OPEN SOURCE MALARIA RESEARCH PAVES WAY FOR CHEAP MEDICINE

BY MS VIVIENNE REINER

Once the domain of IT, a crowd-sourced approach to drug discovery has been shown to work.

A real-time drug discovery project involving some 50 researchers in nine countries has shown open source malaria research works – providing a potential alternative for medicines similar to the way in which open source products compete with proprietary products in software.

Malaria is one of the leading causes of mortality in developing countries – last year killing more than 400,000 people. Researchers worldwide have found the solution for drug discovery could lie in open, “crowd-sourced” science.

The current gold standard antimalarial treatments are based on artemisinin – a compound developed in the 1970s in China, combined with a partner drug. Resistance to artemisinin and its partners has already emerged in some parts of the world where there are concerns that if the resistance spreads, there will be no viable replacements.

Given the lack of commercial incentive for industry to develop drugs for neglected diseases – and because academic researchers often lack resources to move compounds forward – there is a need for new approaches.

In response, Associate Professor Matthew Todd from the University of Sydney’s School of Chemistry, together with the not-for-profit research and development organisation Medicines for Malaria Venture, proposed a solution akin to the open source concept used in software development.

Open source drug discovery is an area Associate Professor Todd has been leading, launching and developing the project in Sydney with support from two Australian Research Council Linkage grants. Through this innovative work, Associate Professor Todd has demonstrated that open source research mechanisms work in the discovery of new medicines.

In ACS Central Science, an international consortium of researchers unveiled its findings for the project that has been five years in the making.

“Can this mechanism be used to break the deadlock of discovery in other areas, such as Zika?”

- A/Prof Mat Todd
The University of Sydney’s Deputy Vice-Chancellor (Research), Professor Duncan Ivison, said the implications for this unique research were far-reaching: “This is thought-provoking research,” Professor Ivison said.

“Can an open-source mechanism be used to break the deadlock of discovery in other areas, such as antimicrobials or Zika? How do we marry the efficiency of openness with the often legitimate need to protect intellectual property? Does the open-source research mechanism provide a genuine alternative to the traditional way of doing things, in the way in which open-source products compete with proprietary products in software?”

“We need to be constantly testing and trying new models for enabling our research to be translated in ways that benefit our community.”

Associate Professor Todd said the openness of the research stimulated inputs from around the world that were of high value. “A thrill of doing this research was showing that an open source approach to drug discovery actually works: talented and committed people spontaneously worked together to accelerate the science,” Associate Professor Todd said.

“The diversity of the paper’s author list is clear testament to the community that has come together to advance this project.”

More than 50 researchers from 21 organisations – across Australia, USA, India, Switzerland, Spain, England, Scotland, Belgium and Canada – added their research to the project, which started with a large set of potential drug molecules made public by the company GlaxoSmithKline.

First author on the paper, Dr Alice Williamson from the University of Sydney’s School of Chemistry, said it was a big job coordinating the inputs the consortium received but was well worth the effort to create a legacy of research for use by anyone for any purpose and which allowed contributors to influence directly the course of the project in real time.

“Scientists love to share their results but all too often we only share the positive outcomes and at the end of the research process,” Dr Williamson said. “Under the traditional model, vast amounts of publicly funded research is lost.”

Medicines for Malaria Venture chief scientific officer Dr Timothy Wells said there was a huge amount of goodwill and intellectual input and this publication was just the start. “We look forward to working with partners like Mat to continue to develop this new open approach to drug discovery, with the ultimate goal of identifying a new drug candidate,” Dr Wells said.

The authors acknowledge funding from Medicines for Malaria Venture, the Australian Research Council, the Australian National Health and Medical Research Council, the European Molecular Biology Laboratory member states, the National Science Foundation and the Wellcome Trust.

Read more in The Conversation explainer by A/Prof Matthew Todd and Dr Alice Williamson at http://bit.ly/2cMwkWO.
A chemistry breakthrough has demonstrated it is possible for conducting nanomaterials to operate as qubits at room temperature.

Co-led by Dr Mohammad Choucair – who recently finished a University of Sydney Research Fellowship gained as an outstanding early career researcher in the School of Chemistry – the 31-year-old has been working with collaborators in Switzerland and Germany for two years before the breakthrough.

The team has made a conducting carbon material that they demonstrated could be used to perform quantum computing at room temperature.

The results are published in the high-impact journal Nature Communications1.

A modern-day computer represents information using a binary number system of discrete bits, as either 0 and 1. A quantum computer uses a sequence of quantum bits, or qubits. They can represent information as 0 or 1 or any of a series of states between 0 and 1, known as quantum superposition.

It’s this leap that makes quantum computers capable of solving problems much more quickly and powerfully than today’s typical computers.

An electron has a charge and a spin – the spin determines if an atom will generate a magnetic field; the spin can be used as a qubit.

The quantum information qubits hold is extremely susceptible to external noise, like vibrations from neighbouring atoms and even the Earth’s magnetic field.

