

## The Human Genome Project: Undervalued Ingenuity

Personal View / Commentary Piece

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### ABSTRACT

This article aims to inform medical students and clinicians about the Human Genome Project (HGP). The article discusses the barriers that have been broken down to allow for wider access to genetic testing and the potentially negative effects that an increase in genetic testing may have on patients. It is hoped that by contrasting the triumphs of the HGP (such as personalised medicine) with the potential pitfalls of the project (such as genetic discrimination), readers will develop an enhanced understanding of the HGP.

**Key Words:** human genome project; genetics

### Introduction

If you were to take a group of medical students and ask them to identify the single greatest breakthrough in medical science, I am quite certain that the Human Genome Project (HGP) would not feature highly.

The reason is quite simple: people do not know what it is. The HGP was a scientific project that boasted the aim of sequencing all 3 billion base pairs in the human genome – the blueprint of life. It began formally in 1990 and was declared complete in 2003. The HGP remains the largest collaborative research project in human history and it is therefore surprising that future doctors know little about a study which has its roots in all walks of medicines (genes play a role in virtually all diseases). The scale and impact of the HGP is made even more impressive when you consider that DNA itself is a relatively new discovery: the double helix structure was only discovered in 1953 by James Watson and Francis Crick.<sup>1</sup> Now, 60 years on, we all have a basic understanding of DNA and the world is a better place for it. Or is it? With genetic testing becoming more widely available, how can we ensure that this information is used appropriately and ethically so as to prevent discrimination on a genetic basis? In this article I consider the breakthroughs and drawbacks of the HGP and the challenges that lie ahead.

### Angelina and BRCA

Since its completion, the HGP has helped us to identify the root of many monogenic diseases. Monogenic (or Mendelian) diseases offer the best chance of predicting life-time risk of disease or providing personalised therapy as the single gene mutation involved often makes for an easier predictive or therapeutic target.

Earlier this year Ms Jolie elected to have a double mastectomy to reduce her risk of developing cancer after discovering that she carries the BRCA1 gene.<sup>2</sup> BRCA 1 & 2 are good at predicting life-time risk of breast or ovarian cancer (a female carrier of a mutation on one of the genes has a 50-85% risk of breast cancer and a 15-60% risk of ovarian cancer).<sup>3-4</sup>

However, as with everything in medicine, predicting disease is not as straightforward as this and indeed Genome Wide Association Studies (GWAS) have shown that there are other genetic factors which have a role in determining the risk of developing cancer, and that only

a small number of genetic variants with a role in BRCA1/2-related cancer have been identified to date.<sup>5</sup> However the complexity of genetics should not be seen by medical students as a reason to run for the hills but rather as an exciting area of research in which there is still much more work to be done, with the BRCA genes representing a piece in the puzzle of targeted drug therapy.

### **Monopoly: one winner, many losers**

Indeed if ever there was a time for BRCA testing to become more popular, it is now. On the 13th of June 2013 the US Supreme Court ruled that the previously patented BRCA genes were no longer eligible for patent, as they are a naturally occurring biological material.<sup>6</sup> This was a major breakthrough for American women as BRCA testing previously cost \$3,340 when Myriad Genetics held their legal monopoly on the gene<sup>7</sup>. Just hours after the announcement, competing companies stated that they would offer the test at a cost as low as \$995.<sup>8</sup> It is hoped that the dissolution of other gene patents will follow this historic move and thus genetic-based medicine will become more widely available by way of competition driving prices down. The counter argument is that by allowing these molecules to remain patentable, we provide researchers with financial incentive to discover new and innovative gene therapies that will ultimately benefit patients. Whatever your own opinion, affordable genetic testing is the only way that patients will be able to fully reap the benefits of personalised medicine.

### **What *exactly* is 'personalised medicine'?**

Personalised medicine is the art of tailoring treatments to individuals based on their genetic profile. Personalised medicine has the potential to revolutionise clinical decision-making and prescribing, and could mean the development of new drugs targeted at a particular group of people, such as a specific race or even individuals with certain blood properties.<sup>9</sup> It could even mean better use of drugs already in use or which failed in trial stage. There have been many developments in the field of personalised medicine in recent years.

