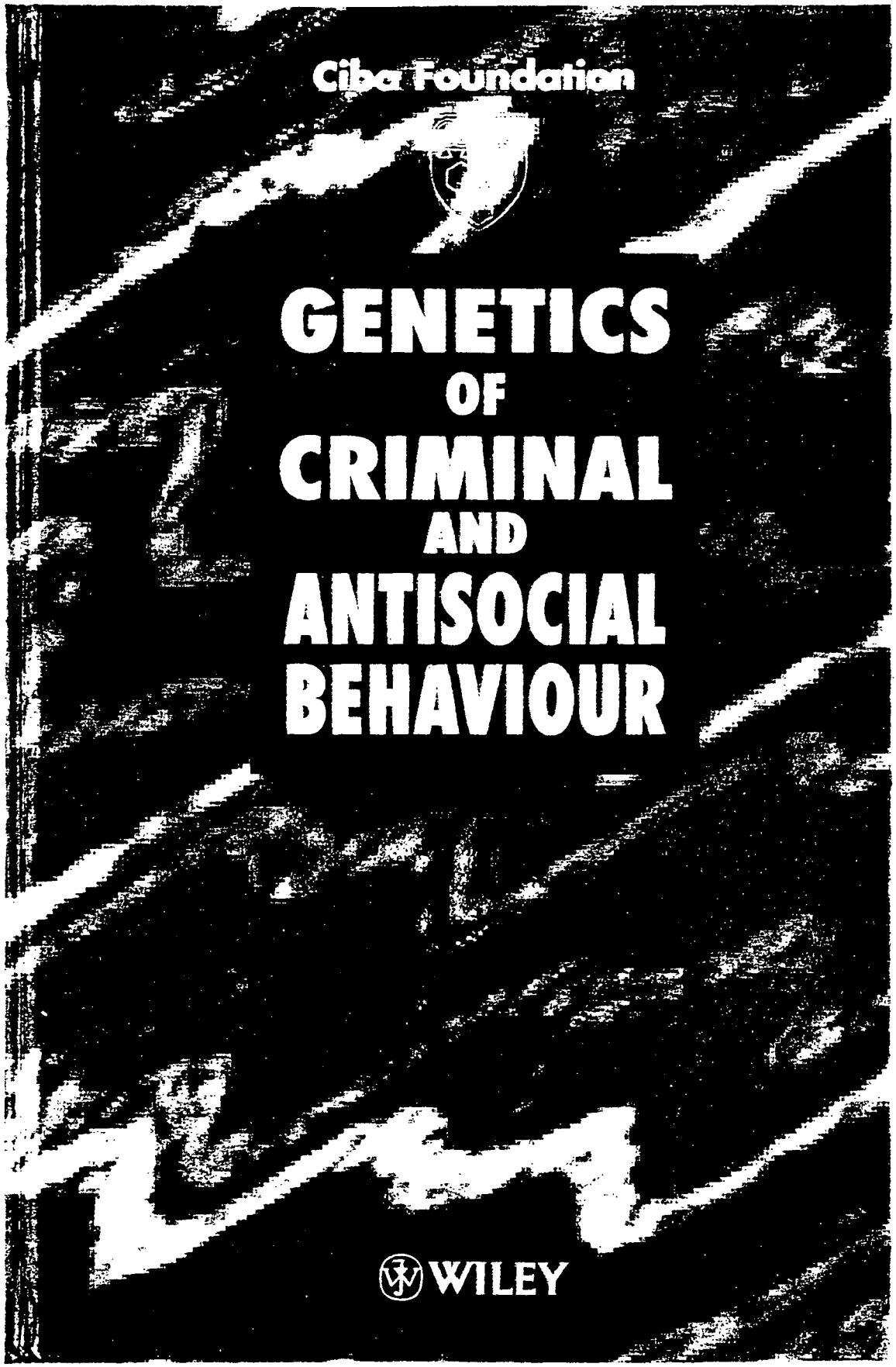
From the launching of the HGP in 1985 , science has made huge promises world's most prestigious scientific journals. The Koshland editorial in Science back in 1989 promising to cure everything from cancer to homelessnes today strikes most of us as absurd bordering on hubris, while a decade on the promises still need qualifying

Koshland Science (1989) claim

Even adverts for DNA technology maintain the promise-making activity.