This is why some qubits, such as those made from silicon atoms, only work at super low temperatures. Cooling down materials slows there vibrations almost to a complete halt once you near absolute zero, or -273 ºC. Other materials require specially designed magnetic shielding to protect the quantum information from being lost.

This requires some heavy-duty and expensive refrigeration and some very sensitive buildings – not so practical if quantum computing is to make it into phones and laptops.

Qubits have been manipulated at room temperature, but the problem with the materials employed was that they were insulating – in other words, the electrons can’t move so won’t conduct electricity. Technology requires conducting circuitry.

Other materials require techniques involving extremely precise engineering, where a single atom must be removed and replaced with another atom. These techniques require special instruments that are really expensive.

Yet other qubit materials need what’s called ‘isotopic engineering’, where they’re hit with particles fired from a nuclear reactor.

Instead of trying to work with the stuff around a qubit, Dr Choucair made a qubit that’s stable at room temperature without any extra fiddling around.

Dr Choucair simply burnt naphthalene, the active ingredient in mothballs, to create spheres of pure carbon, around 40 nanometres wide, filled with disordered carbon atoms.

Their disordered interior was the key to metallicity, or the ability to conduct electricity.

To be used in quantum computing, qubits must hold their spin longer than 100 nanoseconds. These carbon-based qubits retained their spin for 175 nanoseconds.

The next step is to incorporate what’s called a quantum logic gate – essentially a switch, much like a transistor in an electrical circuit – to manipulate multi-qubit systems.

Still, the carbon qubits can be integrated into existing silicon technologies or be part of an all-carbon device.

1Nature Communications, 7 (2016).

http://go.nature.com/2cF1HlG
First developed in 1979 Li-ion batteries function by the transfer of lithium ions from a cathode material, through an electrolyte to an anode. Electrons flow in the same direction, which provide power to connected electronics. The main strength of the Li-ion battery is that this intercalation of Li-ions is reversible, allowing for the battery to be recharged.

Controversy has arisen recently due to Li-ion batteries combusting or exploding. In order to test whether concern is warranted a series of experiments were conducted in order to determine the conditions required for immolation or explosion of Li-ion batteries. For these tests exclusively Li-polymer batteries were tested. Li-polymer batteries are a class of Li-ion batteries in which the electrolyte is a polymer material and are commonly used in smartphones due to a high charge density. Attempts to ignite these batteries via overcharging were unsuccessful, all modern Li-polymer batteries are constructed with internal protection circuits preventing over- or undercharging. Ignition of batteries was only achieved under extreme conditions, several minutes of heating to temperatures above 250°C or perforation resulted in combustion.

It is important to note that exposure to air does not result in immolation. It is a misconception that exposure to moisture in the air causes the combustion of these Li-ions, while Li metal will combust in contact with moisture. Li-ions used in battery construction are specifically chosen for high stability under high temperatures and pressures. The likely source of an explosion is due to a short circuit between electrode layers, due to degradation or breaking of a separatory film brought about by heat or perforation. This results in a large build-up of heat, vaporising the polymer electrolyte. The massive pressure increase then results in failure of the cell.

It is also important to note that these are very extreme conditions and under normal use a Li-ion battery is extremely safe, most accidents involving Li-ion batteries in mobile phones is due to the phones being either excessively bent or perforated. The odds of a battery igniting under normal use are extremely small, while there are reports of such failures it is important to keep in perspective that the number of mobile phones in the world now exceeds the human population, thus even with a one in a million failure rate, failures do still happen.

Certain news outlets have branded Li-ion batteries as “deathtraps” this cannot be further from the truth, the devices are extremely safe under normal conditions and require significant misuse and mistreatment to fail. The news outlet further stated that in order to better protect yourself batteries should only be purchased from trusted suppliers. All batteries used in modern mobile phones are held to vigorous safety and quality standards and are all extremely unlikely to fail under normal use. Li-ion cells do degrade over time, this does not usually affect the safety of the cell but rather leads to a lowering of the capacity of the cell.
SUPERBUGS MAY KILL 10 MILLION PEOPLE A YEAR BY 2050

A recent 18-month review into antimicrobial resistance warns that superbugs may kill 10 million people a year by 2050 if new antibiotics are not forthcoming.

A new paper by Richard Payne’s research group led by Andrew Giltrap and Luke Dowman, together with their collaborators at the Centenary Institute and Simon Fraser University (Canada), reports the first total synthesis of an antibacterial natural product called teixobactin using solid-phase peptide synthesis. Teixobactin generated worldwide press following the report of its discovery in the journal Nature early last year. The peptide natural product was isolated from a previously uncultivable soil bacterium (Eleftheria terrae) using a technology called iChip. Teixobactin has potent antibacterial activity against a range of Gram-positive bacteria, including drug resistant strains of Staphylococcus aureus (MRSA), responsible for a large proportion of hospital acquired infections. The natural product also exhibits potent antibacterial activity against Mycobacterium tuberculosis (Mtbc), the causative agent of tuberculosis (TB) that is responsible for the deaths of 1.5 million people every year. One of the major discoveries made by the scientists that isolated teixobactin was the inability to generate bacterial resistance to the natural product in a laboratory setting. This is a very important result as it suggests that bacteria may struggle to develop resistance against the natural product if it was ever used as a clinical antibiotic.