However, the usefulness of personalised medicine is limited by the fact that we still have so much to learn about the human genome<sup>10</sup>, and indeed knowledge is only acquired with time. We need only look at cystic fibrosis to see that identifying disease-causing genes is only part of the solution to treating the disorder. It is almost 25 years since the most common mutation in cystic fibrosis -  $\Delta F508$  - was identified and only now are therapies being developed that can treat the disease by targeting the faulty gene directly<sup>11</sup>. Indeed when I sat in on an asthma clinic recently I heard the doctor tell the patient that the reason for changing her medication yet again was "more out of desperation, than scientific rationale" - she had not responded to all of the other recommended treatments and the genetic testing that she underwent for specific beta2-adrenergic receptor mutations had come back negative. It would seem that genetic testing is not as clear-cut as it is often made out to be and there are still many questions to be answered.

### **Opportunity for Discrimination**

There is another side to genetic testing, a darker side where the threat of discrimination looms. Indeed there are some who fear that genetic testing could lead to discrimination by employers who may wish to select against those employees with a genome that may affect their ability to work.<sup>12</sup> The theoretical potential for discrimination is huge, however it is very unlikely that this kind of discrimination would ever be legal. There is however a real risk of genetic testing affecting health insurance. There are insurance companies who would just love the chance to use the results of your genetic test to charge you a higher premium, despite the fact that we are unsure of just how much each "risky" gene actually elevates the

risk of disease. In order to protect individuals from being charged more, there are a number of regulatory frameworks in place although there is debate over how much a risky genome would actually increase premiums, with some suggesting that the increase in cost would be very small indeed<sup>12</sup>.

The Council of Europe's Convention on Human Rights and Biomedicine sets out the laws relating to medical research and states that it "bans all forms of discrimination based on the grounds of a person's genetic make-up and allows the carrying out of predictive genetic tests only for medical purposes."<sup>13</sup> At present the United Kingdom has not signed the treaty however it is recognised that the United Kingdom's regulation of medical research with respect to genetic testing is consistent with the European framework.<sup>14</sup> There is currently a moratorium in the UK - a temporary ban agreed to last until at least 2017 - which forbids insurance companies from requesting that a person undergoes a genetic test when purchasing life or critical illness insurance and also allows an individual the right to withhold the results of previous genetic tests when buying premiums up to a certain value.<sup>15</sup> But what will happen in 2017? Is genetic testing a ticking time-bomb waiting to blow up in our faces? One way to stop the mass introduction of genetic testing would be to follow Germany's lead and to only allow medical doctors to carry out genetic tests, as described in their Genetic Diagnosis Act (GenDg).<sup>16</sup> This may serve to curb the recent increase in whole genome sequencing which has now become more popular on account of its ever-decreasing price-tag.

There are number of other concerns also relating to genetic testing. For example, whilst an individual may purchase a genetic test to learn of their susceptibility to one condition there may be other conditions to which they learn they are susceptible, despite them not wanting to know this 'additional' information.<sup>17</sup> There are also likely to be implications for all family members if one member is found to be susceptible to a disease<sup>18</sup> and so the impact of the result should be fully considered before the test. There are also concerns that the increase in genetic testing could lead to a greater number of abortions, with many prospective parents potentially choosing to abort children with profound disabilities (as is already often the case with diseases such as Down's Syndrome). It is clear that genetic testing is an ethical and legal minefield with many considerations.

## Conclusion

Twenty years after its completion, the HGP remains a hot topic that divides opinion. There are clearly many benefits to be reaped from genetic testing but at what cost to patients? I believe that if genetic testing is to become more commonplace then it must be tightly regulated to protect individuals from discrimination. There have been many breakthroughs in medicine as a result of the HGP, such as the beginnings of personalised medicine. Indeed, personalised medicine has the potential to prevent 100,000 deaths caused by adverse drug reactions each year in the US.<sup>19</sup> Ultimately, your opinion of the HGP is likely to be as individual as your DNA, but ponder this: where would the HGP feature on your list of the greatest breakthroughs now?

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