Science (1999) *baby deafness gene*

At first sight an advert combining science and social relevance. Genetics is relevant to human problems - but let us read it more closely. First we see a slippage between one and plural genes as causal. To a biologist this is no small difference either in scientific explanation or in the possibility of therapeutic intervention. Then again deafness has multiple causes. Illness in childhood may have retreated in the face of powerful therapeutics but exposure to sheer decibelage - whether inflicted by the pursuit of pleasure or the lack of health and safety measures at work- is a growing cause of deafness in adult life.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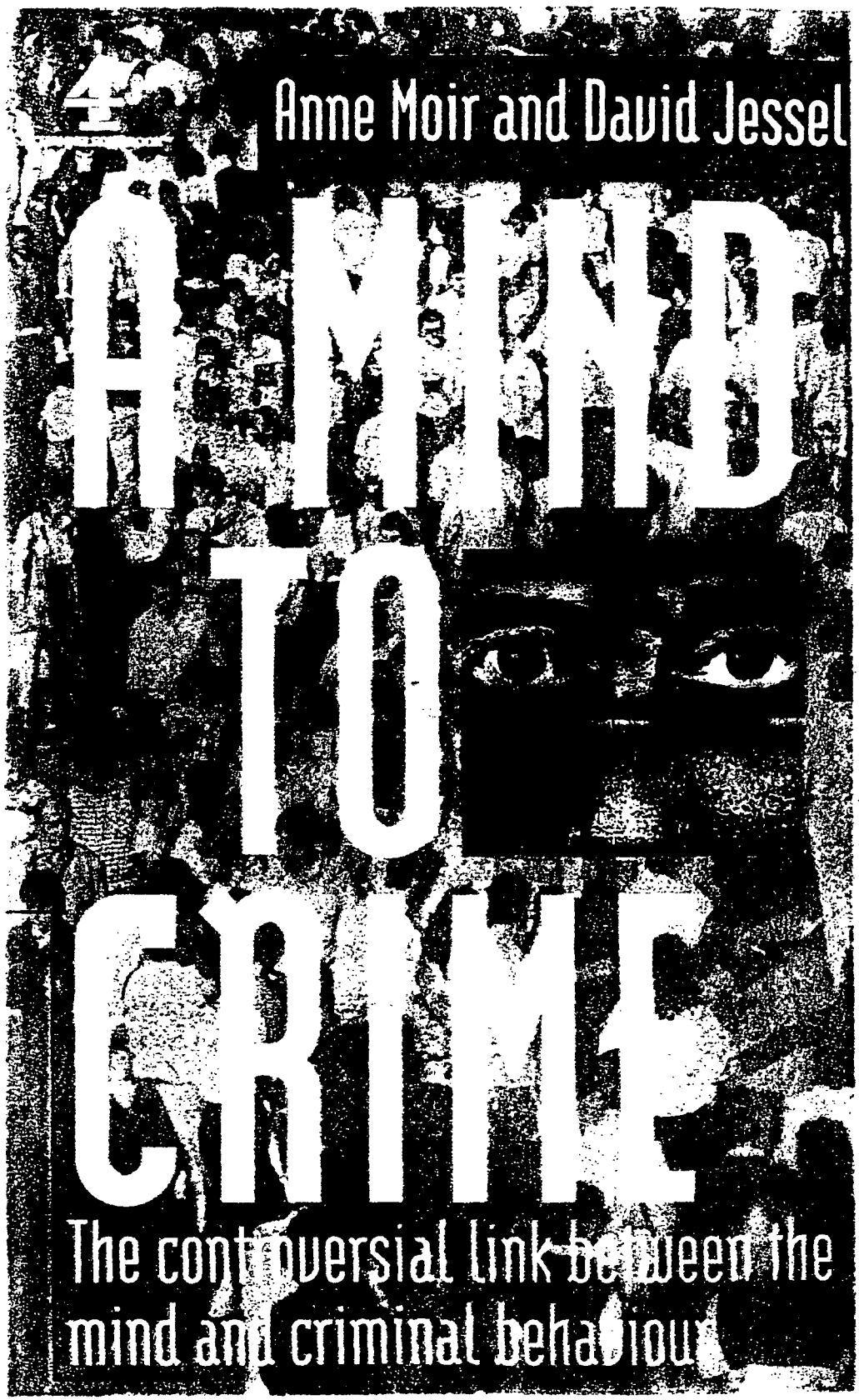
Anne Moir and David Jessel
A MIND TO CRIME
The controversial link between the mind and criminal behaviour

New Yorker

CRIME AND SCIENCE

DAMAGED

Why do some people turn into violent criminals? New evidence suggests that it may all be in the brain.

