Open Science in Drug Discovery: Addressing the Gaps in Traditional Model of Developing New Medicines

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Does the name Linus Torvalds ring any bell? I would not be surprised if the answer is: No! Just to let you know, he developed a "free" operating system as a "hobby" in 1991, while he was a student at the University of Helsinki, which we know today as Linux. Torvalds might have championed Linux, but eventually, it was upgraded by additions and changes introduced by many individuals to its openly available source code. But what is the significance of this development when we are not talking about computer programs or software but an utterly different subject medicine? Before I start to draw the connections, let me make a disclaimer! I will use the term "drug" instead of "medicine" in the rest of the writing and do not confuse it with Cannabis, Cocaine, Ecstasy, and so on.

Now, back to the previous question, why have I started with "Linux" while the title says "drug discovery"? It is because of the philosophy behind "open-source" and "crowdsourcing". So, does a new drug developed using open-source models? Obviously, no. It is generally one hell of a closely guarded process with numerous IP protections. But it would have been best if drug discovery could follow open-source philosophy. We would have been able to afford drugs way more easily, at a much lower price, if not free as in the case of "Linux". Well, I must put a warning before we get over-excited. Drug development processes need access to wet labs and clinical trials and, finally, approval by the appropriate authorities, so the whole process is way more complicated than developing software!

Traditional Models of Drug Discovery & Development

The COVID-19 pandemic has evoked a lot of curiosity around vaccine and drug developments. How is a new vaccine made? How effective are the new drugs in treating COVID? It takes a lot of effort, time, and money to discover new medicines and finally produce and bring them to the market. Let me explain the traditional drug discovery process- a tried and tested model used for nearly 70 years by all the large Pharma companies. These companies, like GlaxoSmithKline, Johnson & Johnson, Pfizer, Novartis, etc., all operate mostly in-house while developing a new drug for any disease.

The R&D process pipeline, clearing the regulatory hurdles and finally bringing the life-saving treatment to the market, takes about 10-15 years and costs around $2.6 billion. But that is not the end; it further involves post-marketing monitoring and development costs which amount to around $300 million. According to estimates, an entire lifecycle of R&D of a new drug takes up to three billion per drug. So it is no wonder many life-saving drugs are expensive. But what about the cost of human lives? Can we just continue



The Drug Development Process

with the same old calculation of checks and balances, or should we start looking for alternative models? The need to update the traditional approach to drug development is more apparent when we consider that the cost of developing a new drug has increased exponentially in the last decade. Still, the total number of new drugs remained relatively constant on the output side.

Open Science in Drug Discovery

The good news is that the open and collaborative drug discovery models have started to take shape based on the open-source philosophy, also referred to as open science in a more generalised term. For example, Prof. Aled Edwards from the University of Toronto established a start-up Medicines4Kids (M4K) Pharma, in late 2017, along with his business partner Owen Roberts. The focus of M4K is to develop a new treatment for a rare, incurable, and fatal pediatric cancer called Diffuse Intrinsic Pontine Glioma (DIPG). They also founded another start-up, Medicines for Neurodegeneration (M4ND) Pharma. This one is dedicated to developing drugs for neurodegenerative conditions such as Parkinson's disease and amyotrophic lateral sclerosis. These companies are among the very few in the world of Pharma to employ an open science approach in their R&D strategy. Their drug development process is based on collaboration that emphasises the open sharing of data with partners and the public. COVID Moonshot is another grand open science experiment that aims to develop accessible and affordable antiviral drugs to combat SARS-CoV-2 infection. Moonshot is a non-profit open science consortium that started spontaneously in March 2020 through virtual collaboration. Around 150 experts from diverse backgrounds and fields joined hands for the Moonshot, crowdsourced ideas on novel molecular entities, used modelling techniques to evaluate effectiveness against the virus, and so on without claiming intellectual property. The first clinical trials of the identified drug molecules are expected to begin soon.

Open Science-Based Drug Discovery for Neglected Diseases

The Open Science approach to drug discovery is more prevalent in neglected disease areas, such as malaria, tuberculosis, etc. Big pharma companies are not interested in this domain as they are not profitable disease profiles for investment. Open Source Malaria project is engaged in finding cures for malaria. Guided by open source principles, all data from the project is available in the open domain, and anyone can contribute to the project. Open Source Pharma Foundation (OSPF) is another open-source drug discovery platform. OSPF received funding from the Tata Trusts, an India-based philanthropic group, in 2018. OSPF has successfully

repurposed the generic diabetes drug metformin as a tuberculosis treatment and moved it into Phase 2B clinical trials. The development process of this repurposed drug is quite fast compared to the traditional ways, and the cost is reported to be remarkably low in contrast to an estimated cost of $2.6 billion typically needed to make a new drug. These successes give us hope for a better future. But many such open science-based drug discovery initiatives saw untimely closure as well. Open Source Drug Discovery (OSDD), an initiative from CSIR, India, is one such example. The last updated event on the website of OSDD dates back to 2015. The publications listed on the site also date back to 2014. But failed initiatives are also essential to building a successful one, especially understanding the challenges in terms of costs, timelines, partner contributions, credit sharing, etc.

Funding of Open Science Projects

Another essential question is how open science-based projects are funded. A vast majority of funds for research comes from taxpayers' money in the Indian ecosystem. The government contributes almost entirely to R&D at public universities and institutions. The private sector has a minuscule percentage in R&D expenditure. Nowadays, crowdfunding is emerging as a viable alternative for funding scientific research. Crowdfunding is a known concept in the global north but is still in its infancy in the global south, including India. Experiment, USEED, Consano, etc., are a few online crowdfunding sites for scientific research.

A few universities and institutes have initiated their own online efforts. They utilise their alumni network for funding. Another approach is via open innovation models, where universities/ institutions can develop a formal collaborative partnership with industry and co-create knowledge. In such cases, IP-related queries are handled through various legal agreements. Open Innovation is a concept first introduced by Henry Chesbrough and is a widely used model in the R&D ecosystem.

However, when we are discoursing developing new drugs, the sheer volume of funding needed for such initiatives makes it harder to achieve entirely through crowdfunding. Therefore, such open science-based drug development projects are generally funded by NGOs or philanthropic trusts. For example, the COVID moonshot project is funded by Wellcome Trust UK, Bill & Melinda Gates Foundation, COVID-19 Therapeutics Accelerator (CTA), LifeArc, and crowdfunding as well. As mentioned previously, in the COVID Moonshot project, all collaborators contributed to the knowledge pool through an open platform without claiming any rights over intellectual property for the greater good of society. A few COVID Moonshot project participants are the University of Oxford, the University of Cambridge, the Weizmann Institute of Science in Rehovot, Israel, the University of Johannesburg, the Drugs for Neglected Diseases initiative (DND*i*) in Switzerland, and many more. Sai Life Sciences of India also contributed to this project in terms of chemical synthesis.

In conclusion, it will take time to create awareness and bring changes in the overall traditional models of developing new medicines. But open science and crowdfunding have a bright future and are the best way to look forward.