Part I. Horizontal Gene Transfer: What is going on?

Horizontal gene transfer, the transfer of genetic materials between different species, gradually becomes a research hot spot over past decades. Although Genetic engineering microorganisms have sprung up in recent years and raised some safety issues when released, it does not necessarily indicate that HGT is good for nothing. In contrast, horizontal gene transfer has significant biological meaning. The evolution of species progresses rapidly not only by mutation and multiplication, but also by transfer of DNA.[1] Now it is believed that successful horizontal gene transfer could provide a selective advantage to either the host or the gene itself. [2]

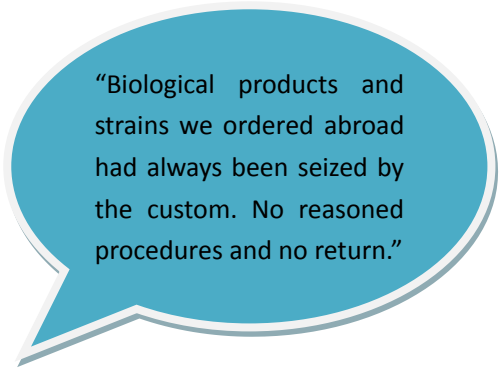
Does horizontal gene transfer happen often? Through conjugation, transformation and transduction, [3] any segment of DNA in a large bacterial population have opportunities to be horizontally transferred. However, the possibility of HGT is extremely low. Only a minor proportion of the DNA transferred between species is likely to be maintained in the new host over generations, and many factors influence horizontal gene acquisitions, including biological mechanistic barriers, temporal and spatial limitations.[1] Therefore, theoretic calculation and laboratory-observed HGT events are rarely linked to serious consequences.

The relevant biosafety researches of many aspects could also help us evaluate the probability of horizontal gene transfer with rational criteria. From results and observations obtained under current studies, it can be concluded that there is little chance to cause hygiene problems and horizontal gene transfer in laboratory,[4] as long as principles of biological safety are well kept. [Table 1]

Name	Evidence	Conclusion
DNA extraction procedures[5]	No viable microorganisms were detected in key stages	the protocol used during the extraction process is safe
Autoclaving procedures[6]	No viable microorganisms were detected in key stages	Autoclaving could eliminated the virulence of microorganisms
Plasmids injection in vivo[7]	organs under observation showed much lower quantities and eliminated soon	The possibility of plasmid integration in vivo is slim

Table 1. Evaluation results of some routine operations. It indicates low probability of horizontal gene transfer with rational criteria.

Nevertheless, from the investigation and interviews, a great many scientific researchers hardly learn national regulations of China, and the meaning of gene transfer, only knowing that many projects are hard to carry on or apply funding. (**More details can be seen on the page of Special feature: HGT investigation**) Almost all Professors complained about unfair treatments and law enforcement. Officials also confessed that regulations and laws on bio-safety, gene transfer and management system should be better formulated and implemented. The public tends to overreact to gene transfer could



"Limitations appropriate or not, wasted time and efforts to overcome inconveniences would, more or less, affect research progress and the development of synthetic biology."

affect the development the genetic engineering industry and synthetic biological science, especially in developing countries, such as China who is just a beginner of synthetic biology. In a larger sense, the innovation room might have been narrowed by officials and public's "crippling" over-concern with the potential abuse of -- not its effective use.

Of course, scientific development has not come without costs. Apart from the harmful byproducts such as prevalence of resistant gene and environmental destruction, it is worth noting that despite much focus on probability of HGT, effective estimates of HGT rates are hardly obtainable, so it is with the evaluation of long-term effects of HGT events.[8] Since rare HGT events could not be ignored within current understanding, people should have cautious consideration of HGT and careful use of GMO. Here's a piece of good news is: horizontal gene transfer is detectable. [BOX 1] Usually, target cultures would be identified by PCR to detect specific sequences, fragment of characteristic protein, or examination of its restriction enzyme profile.[5] Again, overly concern is not necessary, when negative consequences would be avoided to a great extend if one does experiments and uses methods with great care and restraint.

BOX 1 New approache to detect plasmid transfer

In recent years, new approaches such as reporter-gene technology to detect plasmid transfer are developed. Various reporter genes have been used to examine HGT without need of bacteria culturing, including luciferase gene, β-galactosidase gene and fluorescent protein gene. Though with several pitfalls, they provide new platforms for HGT studies and prevention.

(Want to know more methods that could limit risks of HGT? see the page of PartII: Youth Team, Our Future)

In conclusion, horizontal gene transfer is indispensable in the world of microorganisms, and understanding the character and current situation of HGT involved in synthetic biology would be helpful for human beings when doing researches and industrial applications. Development of strategies in the future, including more techniques to detect HGT events and solutions to prevent risks, would definitely contribute to a safer area of scientific researches as well. Don't worry too much when you conduct synthetic biological experiments! Do it, and do it right!

References:

[1] Christopher M. Thomas & Kaare M. Nielsen. Mechanisms of, and Barriers to, Horizontal Gene Transfer between Bacteria. *Nature Reviews Microbiology* 3, 711-721 (September 2005)

[2] Peter Gogarten & Jeffrey P. Townsend. Horizontal gene transfer, genome innovation and

evolution. *Nature Reviews Microbiology* 3, 679-687 (September 2005)
[3] Søren J. Sørensen, Mark Bailey, Lars H. Hansen, Niels Kroer and Stefan Wuertz. Studying plasmid horizontal transfer *in situ*: a critical review. *Nature Reviews Microbiology* 3, 700-710 (September 2005)
[4] E. K. Weibel I, B. D. Seiffert. Biosafety investigations in an r-DNA production plant. *Appl Microbiol Biotechnol* (1993) 39:227-234
[5] Claudia Castro, Liliana González, Juan Carlos Rozo, Gloria Puerto, Wellman Ribón. Biosafety evaluation of the DNA extraction protocol for Mycobacterium tuberculosis complex species, as implemented at the Instituto Nacional de Salud, Colombia. Biomédica 2009;29:561-6
[6] Mark J. Espy, James R. Uhl, Lynne M. Sloan, Jon E. Rosenblatt, Franklin R. Cockerill III, and Thomas F. Smith. Detection of Vaccinia Virus, Herpes Simplex Virus, Varicella-Zoster Virus, and Bacillus anthracis DNA by LightCycler Polymerase Chain Reaction After Autoclaving: Implications for Biosafety of Bioterrorism Agents. *Mayo Clinic Proceedings* July 2002 vol. 77 no. 7 624-628
[7] Florence Faurez, Daniel Dory, Vincent Le Moigne, Rodolphe Gravier, André Jestin. Biosafety of DNA vaccines: New generation of DNA vectors and current knowledge on the fate of plasmids after injection. *Vaccine* 28 (2010) 3888–3895
[8] Kaare M Nielsen & Jeffrey P Townsend. Monitoring and modeling horizontal gene transfer. *Nature Biotechnology* 22, 1110 - 1114 (2004)