Open Source
The Future of Drug Discovery

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In the world of big pharma, it used to be the case that secrecy paid off big-time. Why risk revealing your drug-discovery pipeline when your competitors may just jump on the band-wagon and eat into your market-share? This model no longer holds water in an era of spiraling healthcare costs and the increasingly inter-disciplinary nature of medical science. Secrecy and counter-productive, profiteering IP policies have now given way to a model that literally seeks openness in both name and function. Established in 2008 under the auspices of India’s Council of Scientific and Industrial Research (CSIR), the Open Source Drug Discovery (OSDD) network has gathered resources for developing drugs that pharmaceutical companies don’t find attractive enough. In an exclusive interview, OSDD’s founding father, Professor Samir K. Brahmachari tells APBN why it pays in more ways than one, to be open.

APBN: How did you come up with the idea of OSDD?

Samir Brahmachari: I was involved in genomics and as director of the Council of Scientific and Industrial Research’s (CSIR) Institute of Genomics and Integrative Biology, I realized that we have to develop a systems biology approach to understand complex diseases. I saw that TB is the most devastating disease in India – a 1000 people die every day yet the genome sequence of the TB-causing microbe has been available for almost a decade, which means it should have been easy to target genetic vulnerabilities of the microbe. At the same time, I could also see the cost of human genome sequencing coming down, so I simply asked, if human genome sequencing and its analysis was done in public domain and made open source, why can’t we take drug discovery to open source? What are the hurdles that we face? I knew that Indian laboratories had done exceptionally well to do generic drug synthesis and Indian companies had been successful in taking those generics to market. That means we are very good at development – specifically low-cost development. CSIR has the tradition of drug development at affordable costs to make Indian generics the world leader. So what is missing? We did not invent new drugs. So the idea was very simple, OSDD is open source drug discovery. If I can make a drug discovery cheaper with high efficacy without side effects, using a systems biology approach, we should then be able to take it further to development at a low cost.

APBN: Why is open innovation the future of drug development?

Samir Brahmachari: The reason is that difficult problems need multiple expertise. It is very difficult to gather them together physically but it is easy to gather them on cyber-space. Look at the way Facebook users work and interact and it’s easy to see why open innovation is more successful. Another reason, is if we look at the way we develop an F1 car, we don’t build a car and then drive the car. Instead, we simulate the car on the computer and then make 5 prototypes which are then put into the wind tunnel and finally 2 cars are manufactured and one runs the race and wins it.

I believe the drug discovery of tomorrow will be heavily dominated by the in-silico experiments where one should be able to simulate everything and see where the drug is going, what are the pathways what are the other possibilities and based on that eventually molecules will be made whose failure rate will decrease by a factor 10 or 20. This will
reduce the cost from a billion dollars to a few million dollars. Furthermore, if the Indian generic industry has demonstrated that even a generic drug can make substantial profit, there should be no reason why companies will not participate in taking up new invented molecules which will become generic because it will be shared by others.

APBN: What are some unique features of India’s bio-research landscape that make OSDD a success?

Samir Brahmachari: India is still a resource limited country. Our resources might have increased, but it is still much less than anywhere in the world, particularly when compared to developed countries such as America, Japan and even China and European countries. But I think we have a very large student community that is very hungry to learn and which is really passionate. I think OSDD has been able to convert this activity from a professional enterprise into an emotional enterprise and young people are committed emotionally. And that, I think, is the strength of OSDD in India. Overall however, in India, we do not have too many experienced scientists who have actually discovered new molecules for drugs. This is something I hope to change with OSDD.

Another factor is India’s strong tradition of supporting anything that benefits the poorest of the poor. Profiteering is not the ultimate motto. You are more respected if you have been able to provide benefit to the bottom of the economic pyramid. It also helps that the government has invested heavily in a high GB bandwidth connectivity across the country that is available to people at zero cost. All these things make India an ideal place for OSDD to flourish.

In India, our science and scientists are very hierarchical. We respect our seniors, even if our senior is not making a right statement we will not argue. Instead, we will respect it and that’s the way our culture and family is. This is not good for science. Respect and seniority should not impede science. In cyberspace, something happens to us. We get out of our own cultural roots and try to become different. Things that we hesitate to tell our wives face to face, we have no difficulty communicating to them on social media. This is an interesting phenomenon that is advantageous for the development of Indian science which has been hampered for too long by a respect for hierarchy and seniority.

APBN: What are some of the challenges to the open source model of drug discovery?

Samir Brahmachari: OSDD is sharing drug discovery data and I believe we can do open source clinical trials, but I need to convince regulatory authorities that once the safety phase 1 is cleared, phase 2A where there is a limited number of patients, demonstrates safety. We also need to go into e-clinical trials where the data will go up and volunteer patients will join looking at the public domain data and then decide whether they want to participate or not. It is happening in various diseases, where there is no treatment even in the USA. Patient groups are taking an interest in any new molecules at the laboratory level. I think this would be a new challenge as it represents a fundamental shift in both patients and doctors mindsets at the clinical level.

APBN: There has been a lot of talk about the big pharma model of drug discovery falling apart. Why is this happening?

