Can open-source drug development deliver?

Open-source drug development involves open data sharing, collaboration, and results sharing. The aim is to produce new drugs for neglected diseases. But can it work? Tatum Anderson reports.

A research chemist has a problem. He wants to make a better version of an existing drug that comes as a mixture—one with side-effects and a horrible taste. But it is a drug for a neglected disease, so it's unlikely that a pharmaceutical company will step in to work on it. So, he posts the problem on the internet, and solutions begin to appear from scientists around the world. Using them, he modifies the molecule in his laboratory and posts results back online for them to critique. Gradually, a pure tasteless form without side-effects is developed and handed to a manufacturer for production.

This is how open-source drug development is supposed to work. It is a concept borrowed from the IT world, which harnessed a voluntary global army of coders to produce software for a fraction of the development costs of commercial rivals. Open-source methods speed up drug discovery and could make drugs far more affordable, says Matthew Todd, the scientist at the University of Sydney, Australia, who has posted just such a drug—against schistosomiasis—on the internet and is now working on two open-source malaria molecules.

Specifically, open-source methods widen the pool of researchers applying their expertise to a problem and cut down duplication. And just like open-source software, any modifications are also open and not patented. "The question is whether it was worth abandoning secrecy to get input from people. And, yes, it is worth it because research is accelerated by strangers", Todd tells *The Lancet*.

Alternative way

Todd is taking the concept further; he has helped establish the Open Source Pharma Foundation (OSPF), which will develop open-source drugs and run the first open-source clinical trials. It plans to establish an alternative drug discovery route for neglected diseases where the research and development (R&D) incentive is weak. "We are unrealistic in expecting tools for something [like] Ebola to arise from the private sector. It's just not in the business plan", he says. "We need other ways to generate the [drugs] that are going to help us."

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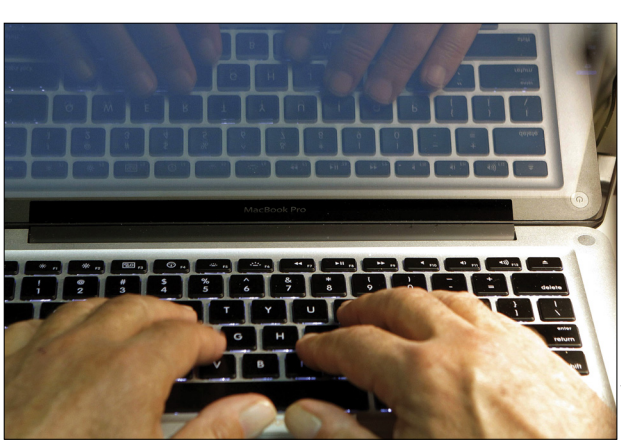
OSPF is a fledgling organisation with credentials. Founders include Bernard Munos, ex-adviser on corporate strategy at Eli Lilly, and Jaykumar Menon of McGill University, Canada, a human-rights lawyer who has turned his attention to drugs for neglected diseases. Ex-head of R&D at AstraZeneca India, Tanjore Balganesh, will run product development partnership (PDP) for OSPF to manage development and manufacturing from Bangalore, India.

The wider global health community—from Médecins Sans Frontières to Sanofi-Aventis—has attended its meetings, a roadmap is agreed, and seed funding secured from India's Tata Trusts. "We are going to prove that there is an alternate way by applying open-source principles at each stage of the process", says Menon. So, for clinical trials, OSPF will use existing platforms; including one that crowdsources clinical trial protocols and an online laboratory notebook that allows data to be regularly posted from clinical trials. OSPF will also work with the European and Developing Country Clinical Trials Partnership, which runs clinical trials for neglected diseases in Africa. Menon says their clinical trial costs will be significantly less than pharma's by using open platforms, carrying them out in cheaper, endemic countries, and securing innovative funding schemes.

Old roots

OSPF is not the only drug project using open methods. It is actually a direct descendant of Open Source Drug Discovery (OSDD), an Indian Government consortium that has, since 2008, led thousands of academics and undergraduates across India to work on tuberculosis (Balganesh was OSDD's project head).