BY MALCOLM GLADWELL

On the morning of November 18, 1996, Joseph Paul Franklin was led into Division 15 of the St. Louis County Courthouse, in Clayton, Missouri. He was wearing a pair of black high-top sneakers, an orange jumpsuit with short sleeves that showed off his prison biceps, and a pair of thick black-rimmed glasses. There were two guards behind him, two guards in front of him, and four more guards stationed around the courtroom, and as he walked into the room—or, rather, shuffled, since his feet were manacled—Franklin turned to one of them and said "Wassup?" in a loud, Southern-accented voice. Then he sat down between his attorneys and stared straight ahead at the judge, asm-

imprisoned in Marion Federal Penitentiary, in Illinois, he confessed to another crime. He was the one, he said, who had hidden in the bushes outside a synagogue in suburban St. Louis in the fall of 1977 and opened fire on a group of worshippers, killing forty-two-year-old Gerald Gordon. After the confession, the State of Missouri indicted him on one count of capital murder and two counts of assault. He was moved from Marion to the St. Louis County jail, and from there, on a sunny November morning last year, he was brought before Judge Robert Campbell, of the St. Louis County Circuit Court, so that it could be determined whether he was fit to stand trial—whether, in other words, embark-

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In 1989 Daniel Koshland the editor of Science, the world's largest and most influential scientific journal claimed that the Human Genome Project would solve many problems - his list included

Cancer

Schizophrenia

Ageing
&
Homelessness

Daniel Koshland 1989

To a sociologist the advert suggests a different more hopeful future. This - it is implied rather than said - is a future without deafness. To most hearing people or someone who has lost hearing this may look like an unqualified gain. The promise that we would want from biomedical research. But deafness in a new baby born to genetically deaf families (c.f. last week's TV documentary Deaf Century showed that many deaf families actively welcome a baby who is deaf. They know that such a baby will be able to be a full member of the deaf culture and community to which they themselves belong. So how is such a family to read the advert? Minimally it is seen as increasing the stigma of deafness; maximally given that there are few therapies and a proliferation of DNA tests it is seen as increasing a subtly genocidic pressure on all families carrying genetic problems of deafness. If a society without deaf people is the goal then the pressure on the well informed woman carrying a foetus genetically predisposed towards deafness subtly encourages her to choose an abortion. For this reason, as we shall explore later with the eugenics history, many argue that historically we may have left the old eugenics behind and have now entered a period of consumer eugenics. Lastly we walk a cultural tightrope - we want to offer help to families with genetic disorders such as some forms of deafness, without stigmatising deaf people in our culture. My reading would be that this advert falls off the tightrope.