Samir Brahmachari: I have not worked in a big pharma so it will not be possible for me to reveal internal information but from what I understand, pharma companies are big on confidentiality clauses. It gives the company a big advantage over others but the weakness of the system is that it does not allow everybody’s brain power to come together. In contrast, look at the success of IT, whether it is Apple or Zuckerberg’s Facebook, all of this is possible because of youth – not some company. Pharma by virtue of its structure of organization, is not able to utilize the brightest. Young students never join pharma and anyone who joins pharma, joins as the technical support or as a middle-aged person after a certain amount of time in academia. I do not know of any 22, 24, 25 year-old fresh PhD rushing to pharma,
whereas in IT it happens the other way. Somebody who could have been an assistant professor in Berkeley or Stanford is actually coming up with new innovations and spinning out MNCs. I think this is the problem with big pharma – it’s failed to attract young people with fresh ideas because its processes are obsolete.

APBN: Even if OSDD is open source and online, any user still requires a number of years of experience in medicinal chemistry and cell biology to understand and contribute to the field constructively. Doesn’t this platform still favour the more experienced researchers?

Samir Brahmachari: You would be quite surprised to know that on our OSDD platform I think 70% of people are below the age group of 35 and these young people are undergrads. And even those who are studying their bachelors of science and master of science, are participating in complete genome annotation, pathway analysis and we are picking up very unusual and bright kids. Since every contribution is recorded I can see on my computer who is contributing so I can always pick up a bright student sitting in a remote place and I can say hey, come and join this program as a PhD student or young faculty staff. So it is very easy to identify people who might have not done very well in their exams and university grades who might have difficulties in getting admission to organizations or getting into a fellowship, yet are fantastic at coming up with solutions to complex problems.

I just wrote a paper with 50 students from 26 institutions and I don't know them. I only know 3-4 of the important ones and, yes they needed guidance. But they have the drive to do things and get back to you. I personally feel empowered that I can sit in a small building and make my world my laboratory and get a project in and review it and have India’s youngest best minds to tap on.

APBN: One of the principles governing the conduct of clinical trials under the CSIR/OSDD umbrella but with the Open Source concept is that private pharma will be stakeholders. Tell us why this is important.

Samir Brahmachari: Indian pharma companies have demonstrated that they can make molecules at low cost on an industrial scale and maintain quality and market it. The idea behind the principle is that we should be able to take more than one partner who would contribute to the clinical trials cause. The general idea is to take 20% cost from the company and 80% will be borne by OSDD and of the 20% maybe 4 companies will come in together so that brings it down to 5% each. There will be various teams doing the clinical trials. They will all get the manufacturing rights along the way.

APBN: After TB and malaria, what other diseases does OSDD intend to target?

Samir Brahmachari: We have already initiated for malaria and we have no problem and anybody can call it OSDD as long as the drugs produced become affordable and so we are working with others. We believe that leishmania should be the next one which is also a problem in India, next only to cholera. Beyond that, I think the most interesting and challenging will be to discover drugs for chronic long-term diseases which are always very expensive. Pharmacogenomics principles may be applied to identify the right drug for the right patient.

APBN: Besides OSDD, what other kinds of open source development models do you foresee for biomedical science?

Samir Brahmachari: We have prepared open source pharmacogenomics and some of my young colleagues have already started and we have taken the initiative with global effort again. If everybody shares pharmacogenomics markers, in a public domain, patients can actually get the benefits for a particular low cost drug for cancer it might have some side effects in x% of people, wouldn’t you like to know that you don’t belong to that percentage and thereby effectively you can reduce the public health costs significantly?
APBN: When you speak of drug development expertise, what specific qualifications and skills are you looking for?

Samir Brahmachari: This is a question I asked myself before Sanger introduced DNA sequencing, as he was an expert on protein sequencing and that’s why he got the Nobel Prize. If we were to advertise we wanted somebody who has relevant to discover DNA sequencing knowledge then we might not have selected Sanger - Cambridge might not have selected Sanger. My point is that drug discovery is a new science and we are trying to use a systems biology approach. So it will need people with a medical background, medicinal chemistry background, techniques and systems level understanding background, mathematical and computing and simulation, chemical engineers and electrical engineers who know how to create the simulation, in short, all the faculties are needed. We also need to write protocols for new molecules in clinical trials for phase1 and phase 2 which is an expertise that we need to look at.

Perhaps most importantly, we need people who want to solve problems. With such a heterogeneous, inter-disciplinary team – fun in its own way – managing it can be an uphill battle. Leadership with strong goals of solving problems is lacking. What we are looking for is somebody who has at least 2–3 domains of expertise, somebody who is an IT person, who understands networking as well as hardware, software and biochemical pathways. It could even be someone who understands chemistry, computing and docking. Classically these are compartmentalized subjects and there’s a flow of molecules that goes through these compartments of knowledge. In Osdd we realized that we needed inter-disciplinary minded people and that’s what we are looking for. We are also looking for one person to be a brand ambassador for Osdd. This person will be a great communicator and write about Osdd.

I believe Osdd is not a research project – it is a movement, an emotional enterprise, with clear, well-defined, worthy, real-world goals.

APBN: What can Indian universities do to develop more inter-disciplinary minds?

Samir Brahmachari: We have realized that our education system is reasonably compartmentalized and not enormously multi-disciplinary but my CSIR laboratories are a chain of laboratories from biology to engineering to chemistry all put together, providing a unique opportunity to expose graduate students to get exposed to this type of multi-disciplinary type of environment. Very recently we have approval from parliament to set up an academy of scientific research which is called APSIR. It is like a mega university but it is a network environment because these laboratories already exist. The students will come and work in the same laboratories but the academy is an umbrella organisation which makes sure the posts are connected, standards maintained, comprehension is done and the students go to the programs and eventually participate and get a PhD. This is a step in the right direction to develop inter-disciplinary thinking and an innovative culture – both bywords of 21st century science.