Personalised Medicine

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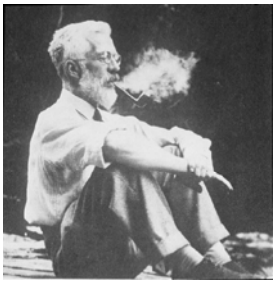
Vision for health

- "*…we can now see a future where the doctor will swab a few cells from inside your cheek, put them into a DNA-sequencing machine and a computer will spit out a complete reading of your unique genetic makeup – all 30,000 or so genes that make you who you are. From that, doctors could pinpoint flawed genes and gene products and predict what diseases you are likely to develop years in advance of any symptoms – and how to help you avoid them*". (Tony Blair, 'Science Matters' speech, 23 May 2002).

- **Eugenicists** and heritability
- **Blaming genes for cancer, hypertension, diabetes, obesity**: History of funding by tobacco, chemical, nuclear, and food industries.
- **Personalised marketing & expansion of 'health' market** Shift to 'pre-symptomatic' treatment by pharmaceutical, food & health industries (rich, well people are a better market).
- Allows governments to create **DNA databases** of whole populations.

Ronald Fisher



Fisher RA: **The correlation between relatives on the supposition of Mendelian inheritance.** *Trans R Soc Edinb* 1918, **52:**399-433.

The case of the missing heritability
When scientists opened up the human genome, they expected to find the genetic components of common traits and diseases. But they were nowhere to be seen. [Nature 6th November 2008]

- "*Finally, some of the missing heritability may simply be an illusion. Heritability is estimated by applying formulae for inferring additive genetic effects from epidemiological data. The estimates may be inflated because the methods are not very effective at excluding the (nonlinear) contributions of genetic interactions or gene-by-environment interactions, which are likely to be significant*." Lander E (2011) Initial impact of sequencing the human genome. *Nature*, **470**, 187-197.

Blaming genes

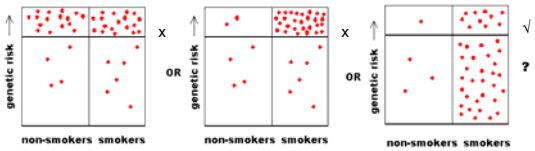
- **Fisher became a tobacco industry consultant in the 1950s**
- The industry supported "individualised prevention" because it would be good for business
- In the run up to the Human Genome Project scientists had to convince the Reagan and Thatcher governments of "industrial applicability".
- They did this by teaming up with the **tobacco industry**…and the **food, chemical and nuclear industries**
- Instead of being about genetic damage caused by radiation, tobacco smoke etc, **they changed the story of the HGP**: genetic screening would identify heritable genetic risk and allow 'at risk' individuals to be identified.

BAT minutes of meeting with Sydney Brenner, March 1988

Wallace HM (2009) Big tobacco and the human genome: driving the scientific bandwagon? *Genomics, Society and Policy*, **5**(1), 1-54.

Gundle KR, Dingel, MJ, Koenig, BA (2010) 'To prove this is the industry's best hope': big tobacco's support of research on the genetics of nicotine addiction. *Addiction*, **105**, 974-983.

By 1994, the Council for Tobacco Reseach had awarded nearly $225 million to approximately 1,000 researchers. BUT…there is no significant inherited component to lung cancer



M.M. Braun, N.E. Caporaso, W.F. Page and R.N. Hoover. A cohort study of twins and cancer. *Cancer Epidemiol Biomarkers Prev* 1995; **4**(5):469-73. See also: Lichtenstein et al. 2000.

- In April 1996, 'Science' reported that Philip Morris was about to fund a new institute for Brenner at La Jolla: $15m a year for 15 years.
- In 1998, key funders of the HGP (Wellcome Trust, NIH) distanced themselves from the tobacco industry and stopped co-funding research.
- From 1999, GlaxoSmithKline – led by its former Chair **Sir Richard Sykes** and then Director of Science **Sir George Poste** – lobbied to build a database of everyone's medical records and DNA in the UK NHS (to compete with DeCode).
- GSK wished to massively expand the drug market for healthy people. £12bn was wasted on e-health records. An attempt to get access to all NHS DNA without consent failed in 2009.

- **From a presentation by Burrill & Co. (December 2009)**
- **Centrally Delivered e.g. genetic screening at Walmart, with home diagnostics & monitoring**
- **Longer Term Risk Assessment (prediction) Driving to Prevention:**
  - Genome wide association studies
  - Navigenics, DeCode, 23andMe
- **Smart cards with electronic health records & sequenced DNA**
  - Consumer driven personal health planning PHR
  - Microsoft -HealthVault™, Google Health and others
- **Tracking & Feedback**
  - Nike/Apple –iPod Nano and online workouts/equipment/fitness linked
  - Tools to monitor medication regiments to drive compliance
    - Tools to measure Activity, Sleep, Food consumption

How are the risks distributed for different common diseases?

- "*The overall conclusion based on these arguments is that the predictive value provided by genetic screening tests for either disease susceptibility or normal variation will be too low to have widespread medical or social application*". Wilkie A (2006) Polygenic inheritance and genetic susceptibility screening. Encyclopedia of Life Sciences. DOI: 10.1002/9780470015902.a0005638.
- "*Many authors have recently commented on the modest predictive power of the common disease susceptability loci currently emerging. However, here it is suggested that, for most diseases, this would remain the case even if all relevant loci (including rare variants) were ultimately discovered*." Clayton, DG (2009) Prediction and Interaction in Complex Disease Genetics: Experience in Type 1 Diabetes. PLoS Genetics, 5(7): e1000540.

- "*Some seek a secondary goal: to provide patients with personalized risk prediction. Although partial risk prediction will be feasible and medically useful in some cases, there are likely to be fundamental limits in precise prediction due to the complex architecture of common traits, including common variants of tiny effect, rare variants that cannot be fully enumerated and complex epistatic interactions, as well as many non-genetic factors*." Lander E (2011) Initial impact of sequencing the human genome. *Nature*, **470**, 187-197.

Conclusions

- In general, genetic sequencing will not be useful to 'predict and prevent' disease
- The (unregulated) gene tests on the market now are at best a waste of money
- This idea has been promoted by a wide range of vested interests without assessing the potential costs or benefits to health
- The benefits of screening everybody's genome do not outweigh the privacy risks
- BUT some gene tests are useful for some people e.g. before taking specific drugs, or to test for rare familial forms of diseases.