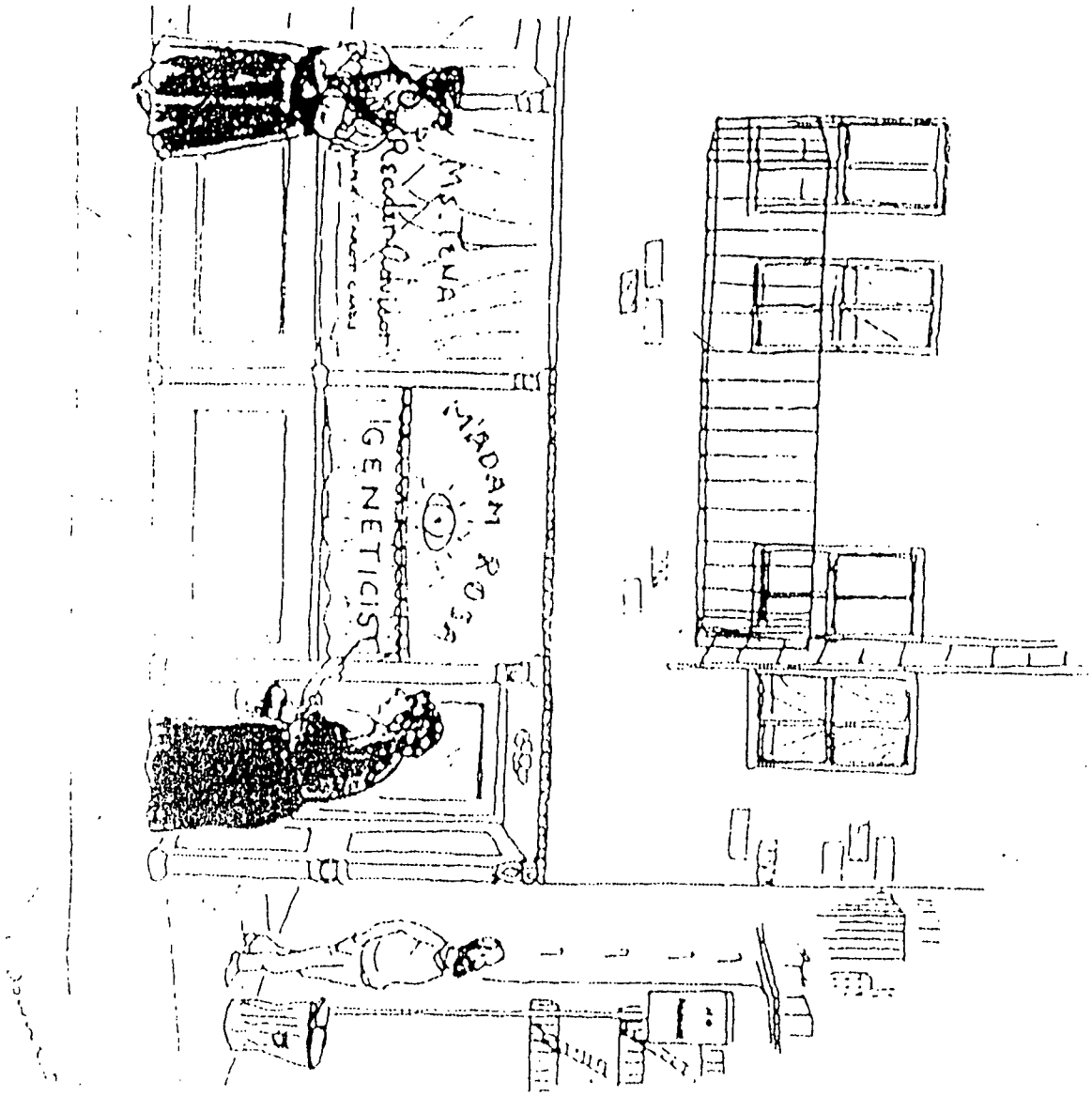
Jokes wonderfully sum up the claim of genetics to predict our future health and illness

Madam Rosa cartoon

or seriously, as in the front page news story in this Sunday's Observer, and the leading article that it generated:

Observer story

What this claims to describe is one stage in the international programme to sequence the human genome - just what this means in technical terms is something we will come to in later lectures - for now we may just take it as listing the order in which the 3 billion strings of the letters ACG and T, the constituents of DNA, appear along the 23 pairs of human



From *The DNA Mystique*

OBSERVER October 3

Front page news item

"Researchers are on the threshold of unravelling the full DNA code of a human chromosome - a breakthrough that could lead to improved treatments for schizophrenia, several forms of cancer, and many other diseases. The achievement ranks as one of the most important in the history of science."

OBSERVER October 3

Front page news item - ctd.

"Think of the human genome as the Book of Life," said John Sulston... "We are about to read the first chapter, as important an accomplishment as discovering the earth goes round the sun..."

OBSERVER - October 3

Editorial

Already, the knowledge uncovered from Chromosome 22 is staggering. We know th DNA cell sequences that respond to heart medicines and those linked to schizophrenia. When the project is complete, we will be able to explain and predict every human being's health experience.

"...we feel that our proposed structure for deoxyribonucleic acid may help to solve one of the fundamental biological problems – the molecular basis of the template needed for genetic replication. The hypothesis we are suggesting is that the template is the pattern of bases formed by one chain of the deoxyribonucleic acid and that the gene contains a complementary pair of such templates."

