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RESPONSE

Support the *Manchester Manifesto*: a case study of the free sharing of human genome data

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Professor Huanming Yang is co-founder and president of BGI Shenzhen (formally the Beijing Institute of Genomics). BGI made China's contribution to the human genome project. From 1% of the human genome project, it is now a key player in many of the world's megasequencing projects. Professor Yang also has a strong interest in bioethics and society. He is a former member of UNESCO's international bioethics committee and has recently been appointed to President Obama's international research panel of the presidential commission for the study of bioethical issues.

The issue of the 'ownership of science' raised by the *Manchester Manifesto* is the right issue raised by the right people, at the right time – at least in the field of biomedicine. I would like to present the ownership of the human genome data and their free sharing as a case study in discussing the ownership of science.

The human genome project (HGP) will go down in history as one of the most important projects ever in biomedicine. Because of its research scale, heavy cost and significant impact, it has raised serious issues relating to the ownership of science and human genome information. However, thanks to the efforts of the human genome sequencing consortium, as well as its sponsors and supporters, a brilliant example was set for future international collaborations and how to balance intellectual property rights and innovation.

First, following the spirit of the HGP – 'owned by all, conducted by all, shared by all' (Muzny *et al*., 2006) – it has been generally acknowledged that the human genome is the common heritage of mankind, at least symbolically (UNESCO, 1997). The HGP is undoubtedly a scientific project, and the ownership of the HGP is therefore crucial to the ownership of science.

Who should do the science of the HGP? The HGP was initiated by scientists in the US, the UK and other developed countries. I, personally, would like to take this opportunity to thank the HGP consortium for accepting China, then and now a developing country, into the project, especially as the work was already well underway in other countries, and China was way behind the curve. China might well not have been accepted because it had not proved itself, or more correctly, had not yet

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had the opportunity to prove itself in such a great scientific undertaking. The acceptance of China by the HGP was the beginning of a changing international landscape of scientific collaboration. Science should be done by all, and big science should be done by vast and inclusive collaboration, including those countries that might be judged to be lagging behind by the usual historic and economic measures.

As stated by the *Manchester Manifesto*, the HGP was not anti intellectual property rights (IPR), but it did question to what extent IPR have been helpful in the delivery of important public goods and services that are essential for human advancement, and what changes should be made to correct any shortcomings. At that time, genes were patentable, and subsequently, a significant proportion of identified human genes were patented, including many fragmented, incompletely sequenced genes lacking any characterization of the gene function.

The formulation of the *Bermuda Rules* (US Department of Energy Office of Science, 1996) for the release of all scientific data immediately for free use by all people marked a milestone in the debate on the ownership of science. It was the first time that, no matter how much funding and effort was contributed, achievements had to be freely shared with others. To some, the agreement might have been dismissed as just the ideals of scientists, but its product has been crucial to mankind. It is upstream of many things, the fundamental bedrock, and it marked the beginning of a biotech, bioindustry and bioeconomy throughout the world.

The immediate release and free sharing of the human genome data placed all countries, both rich and the poor, both developed and developing, at a similar starting point in the developing bioindustry. We all have reasons to sing the praises of the HGP, not only for its contribution to science, but also for its attitude towards the ownership of science. My perspective at the time regarding the free sharing of this data was simple: I was not interested in what group of people would gain the credit for it. I was deeply impressed by a poster in the Sanger Institute at the time, which read: 'Human genome, to buy it, or to get it free?'.

There is no denying the fierce debate about the ownership of the human genome. Take as just one example, one argument that made it very difficult for me to persuade the relevant authorities in China to support joining the HGP: if the HGP consortium failed and we finally all had to pay to access the human genome sequence data, why should China pay for nothing? If the HGP consortium won, the human genome sequence data would be free to all, so why should China pay?

However, there was another argument: gene patenting and the potential to sell sequencing data were the crocks of gold at the end of the genomics research rainbow. This was especially tempting for China at that time since China had begun to show its potential in many areas and was drawn to the idea of you patent the human genes: China will patent the rice genes, or you charge for using the human genome database: China will charge for using the rice genome database. According to this argument, China should have supported those opposed to free sharing. This was a common argument put to my own institute, the BGI, which has subsequently grown to become one of the biggest genomics research centres in the world. We all understand that history goes in its own way. No matter what choices you make before an event, they will not determine what happens. However, I announced at the beginning of applying to join the HGP: 'We are on your side by joining you!'. BGI was actually born out of the HGP.

We have therefore changed history together. Together we have won. China joined the effort to protect the human genome, and also to protect the ownership of

science. China contributed greatly to the Statement on Free Availability of Human Genome Data (UNESCO, 2000), supporting the HGP consortium. This was followed by the G8 Communique (G8 Information Center, 2000), which stated that the HGP was 'critically important for all humanity'. It called for 'the further rapid release of all raw fundamental data on human DNA sequence as such'. The United Nations Millennium Declaration (The General Assembly, 2000) followed, promising 'free access to information on the human genome sequence'.

I wish to give another example, that of the rice genome project carried out by the BGI and its collaborators (Yu *et al*., 2002). In the spirit of HGP, all the sequence data were released for free sharing. Globally, there was historically much more research carried out on wheat, a crop of equal important to rice, than on rice. However, there is now much more research carried on rice than on wheat, obvious evidence that the research on rice was promoted by the free sharing of the rice genome data (Figure 1). This phenomenon is even more evident in developing countries; before 2002, almost the same amount of research was carried out on both rice and wheat in these countries. Since the free sharing of the rice genome (Figure 2), research is more focused on rice than on wheat. The reason is not because of more funding of rice research by the economically emerging entities, but because of cloned genes and the quantitative trait loci (QTL) of rice, created by taking advantage of the rice genome sequence being freely available to all (Figure 3).

