

Commentary: Tony Sedgwick**Thought disruption in R&D discovery**

Every company in the pharmaceutical industry today is seeking to find technologies that will deliver new therapies capable of changing patients' lives. Typically this process starts with the search for unique biology that can be transformed into potential small molecule or biologic drugs. In this article, I argue that we have exhausted current methods and need to think more holistically about whom we are trying to serve.

Drug discovery is a complex process that often starts with a scientific project. Researchers skilled in a particular area of biological science take a deep dive into the literature to find out what subjects are current and need further elucidation. This is followed by a search through databases for more detailed information. The same scientists then seek to connect with globally recognised experts in the field of inquiry. With the use of databases and old fashioned networking, the scientific team is able to top up its knowledge of what is known and unknown about a subject. The research also includes a thorough investigation of outstanding patents. In the end, the goal is to spot opportunities for innovation.

Innovation comes in different forms. It could be based on new technology, or it could be the repackaging of an old idea with a really new twist. Individual scientists obsessively champion an approach until there is a fusion of ideas, and everyone agrees on a line of scientific attack.

Once a starting chemical, or a target biological process is determined, the discovery process takes over with classical chemistry and/or antibody creation. This then leads to the use of tests and screens to find a candidate drug.

But does it work?

The industry has spent billions of dollars on classical discovery in a bid to identify more and better drug candidates. Most executives, and those that give them advice, have swung from the belief that drug discovery is best done in-house, to the notion that it should be acquired externally from small, innovative biotech companies. The pendulum is still swinging from one approach to the other.

The industry says that it wants to identify and invest in disruptive technology. It is worth pausing for a moment to consider what the term disruptive really means. According to most dictionaries, it is something that disturbs, disorders or unsettles the existing order. In other words, it can be an uncomfortable process. At the very least, it involves energy and the courage to see things differently. Richard Branson has tried to capture this energy in seeking to introduce changes to the music industry. This can be done in pharma as well, but we also have to recognise our unique circumstances.

The pharma industry is heavily regulated because it produces products that seek to improve the public health. New drugs should deliver a benefit. But this has to be weighed against the risk of unexpected adverse events. The regulation is there to ensure safety and also to promote long-term investment in science.

This means that disruption in life science takes a different

form than in the music industry. I would call this 'thought disruption.' Put simply, it is the act of putting old research habits aside and drawing on new people and new ideas to rediscover the drug discovery process.

I would start by engaging experts in different disciplines to apply their minds to the challenge of finding a new drug. They might be computer engineers or retail experts who are accustomed to dealing with the customer, or the end user.

We could start by thinking more holistically about patients. How many of us who have worked in laboratories actually understood the physical discomforts and anxieties of patients with a chronic disease? More importantly, how many of us experience the hope that many patients feel about the efficacy of new medicines? Perhaps discovery should start by logging the observations of patients rather than in a medical library.

Greater patient engagement may be possible to achieve in the emerging field of bioelectronics. This describes the convergence of biology and electronics enabling things like silicon chips to identify tiny biological particles that can predict disease. Bioelectronics also enables the creation of wearable devices that help patients monitor a disease like diabetes.

On its own, computer technology could contribute much more to drug discovery and development than it does at the moment. Making chemical entities manually and testing them manually has its strengths. But we could take this process much further by using computers to model drug interactions at a preclinical level.

Moreover, it should be possible to use systems biology to understand pivotal biological processes better. In the current discovery process, the number of potential biological systems available for manipulation is very high. The body is uniquely capable of responding to change by using homeostatic mechanisms to abort a therapeutic intervention. However, by using computers to simulate this process, it should be possible to identify these resistance mechanisms, move on and radically change the discovery process.

Finally, the disruption in thinking that is necessary to recharge drug discovery will need to start in universities. Although universities and courses have been modernised, the career path for a scientist continues to depend on knowledge of biology rather than knowledge about industrial science. New courses in digital biology and a discussion about different treatment paradigms may start to break this mould and prepare scientists for innovation in the centuries to come.

Tony Sedgwick started out as an academic and then moved into industry, becoming chief executive of four biotechnology companies and a senior executive at Roche Pharmaceuticals. He currently is an advisor on R&D to the industry. He is a partner at Novasecta and an advocate for thought disruption through the website www.thoughtdisrupter.com.