

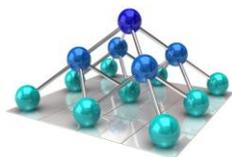
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Open Source Drug Discovery (OSDD)— Collaborative Innovation

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Abstract

Open Source Drug Discovery (OSDD) is a Council of Scientific and Industrial Research (CSIR) Team India Consortium that provides a global platform for collaborative discovery work into novel therapies for neglected tropical diseases including malaria, tuberculosis, and leishmaniasis. OSDD enables the sharing of information, including but not limited to, ideas, articles, papers and other literary work, data, software, applications, notes, results of experiments, patented inventions, and other materials submitted by users. OSDD has more than 4500 registered participants and more than 150 projects on TB drug discovery. Participants formally register and agree to the terms outlined by the OSDD including those referring to the management of knowledge assets and the associated intellectual property. These participants post innovative projects online, actively engage in ongoing scientific projects, share positive and negative results, as well as participate in the review process of other projects posted on the OSDD portal

Two pharmaceutical companies have expressed their desire to be a part of Council of Scientific and Industrial Research's (CSIR) open source drug discovery (OSDD) project for tuberculosis (TB). If the proposals are accepted, bulk of the cost of the clinical trials will be borne by government. If the drug is developed using the resources of OSDD, the parent organization will determine the pricing. The private company that develops the drug cannot apply for a patent.

The early success of the Mtb OSDD programme has presented a model for drug discovery research for infectious diseases with the next target being Malaria.

1.0 Introduction

Open Source Drug Discovery (OSDD) is a Council of Scientific and Industrial Research (CSIR) Team India Consortium that provides a global platform for collaborative discovery work into novel therapies for neglected tropical diseases including malaria, tuberculosis, and leishmaniasis (www.osdd.net). OSDD anticipates providing affordable healthcare to the developing world by providing a platform where the best scientific minds can collaborate and collectively endeavour to solve the complex problems associated with discovering novel therapies for such diseases. Specifically, through the aggregation of and open access to biological and genetic information for scientists, the goal is to enable faster downstream drug discovery (www.osdd.net).

The OSDD portal is the platform supporting this collaboration effort. Challenges are well-defined problems posted on the website. Each of the solutions to these problems is then peer-reviewed. Appropriate rewards are assigned for the respective contributions; in this sense, the OSDD model appears to be emulating the InnoCentive model. (www.osdd.net; www.innocentive.com) Based on the points accrued by contributors, four levels of membership cards are awarded. Each type of card entails a certain sets of rights, privileges, and responsibilities in the entire process (www.osdd.net).

2.0 Knowledge Assets and Management

Knowledge Characteristics:

OSDD enables the sharing of information, including but not limited to, ideas, articles, papers and other literary work, data, software, applications, notes, results of experiments, patented inventions, and other materials submitted by users. In this case, both disembodied pure knowledge including papers, data, software, notes, results and embodied knowledge in the form of biological materials such as molecular libraries, are donated by participants. Interestingly, collaborative resources such as laboratory access and computing time/bandwidth/compute- resources can be contributed to the network. Perhaps then it is more effective to use the following categorization to describe OSDD assets: assets that enable knowledge production while tangible are not tradable (in the traditional sense of trading goods) and those that are an outcome of these knowledge production activities existing in tangible and tradable form. Furthermore, it is worthwhile to note that any intellectual property rights (IPR) are likely associated with software, databases, biological materials, other technological resources (www.osdd.net).

Participant Type:

OSDD is a community of public and private stakeholders—all committed to the open source discovery of drugs. The OSDD project is managed online. All project documents and tracking are done through the OSDD portal. Principal investigators report directly to the project director through this portal. In addition, the core OSDD team meets monthly; at this time the chief mentor reviews the progress of the platform along with the board of mentors (www.osdd.net).

OSDD has more than 4500 registered participants and more than 150 projects on TB drug discovery. Participants formally register and agree to the terms outlined by the OSDD including those referring to the management of knowledge assets and the associated intellectual property. These participants post innovative projects online, actively engage in ongoing scientific projects, share positive and negative results, as well as participate in the review process of other projects posted on the OSDD portal (www.osdd.net).

Rules for Knowledge Production:

The OSDD's objective is to create a collaborative online platform including: a Wiki based genome annotation service; a platform for open source tools for drug discovery; integrative genomic maps; an open access document repository; and a metadata archive and search engine for open access to theses and dissertations. Contributions can be made in the form of database, molecular library or other biological resource donations, laboratory access or the sharing of technological capabilities, computing time, bandwidth or other computation resource access, monetary or in-kind rewards for contributions themselves. Collaboration spaces enable participants to post ideas, to discuss methodologies and possible solutions to the problems, bookmark web based resources for drug discovery, and share experimental data (www.osdd.net).

