UNIVERSITY OF OXFORD

A novel diagnostic strategy for Chagas disease

Cell-Free Report

Report on the Use and Regulation of Cell-Free Technologies in Synthetic Biology

Overview:

- Synthetic biology products are just coming to market and being considered as solutions to many problems.
- There has been little discussion of cell-free technologies specifically thus far.
- Addition to the Cartagena Protocol is a viable option
- The problems of dual-usage and the FINK report

'*Synthetic biology provides a prime example of technology outpacing regulation, and highlights the need to identify the risks posed by new and emerging technologies via early warning systems. As with many such technologies, it is too early to foresee all the possible developments of synthetic biology. Developments could generate unexpected (and undesirable) side effects*.' [1]

Synthetic biology can include anything from well-established genetic modification to the creation of entirely novel organism (not yet achieved). It involves using engineering principles such as the design build test cycle, and integrates computational tools to assist in building biological systems. Most of the time this involves the genetic material (DNA or RNA) that acts as the information store and can confer specific functions to organisms. We can tailor these functions to something that we require such as the production of opium in yeast for medicinal purposes [2]. Different DNA 'parts` are often stored as 'bio bricks` in libraries so that the different elements can be improved or put in a different context, eg. The Registry of Standard Biological Parts [7].

According to the European commission report on synthetic biology and biodiversity '*future developments in synthetic biology will* ***require changes to existing regulation, or entirely new legislation****, and there is a pressing* ***need to explore other biosafety frameworks and identify the gaps*** *in current risk assessment methodologies.'* [1] One such development that is becoming more popular is cell free technology.

It is a common problem in scientific literature that there are various definitions of the same thing that are used differently or interchangeably, this happens especially in synthetic biology which is a relatively new field. [4]

Even within the small area of cell free based technology there are different areas of research, for example those that contain genetic information in their final design and those that do not. There should be a clear distinction between these technologies especially. In this review we will focus on cell free technologies that contain genetic material.

Some definitions of synthetic biology specify the manufacture and modification of genetic material in *living* organisms. Cell free systems do not use living organisms; however, they cannot be treated as simple chemical compounds as they can interact with biology under the right conditions (i.e. uptake of genetic material in bacteria by horizontal transfer mechanisms).

The key thing to consider here is whether cell-free technologies are deemed 'living' in a legal sense even if not in a biological sense. Because this will determine

how they will be treated by governance agencies and thus the regulations put in place.

It may be seen that perhaps different precautions and safety measures must be put in place when dealing with cell free technology and they may not be the same or as stringent as the regulation of the use living organisms. However it is something that needs to be discussed by the relevant bodies in order to ensure the safe and legal use by all.

If there were less barriers to the transport and use of cell-free technology, this could in fact give us a way of fast-tracking synthetic biology technologies so that they can be used in the field sooner. This should give incentive to governments to draw up appropriate guidelines and bring cell free systems into policy discussions surrounding synthetic biology.

A potential problem there may be is the application of the precautionary approach by states, where there are threats to environmental degradation. [3] If there is no clear regulation in place then this expanding technology may not be able to be used or developed. With better infrastructure the application of this technology that spans many fields can be utilised to its full extent enabling all the benefits to be reaped whilst safeguarding the health of the public and the environment.

Existing regulatory framework such as the Cartagena Protocol cover the use and handling of living modified organisms. [6] The scope of this does not extend to cell free technologies and so the protection of biological diversity and human health could be compromised. 171 countries are parties to this protocol and have signed and ratified the supplementary protocol; so, an addition to this could be a good way of ensuring that cell free technology does not fall beneath the radar.

The processes to make these systems will nearly always require the use of genetically modified organisms and whilst these may not be transported or released into the wild they need to be acknowledged in some way. There is the option of going for regulations that are product centred (like the Food Standards Agency), or process centred.

The 'FINK report' represents the views and concerns of the scientific community on the dangers of bioterrorism. The consensus was that research with dual use, whilst not being prohibited, should be undertaken with structures in place in order to safeguard the community. We must ensure therefore that any new regulations in this area still monitor and mitigate the risk resulting from dual use research and that this danger is not overlooked.

There are 2 potential ways forward for considering cell free technology which is either to extend the scope and risk assessment of existing regulations, or to take the form of entirely new regulations that discuss this type of biotechnology specifically. The 2 options have different benefits and it is important to consider the ease of implementation on a political and legal level, as well as matching the biological needs.

References:

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