

**BSEM submission to the House of Lords Genomics Enquiry**

**House of Lords Science and Technology Committee  
Enquiry into Genomic Medicine**

**Submission by the  
British Society for Ecological Medicine**

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## **1. Context**

1.1. Since the international human genome project was completed in 2003, we have seen the increasing application of genetic knowledge to daily life. Two different fields are now emerging in genetics:

- traditional genetics, concerned with prenatal diagnosis, severe hereditary diseases, monogenic pathologies such as cystic fibrosis, Huntington's chorea, etc.;
- genomics, which looks at multigene, multifactorial patterns, and whose main consideration is the two-way interaction between genes and the environment. This approach is fundamentally different from traditional genetics, in that it does not lead to pure determinism, but by acting on the environment allows the expression and functioning of our genes to be modified, enabling individuals to improve their own health and their risk profiles for a number of diseases.

1.2. Within genomics we can distinguish:

- Nutrigenomics, which studies the interactions between the way our genes operate and our dietary intake.
- Toxicogenomics, which examine the differences between individuals with respect to the interaction of their genetic susceptibility with environmental agents (pollutants, ultraviolet light etc.);
- Pharmacogenomics, which studies the effects of our genome on drugs, and of drugs on the expression of genes;

1.3. We are currently witnessing a distinct increase in the incidence of a number of diseases connected with the environment (cancer, cardiovascular diseases, neurodegenerative diseases etc). Recent studies in the application of genetics/genomics have shown that adapting our diet, lifestyle and toxic exposure to our genetic resources can give worthwhile results in:

- Multifactorial disorders such as cancers connected with the environment, cardiovascular risk, asthma, bronchitis, endometriosis, obesity, allergies, osteoporosis, etc.
- Detection of susceptibility to disease in a healthy individual, and instigation of appropriate preventive measures.
- Identification of both therapeutic and adverse reactions to many drugs, enabling better choice of drug and of dosage levels for individuals.
- Adoption of effective anti-ageing measures, notably by taking degenerative processes connected with oxidative stress into account.

These measures make it feasible to increase not only longevity (up to 14 years of life in good health according to some researchers), but also quality of life in the long term.

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1.4. Genomics further enables a change in the very nature of the medical consultation, in that the doctor becomes a health advisor. He/she can now:

- Help healthy patients to remain so by managing and optimising their long term health "capital".
- Offer an individualised and integrative approach, addressing the patient as a whole, both physically and psychologically, and no longer as an organ or a disease.
- Warn a healthy individual about his weak points, enabling him to manage long-term health risks with diet and lifestyle measures.

### **2. Pharmacogenomics**

2.1. According to the online journal *BMJ Clinical Evidence*, 47% of medical treatments are of unknown effectiveness, and only 13% have been demonstrated to have beneficial effect. It was in this context that in 2003 Allen Roses, GSK's Vice President for Pharmacogenetics, said;

*The vast majority of drugs - more than 90 per cent - only work in 30 or 50 per cent of the people.....I wouldn't say that most drugs don't work. I would say that most drugs work in 30 to 50 per cent of people.*

2.2. It was easy at the time to see this as comparable to Gerald Ratner's well-known observation on the quality of his firm's products in 1991. However it soon became apparent that it was in fact a bid for the future; that the pharmaceutical industry saw genetic profiling — pharmacogenomics — as the wave of the future for medicine, enabling the development of new drugs targeted at individual genomic profiles.

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### **3. Concerns**

3.1. There are human rights concerns here that have been well developed elsewhere. Sir David King has stated;

*Public health genomics aims... to open new markets through preventive drugs targeted at genetic (or 'racial', in the case of BiDiI) sub-groups of the population. This co-option of prevention and the incorporation of genetics into public health will greatly intensify the role of 'health' as a technique of biopower. The focus on individual risk will set new standards for individual health performance, and will inevitably lead to an expansion of eugenics.*

3.2. However the principal concern of this society is that sheer financial clout will enable the pharmaceutical industry to set the overall agenda for genomics. In our globalised economy, in which multinational corporations can have more fiscal power than national democracies, the direction of research is largely profit-driven. The pharmaceutical and biogenetic industries are already investing billions in this research. If profit is allowed to be the principal determinant of research priorities, the risk is that advances in genomics that do not lead to profit will be neglected, ignored and even suppressed. In plain terms, patentable drug-based interventions will be chosen over almost-free diet and lifestyle-based ones, and treatments will be chosen over prevention.

3.3. Our healthcare system is becoming unsustainable, in large part due to the dominant role of the pharmaceutical industry, with 650 million prescriptions written by GPs each year, and a total drugs bill of over £7 billion. Moreover 65% of healthcare research is already funded and controlled by the pharmaceutical industry.

3.4. If the pharmaceutical industry sets the agenda, commercial realities will determine that the focus of funding, investment and research will turn to pharmacogenomics, to the detriment of nutrigenomics and toxigenomics.