The total synthesis of teixobactin reported by Payne and co-workers represents an important step as it provides a viable route for future access to customised structural analogues of the natural product with improved antibacterial activity which the group is now pursuing.

Why not receive your newsletter electronically! If you would like to receive our e-newsletter please email anne.woods@sydney.edu.au and she will arrange it for you. To view the e-newsletters please visit: http://bit.ly/1q2J77B
Dr Girish Lakhwani and Dr Asaph Widmer-Cooper have been successful participants in securing an ARC grant for an ARC Centre of Excellence in Exciton Science. The ARC Centre of Excellence in Exciton Science, to be established at The University of Melbourne, will manipulate the way light energy is absorbed, transported and transformed in advanced molecular materials.

Led by Professor Paul Mulvaney, the Centre’s research is expected to produce outcomes and benefits that will focus on ‘full-spectrum’ photovoltaics through to printable electronics and new Australian technologies in solar energy conversion, energy-efficient lighting and displays, and security labelling and optical sensor platforms for defence.

The $35M Centre will include an international team of researchers to drive innovation and improve Australian’s energy production.

With input from across both technical and social sciences, the Centre for Exciton Science will create a dynamic and integrated team which comprises mathematicians, chemical and physical scientists and engineers, as well as leading education experts, environmentalists, architects and business consultants. Research programmes will span high-throughput computational screening, single molecule photochemistry and ultrafast spectroscopy and embrace innovative outreach and commercial translation activities.

For further information, please visit the ARC Centre of Excellence in Exciton Science website at http://bit.ly/2dn2Tqs
Regardless of the application, advances in these areas have been dependent upon the implementation of new synthetic methods. This is exactly what my research group works hard to achieve, inventing better ways to build life-changing molecules. One of our recent success stories has been in the field of plant-signalling molecules.

Food security looms as a major challenge for society. Cereal crops constitute more than 50% of the calories in human consumption, and the Food and Agriculture Organization of the United Nations predicts that a 60% increase in global production will be required by 2050 to meet the growing need for food. Despite being spectacularly successful, the contribution of synthetic organic chemistry to the agricultural sector has been directed towards crop protection rather than growth promotion (i.e. insecticides and herbicides). Promoting crop growth has traditionally been approached by applying fertilisers. We want to change that.

In 2005 strigolactones were identified as the molecules that facilitate plant–fungi communication. Released from the plant’s developing root system into the surrounding soil at picogram concentrations, these compounds cause Arbuscular mycorrhizal (AM) fungi to take up residence in plant roots where they provide nutrients (such as phosphates) to the plant while receiving plant-derived carbohydrates in return. This plant–fungi interaction is the most widespread example of symbiosis on the planet, and enhancing this process is an ideal way to promote plant growth and increase crop yields. The stumbling block was accessing the strigolactone molecules.

We rose to prominence in this field by designing and executing an asymmetric total synthesis of a strigolactone signalling molecule called GR24. Before our work, plant researchers used a mixture of compounds in their assays because there was no way to control the 3-dimensional structure of GR24. We overcame that shortcoming and designed a method to stereoselectively build any GR24 structure (isomer) in just 5 steps. We currently supply single isomer GR24 molecules to over a dozen research groups worldwide. Our expertise in synthetic organic chemistry allowed us to invent a process that can make hundreds of grams of this molecule in one go, which has enabled its use in field trials in both Canada and China. We are eagerly awaiting the outcome of those trials, but have used the intervening time to take on another strigolactone challenge.

We know that strigolactones play vital roles in the growth and development of plants, but we know very little about the mechanisms by which this occurs. In order to see what happens inside a plant, scientists need a fluorescent molecule that behaves just like a strigolactone plant hormone … so we invented one! This molecule is currently being used by our collaborators to monitor the processes by which hormones influence plant architecture under adverse growing conditions. We know that nutrient and water stress causes plants to accumulate signalling molecules that retard growth and put the plant into ‘survival mode.’ This negatively impacts on seed development in cereal crops, the number of seed pods is reduced and the grains do not fully develop. The outcomes are reduced yields and significant devaluation of the harvested grain, which has major financial impacts on the growers, the industry, and the Australian economy. Recently it was shown that the application of strigolactones can inhibit the accumulation of these “stress response” signalling molecules, which results in continued growth under adverse conditions. Using our fluorescent molecule, we can watch what happens inside the plant to stop the stress response. Harnessing this technology for cereal crops would increase crop yields without increasing water and fertilizer inputs.

Organic synthesis sounds a million miles removed from food security, but tomorrow’s food supply is reliant on our ability to build molecules that promote plant growth. My team of dedicated researchers is making great strides to achieve that goal.
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