Many people have been worried that the 'free lunch' of genome sequences would reduce the interest in investment by governmental funding agencies and the private sector. It is true that BGI has had a difficult time in the past getting funding for sequencing projects because many colleagues successfully convinced the government that this kind of free lunch should be offered by the rich countries and a country like China should just wait and take it. Their argument was that China should not be stupid enough to pay for it.

Fortunately, history has proved them wrong. The *Manifesto* asserts: 'It is frequently said that the strengthening of IPR is always good and is essential for

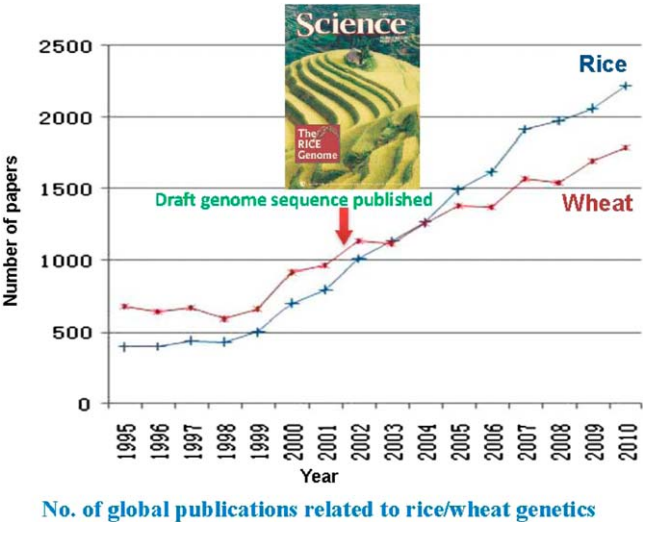

Figure 1. The impact of free sharing of the rice genome sequence data on global rice research

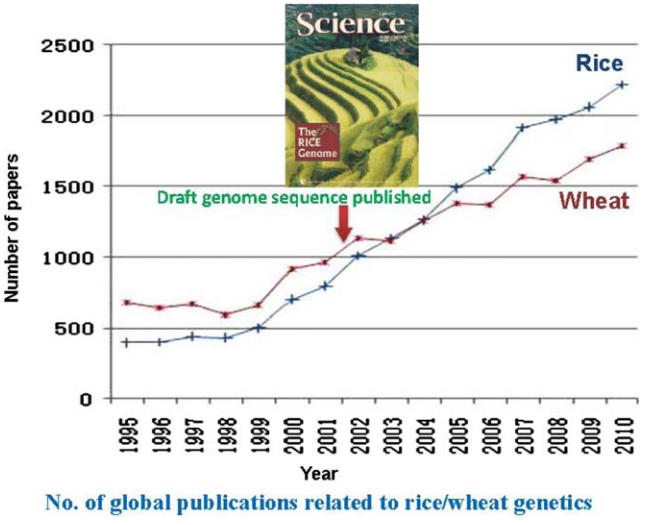

Figure 2. The impact of free sharing of the rice genome sequence data on rice research in developing countries

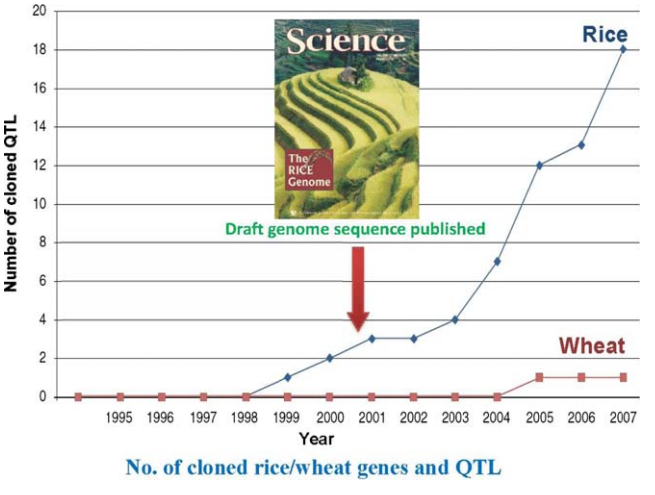

Figure 3. The scientific basis of the impact of free sharing of rice genome sequence data on rice research

promoting innovation. But actually some evidence points the other way'. The archetypal example of this is again in the field of genomics where shared by all has not delayed the development of the field. Instead, it has unleashed a revolution and sequencing boom. With the advent of new generations of sequencing technology, genomics has developed into one of the most prosperous fields of science. BGI has grown into the world's biggest sequencing centre, and has an ambitious mission to 'sequence every (living) thing on Earth and everybody in the world' through its stated goals of promoting widespread international collaboration and free sharing of data.

'Because IPR lie at the heart of the 'knowledge society', there is a widespread unwillingness to consider any problems', states the *Manifesto*. Patenting continues to be a temptation. The saddest example of this was during the global emergence of SARS in 2003. Soon after the decoding of the pathogen's genome, many colleagues rushed into patenting the genome for commercial purposes. Their excuse was the familiar one: only IPR protection can stimulate science and finally serve all. Fortunately, the international community raised the banner of shared by all. This banner has been raised even higher even more recently. BGI and its German partners sequenced the toxic *E.coli* genome; to promote efforts to fight the outbreak, BGI immediately and freely released its data and free diagnostic tests under the most open public domain license without the slightest hesitation (Li *et al*. and the Escherichia coli O104:H4 TY-2482 Isolate Genome Sequencing Consortium, 2011).

To conclude, I strongly support the *Manchester Manifesto* because it raises an important issue related to humanity. Just as I stated in 2001 when I made every effort I could to convince my colleagues to support the HGP, the most important and urgent issue of ethics is to share equally scientific achievements. This is just as relevant now as it was then.

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