JD Watson and FHC Crick (1953)
"Genetical implications of the structure of deoxyribonucleic acid"

"It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

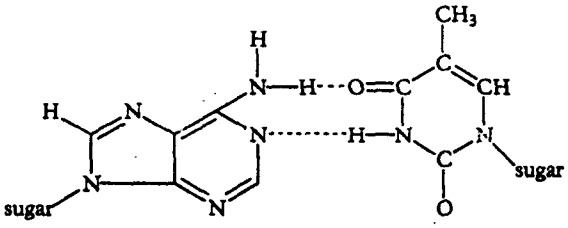
JD Watson and FHC Crick (1953)

"Molecular Structure of Nucleic Acids"

Nature, v171, pp737-738

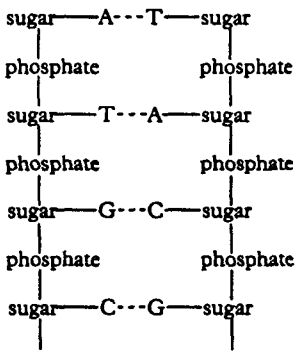
Figure 8

(a) Mortice-and-tenon arrangement of base-pairs.

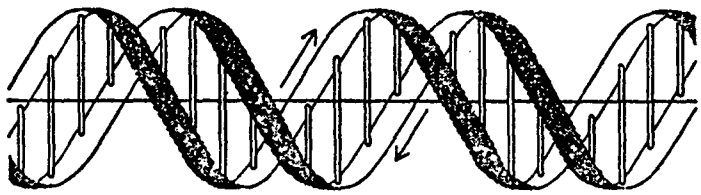


adenine thymine

(b) Bonding of two chains in DNA helix.



(c) Watson–Crick DNA helix



strange tensions that have existed between biochemists and molecular biologists for the getting-on half century since the Watson–Crick discovery can be dated to this episode.

In the structure of DNA shown here, the amount of adenine inevitably equals that of thymine, and guanine that of cytosine, just as the chemical analysis had shown. Despite the restrictions

chromosomes, and how a tiny proportion of them - around 5% in all - can be 'read' as representing genes. The journalist's news story is full of breathless enthusiasm - one of the most important achievements in the history of science. Some claim this for what is no more - or less -than the application of big machines to produce a string of letters for which there is still no clear biological meaning. Decoding the human genome in the next three years is an immense technical achievement. It produces an immensity of information. But what does the information mean for the cell, let alone the organism? As later lectures will discuss, the routes between DNA sequences and living organisms are complex and multiply layered.

And as for the promises, well they need to be read with a distinct handful of salt, if not downright disbelief - the view that we know anything about the genes which may be associated with a diagnosis of schizophrenia is at best premature, at worst highly doubtful.

But the journalist's hype and the Leader's follow up (with its scientifically illiterate reference to "DNA cell sequences" - which is gibberish) pale by comparison with the researcher's own triumphalism. John Sulston is a fine molecular biologist, but identifying a string of letters may at best be compared with learning Egyptian hieroglyphs from the rosetta stone - and then only on the basis of much more work than has hitherto been done. As the social scientists keep telling us, there is an immense cultural change in the style of science. Where Galileo murmured 'but still it moves', and rather more even Jim Watson and Francis Crick (neither known for modesty) in their famous 1953 paper observed dryly

watson and crick transparency

Today's scientists no longer need PR help. They do not wait for history to judge the contribution of the cracking of the HG, they tell us.

Lastly their metaphor for the Genome, The Book of Life draws strangely on religion. Actually the earlier much favoured metaphor of the HG - "The Holy Grail" only disappeared after extensive teasing at the sight of so many secular but ethnically Jewish biologists celebrating the pursuit of

medieval Christendom. The Book of Life has much wider cultural appeal. For what Judaism Islam and Christianity share in common is that that all are religions of the book. When the discourse of science draws on the discourse of religion for its metaphors, we can be pretty sure that something interesting and culturally quite problematic is taking place.

What we have tried to do in this first lecture is to raise two problems: first, that of living in a geneticised culture and second, to begin looking critically at the claims and promises of the new genetics and through this to explore the place of genetics in the study of living processes. In the following lectures we will begin to discuss how we got here, beginning with that old and unpleasant story of the relationship between genetics and eugenics in which evolutionary theory plays a major part.

ENDS