

#### Debate 4: Will the real revolution come from biotechnology?

7<sup>th</sup> July, 2018 Aix-en Provence

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Metamorphosis, this year's theme of the French economy conference, in the biological context describes the process of profound change in form by which insects and some animals develop into the adult form, e.g. a larva through pupa to a beautiful butterfly. The process is strictly controlled genetically in terms of the sequential biological events and their timing. Current and future applications of new biotechnologies may be able to modify biological processes and further may have wide-ranging effects that can stimulate profound change in society.

I shall comment from the perspective of a natural scientist in the field of chemistry and biology. Currently I am carrying out basic research to understand the molecular mechanisms concerning development/differentiation of fresh-water snails at the early embryonic stages using CRISPR/Cas9 gene editing techniques in the laboratory. My aim is to review the current status and possible future development of potentially transformative technologies so that together with the audience we can find some answers to the questions: "Are we under- or overestimating the future impact of advances in biotechnologies on our societies?" and "What role should public regulation play in guiding the development of biotechnologies?"

The rapid development of gene editing techniques and related sciences has already had a substantial impact in many areas including medicine, agriculture, energy and environmental issues. For example, research aiming at the cure of thalassemia and sickle cell anemia has been started to change the pathway of a fetal-stage-hemoglobin production. Commercial applications have also mushroomed. Ripening of tomatoes without pollination, a labour-intensive process, has been achieved, and claimed to be beneficial in an aging agricultural community. A third example involves the protein myostatin, a member of the TGF beta protein family, which acts to inhibit myogenesis, i.e. muscle cell growth and differentiation. Animals either lacking myostatin or treated with substances that block the activity of myostatin have significantly more muscle mass. Furthermore, individuals who have mutations in both

copies of the myostatin gene have significantly more muscle mass and are stronger than normal. What does this mean? There is the hope of therapeutic applications in treating muscle-wasting diseases such as muscular dystrophy, but at the same time, it has been used already to produce particularly delicious and expensive fish faster by fish farming, and in making stronger and faster dogs and racehorses. The application of gene-editing techniques to humans has started in China.

Looking back at history, many new discoveries have had a great impact on us including the DNA double helix structure (discovered in 1953), the genetic code (1966-68), recombinant DNA methodologies relying on restriction enzymes that cleave DNA at particular base sequences and DNA ligase to paste together DNA fragments (1962), Green Fluorescent Protein (1995), embryonic stem cell research (1980), somatic cloning and the birth of Dolly the sheep (1997), and induced pluripotent stem cell research (2008). CRISPR/Cas9 gene editing mentioned earlier was published as recently as 2012.

Further, DNA sequencing techniques were developed in the 1970s leading to greater understanding of gene structure and function. Moreover, tremendous technical improvements have substantially reduced the cost and time required for DNA sequencing. Thus, the cost per Megabase of DNA sequence has been reduced dramatically. It was \$9,000 per Megabase in 2001, \$800 in 2007, \$12 in 2008, \$0.09 in 2012 and \$0.01 in 2015. The cost is now one millionth that in 2007. These advances have facilitated the sequencing of the genomes of many pathogens and of the human genome enabling progress in understanding antimicrobial resistance, vaccine development and inherited gene defects.

Knowledge gained from new biotechnologies widens grey zones e.g. between healthy persons and the handicapped, drugs and food, human beings and cybernetic organisms. We may be underestimating the impact on environmental issues. The pros and cons of the powerful new gene/genome editing techniques must be discussed publicly and agreed legislation must soon be established internationally. The methods may have benefits in some areas but could have adverse consequences in others. We must adopt holistic approaches.

Biotechnology together with the development of information technology may change even our way of thinking- *D'où venons-nous? Que sommes-nous? Où allons-nous* (P. Gauguin).