Access and affordability

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We all want to make the world a better place. For those engaged in pharmaceutical manufacturing, the motivation is to apply scientific advances to the improvement of society. 'Better, faster, more affordable' is a mantra we should all take to heart as we pursue the knowledge that could make it easier to make the drugs to save lives more affordably.

The problem is, not all drug manufacturing practices today are equally well-placed to handle the needs of a growing patient population. One facet of this problem involves the current paradigm for synthesising life-saving biologic drugs using CHO – Chinese hamster ovary – cell lines.

CHO cells have been used for decades in many lab studies – and are popularly used as a host for producing the proteins that wind up in many drugs. Yet, although CHO continues to play a major role in biologic drug production, the industry is recognising that it has now reached the limits of its productivity. As such, it is worth looking at other innovative methods of protein production that could enhance the efficiency of drug manufacturing. Consider the following:

- Next-generation biologics may be produced in a faster and more efficient manner than CHO by harnessing alternative, hyper-producing cell lines that use much lower-cost growth media and potentially simpler downstream processing. No viruses are associated with these cell lines, which eliminates the need for two purification steps typical in CHO.
- One of the most promising alternatives to CHO involves a genetically modified form of a novel fungus known as *Myceliophthora thermophila*, which we nicknamed C1. Although C1 is a proprietary platform of my company Dyadic, it is being made available to academia and industry via R&D collaborations, licensing and other arrangements to help speed up the production of biologics and lower their cost.

To develop C1, our scientists exposed the cells of this species of fungus to UV light. They expanded and reinforced beneficial mutations to drastically change the shape of C1 from long, spaghetti-like strands to short, grain-sized sections. Since C1 fungal cells secrete proteins from the ends of the filaments, there were more secreting ends, multiplying the potential total yield of secreted proteins. Furthermore, due to its new shape, C1 became easier to grow in large tanks.

Our C1 expression platform has already shown in the biofuel space that it can produce industrial enzymes at up to 100 g/L at about 80% purity, and we, along with certain biopharma company collaborators, have already seen C1 achieve record productivity with high purity of biopharmaceuticals. The goal is to produce a quantity of drug – such as a monoclonal antibody (mAb) – in a fraction of the time it currently takes to produce the same drug using CHO cells at a much lower cost with more efficient downstream processing. If successful, C1 has the potential to help speed up the development and significantly lower the cost of manufacturing biologic vaccines and drugs.

So far, the results have been dramatic. In January 2018, for example, the maximum mAb yield from C1 stood at 1.34g/L/d. Two months later, we had raised that to 1.71g/L/d. As of May 2018, this figure had been raised again to 2.46g/L/d – representing an 84% improvement in productivity in only four months. This progress is accompanied by a corresponding 67% drop in the cost of the low-cost, chemically defined medium required to produce the mAbs.

By applying synthetic biology and taking advantage of the rapid advances in biotechnology that are occurring faster than Moore's Law did for IT, we can apply these advances to industrially proven, hyper-productive cells like C1 rather than trying to fine-tune relatively low-yielding cells like CHO. Engineering CHO cells is like trying to tune up a *Model T* engine in a Tesla world. No one in today's world would try and retune a *Model T* engine when you have a better engine available to go faster and farther.

By focusing on these issues today, we may be heading off a looming health crisis in the future. Ensuring that patients have adequate access to the vaccines and drugs they require is a priority in the developed nations across the world and even more of a priority in developing nations. In an era in which scientific authority is sometimes dismissed by top government officials, it is more crucial than ever to focus on harnessing science for the good of the human race.

No one can forecast with 100% accuracy how a new approach to biologic drug manufacturing will impact the world tomorrow. But if it's our responsibility to enhance pharma companies' ability to develop and make these drugs efficiently and more cost-effectively, encouraging them to see the light about CHO and viable alternatives such as C1 is a moral duty. Working together, government, regulatory agencies, academia and pharma and biotech companies can indeed change things for the better.