### **4. Solutions**

4.1. We submit that using all three subspecialities — pharmacogenomics, nutrigenomics and toxigenomics — offers in contrast a great opportunity for the improvement of public and individual health, at relatively low cost. It has a further merit in that it empowers the individual to manage his/her own risk profile, in contrast to the “biopower” approach.

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### 5. Illustration 1

5.1. Gilbert's syndrome is characterised by a mild hyperbilirubinaemia, consequent on a genetic impairment of the UDP-glucuronosyltransferase enzyme (the gene that codes for this enzyme is known as UGT). Individuals with the UGT1\*1 [TA](7)TAA genotype show a significantly higher bilirubin level, and a small study found all Gilbert's cases to be homozygous for this 7/7 allele [ ]. As well as bilirubin, the UGT enzyme also processes a range of endogenous and exogenous chemicals;

- steroid hormones, melatonin
- salicylates, benzodiazepines, paracetamol, valproate, digoxin,
- carbamates, phenols, aniline dyes.

5.2. Gilbert's is generally said to have no clinical consequences; however ecological doctors have noted a high frequency of Gilbert's in their caseload, and Gilbert's-positive individuals appear to exhibit chronic or recurrent non-specific symptoms more often than negatives.

5.3. Animal studies have found that paracetamol is considerably more toxic to rats that are either homozygous or heterozygous for a variation in UGT activity — up to 110-fold more. The paracetamol issue alone has major implications for health; deaths from paracetamol run at about 100 per year in the UK.

5.4. The PRESTO trial using Tranilast to treat restenosis after coronary arterioplasty found that 4% of subjects in the active arm developed hyperbilirubinaemia; 92% of these were homozygous for the 7/7 allele [ ]. Those with impaired UGT enzyme activity are thus demonstrably more vulnerable to the hepatotoxic effects of the exogenous chemicals it processes.

5.5. Using pharmacogenomic strategies to respond to this new knowledge would allow us to identify the individuals at risk for adverse reactions to drugs metabolised by this pathway, and the drugs that would mediate that risk.

5.6. The nutrigenomic strategy would be more "holistic"; it would include consideration of the prescribing implications, but would also address the potentially major health implications, yet to be fully elucidated, of individual vulnerability to exposures to both pharmaceuticals and pollutants that are processed by this enzyme. The latter are already commonly identified in the tissues of the patient population. It would develop lifestyle recommendations to manage the risks and prevent illness.

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### 6. Illustration 2

6.1. Two cellular receptor proteins that respond to niacin (vitamin B3) have recently been identified, termed HM74A AND HM74B. Research currently ongoing at Johns Hopkins University, using brain cortex samples obtained at post-mortem from individuals with schizophrenia or with bipolar disorder and from controls, has shown that brain tissue from schizophrenics produces much less functioning receptor protein — 6% of that produced by controls or bipolar subjects.

6.2. Hoffer demonstrated that simply giving very large doses of the vitamin niacin could be beneficial for many schizophrenics. Hoffer, Osmond and others have published nearly 50 papers on the use of niacin in schizophrenia, including long-term (10 years) follow-ups, and 6 randomised controlled trials; they have consistently shown that high-dose treatment does reduce symptoms, but that early intervention is more rapidly effective, and it needs to be maintained for years.

6.3. The Johns Hopkins researchers are correct in saying that his research has been “inconsistently replicated”;

*The possibility that a deficiency in the high-affinity receptor is a core feature of many individuals with schizophrenia provides a basis for research into more potent receptor agonists and therapies that might significantly increase expression of the fully-functional protein. One important implication of the data we present here is that the early clinical studies by Abram Hoffer reporting a notable degree of success through treatment of unmedicated patients with niacin, but inconsistently replicated in follow-up work by others, should now be re evaluated in the context of the limitation imposed by a deficient receptor.*

6.4. In other words these findings provide a post-hoc rationale for the use of niacin in schizophrenia, as well as explaining the impaired niacin skin flush response which is well recognised in schizophrenia.

6.5. Pharmacogenomics would naturally seek to develop drugs which either “increase expression of the fully-functional protein” or which modulate the downstream biochemical results of this genetic variation.

6.6. The nutrigenomic response would include, firstly, prevention by optimising both niacin intake and general nutritional status in individuals with the variant gene(s), and secondly early intervention with high-dose niacin in the first instance in newly-diagnosed patients.

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## **7. Conclusions**

7.1. According to the American Institute of Medicine (1999 study), there are some 100,000 avoidable deaths, and 3 million medical errors, 2,216,000 adverse drug reactions and 2.2 million avoidable surgical operations every year in the United States. The UK figures are, of course, comparable.

7.2. The global environment is subject to ever-increasing pollution with a range of extracted or man-made chemicals — heavy metals, pesticides, flame retardants, plasticisers to name a few — whose consequences for individuals are often grave, and the totality of which is evident but incalculable.

7.3. The application of strategies based on the full triad of pharmacogenomics, nutrigenomics and toxigenomics would enable the majority of these malfunctions to be avoided or minimised, at relatively low public and personal cost. Concentration on pharmacogenomics to the exclusion of nutrigenomics and toxigenomics would in contrast squander a great and crucial public health opportunity.