Open source has been tried for over a decade, spawning Cambia's open-patent database and Medicines for Malaria Venture (MMV)'s Pathogen Box project among others; MMV posts pathogen boxes—400 compounds that could combat pathogens causing some of the world's most neglected diseases—to research groups worldwide in return for a commitment to put results in the public domain within 2 years (a precursor—the Malaria Box—has already led to 30 published papers).



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Open source is popular too; civil society organisations in March proposed support for it within the Johannesburg Declaration presented to the UN Secretary-General's high-level panel on access to medicines. WHO's Consultative Expert Working Group recommended more open-source approaches to R&D and innovation too; MMV's project is a WHO demonstration project designed to test such approaches.

Proponents say that open-source methods are needed because research fiefdoms have built up around neglected diseases and stalled progress towards new drugs. Researchers have refused to share data during some outbreaks fearing, among other reasons, that they'd jeopardise their own chances for publication; universities rush to patent discoveries even for neglected diseases.

Individual researchers are trying open concepts; some are publishing straight to the internet. Research chemist Isaac Yonemoto, has crowdfunded Project Marilyn—research on an abandoned molecule, which might have oncological effects. He regularly posts results online so that they cannot be patented and began testing in a mouse model this month.

So-called biohackers are working on devising a simpler and cheaper method to create insulin for those who cannot afford it, including poorer Americans. Many work in their spare time at Open Insulin's California laboratories, which have been crowdfunded. Pharmaceutical companies are even opening their drug libraries to outside scientists.

Despite the number of open projects, most concentrate on the preclinical stages of drug development. None have produced drugs. "Nobody is doing drug discovery for neglected diseases in the open", says Aled Edwards, CEO of Structural Genomics Consortium, which resolves the structure of potential drug targets, develops inhibitors (possible protodrugs), and posts them to researchers and into the public domain. He plans an alternative open-source business model that goes beyond the preclinical stage and passes molecules to commercial manufacturers after the proof-of-concept stage, so that they can undertake and pay for phase 3 trials.

> **"…. fiefdoms have built up around neglected diseases and stalled progress towards new drugs."**

Previous projects probably underestimated how ferociously complex drug discovery is compared with software. Development is more expensive too, especially, for clinical trials. So once an open molecule looks promising, it or variations of it often disappear into commercial development, are patented, and taken out of the public domain.

Truly open source?

Open-source labels are often misleading anyway; openness might only apply to a tiny portion of the development cycle, says Christine Årdal of the Norwegian Institute of Public Health, who has studied several so-called open-source projects. "It might be very trendy to say that it's open source when in fact it's not", she says. If a project can boast open data sharing, collaboration, and rules that ensure results remain open too, it's probably open source. If problems are placed in the public domain but the solutions are not, that's open innovation, she says.

Årdal argues that even OSDD—hailed as one of the greatest open-source projects so far—is actually crowdsourcing because it owns everything that is discovered, and the results are not always easily accessible to the wider community to critique or work on.

Labelling a project open source brings great PR and kudos. But it's undeserved if the project merely rehashes age-old scientific methods such as collaborations between grant-funded scientists who would already be working in the field anyway. So says Stephen Maurer, of the University of California, Berkeley, USA, who first proposed the open-source Tropical Disease Initiative as far back as 2004.

True open source should instead unleash talents not already there; the enthusiasm of scientists with day jobs who love problem solving or doing altruistic work in their spare time; female scientists excluded from the workplace who can manipulate molecules on home computers, or even companies that undertake pro-bono work on open-source projects to impress potential clients, he says. Importantly, it must be a viable alternative to pharmaceutical companies. "The definition should mean something. We are trying to design a new institution that performs better than what we already have", he says.

So now OSPF must prove it can bring a drug to market. Fine details will be worked out; pricing models should ensure individual researchers' efforts are vetted and properly attributed. And, importantly, the public funds that it believes are available for open source need to materialise.

That's why OSPF's first clinical trials will focus on repurposed drugs; some existing drugs developed for one disease often show promise against others (an epileptic drug might work against tuberculosis, for instance). Bruce Bloom, president and chief scientific officer of US repurposing organisation, Cures Within Reach, which is working with OSPF, says running trials of repurposed drugs can cost as little as US$500 000 and take just 3–5 years to complete. Funders and the larger global health community will be more inclined to back open source if they can see a real drug, says Todd.

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