The entire process of drug discovery is divided into problems that are open for the entire community to contribute to. Larger complex problem are broken into simpler, smaller set of activities which have a clear and well defined scope and deliverables. The smaller sets of activities are termed work packets or work packages (WPs). Each of these solutions is peer-reviewed—with contributors receiving a reward in form of credit points for correctly solving the

problems. Work packages include: target analysis at a computational level including systems biology research and setting up networks; experimental expression of protein targets bringing together experimental reagents and chemicals into the open space; screening of targets discovered using large chemical libraries often involving the participation of contract research organizations; *in silico* docking and identification of a library of chemicals for specific screening—another computation activity; microarray gene expression analysis on human cells and tissues with the most optimal inhibitors; lead optimization of non-toxic hits—an essential stage of the drug discovery process; medicinal chemistry including the synthesis of analogues; proteomics based lead affinity experiments to check for human cellular protein binding; preclinical toxicity analysis of lead compounds—in order to develop a pharmacological profile of the investigational drug; and finally, clinical development of new molecular entities—to establish safety, tolerability, and efficacy of the entities (OSDD, 2009).

Rules for Knowledge Dissemination:

In formulating the terms and conditions of knowledge access and use, the OSDD explicitly addresses the potential problem of other parties filing, and being awarded intellectual property rights based on the information, data, ideas or other materials available on its website, either pre-existing or generated by the OSDD community (sysborgtb.osdd.net).

Hence, all participants are required to partially assign their right(s) pertaining to the resources they contribute, to CSIR acting on behalf of OSDD, for the sole purpose of taking action against any potential infringement. Such an assignment is partial and only for the purpose of protecting the intellectual property generated by OSDD. This step seeks to

prevent the IPR based on the information, ideas, and intellectual property generated by the OSDD users from being misappropriated. Thus OSDD/CSIR holds the intellectual property over the content generated as protected commons. Information available on the OSDD website in any form is confidential information and the proprietary right of the OSDD. Any appropriation of the information to acquire intellectual property rights, without an explicit license of OSDD, is considered misappropriation of the protected commons, liable to legal action under the applicable laws (sysborgtb.osdd.net). By submitting a patented invention for OSDD, donors agree not to place any encumbrances on products or processes arising out of the use of the patented contribution (sysborgtb.osdd.net). One could argue that OSDD has adopted both an ex-ante and ex-post strategy for the management of contributed knowledge assets.

3.0 Organizational Structure

Typology of OSDD:

R&D marketplaces are exemplified by Innocentive or NineSigma. These are intermediaries that auction R&D questions to a community of registered researchers, some of whom will then submit solutions. The winner is eligible to the promised reward. (OECD, 2009) Knowledge communities can also collectively produce new knowledge, which requires a highly structured approach. These communities include open source modes (notably open source software), expert networks (communities of experts sharing freely their knowledge and experience) and user-innovator communities (in the context of user innovation). (OECD, 2009) I contend therefore, that the OSDD has elements of the R&D marketplace and knowledge community and can perhaps be jointly classified as a collaborative knowledge marketplace. In the case of the OSDD, based on the points accrued by contributors, four levels of

membership cards are awarded. Each type of card entails a certain sets of rights, privileges, and responsibilities in the entire process—entitling contributors to a particular status rather than monetary reward.

Organization of Participants:

The entire process of drug discovery is divided into problems which are made open to the entire community to solve. As an example of an open invitation for submitting drug targets, researchers who are working to identify potent drug targets in Mycobacterium tuberculosis are urged to post projects online. Once projects are posted online they will be open for review by the OSDD community and members of the Science Coordination Committee. The project investigators of the projects receiving positive comments are then invited for an online presentation of comprehensive data. Based on input from the OSDD community, the Committee is then able will shortlist targets that will be taken forward in OSDD.

Having then shortlisted targets, the target proteins will have to be expressed and biochemical assays will need to be developed. Subsequently, these assays will have to be converted into screens for identifying inhibitors towards lead identification. OSDD has recently proposed to take this forward via a public-private partnership. Interested members are encouraged to forward details of their experience in developing assays for eventual presentation before a team of scientists (www.osdd.net).

Supporting Infrastructure:

The OSDD's objective is to create a collaborative online platform. SysBorgTB is the Wiki based OSDD collaboration system and cyber infrastructure for collaborative research. SysBorg stands for Systems Biology of the Organism (Mycobacterium

tuberculosis). It is a Mycobacterium tuberculosis genome annotation service. The SysBorg system assigns roles and responsibilities based on the different TWikiGroups. All participants begin as Blue group members; the Platinum group is the highest role that can be attained. Roles are assigned based on a unique micro-attribution system based on contributions to the SysBorg system (sysborgtb.osdd.net).

Other open spaces enable for resource sharing as well as discussions related to drug discovery. OpenIdeaSpace is a collaborative multi-user blog for users to post ideas and to discuss methodologies and possible solutions to the problems. OpenBookmarks is a social bookmarking tool, which is a collaborative platform for bookmarking web based resources for drug discovery.

OpenLabNotebook is used for experimental data sharing. OpenProjectSpace is for scientists/researchers to post and manage projects online. CRDD (Computational Resources for Drug Discovery) is an important module of the *in silico* aspects of OSDD. The CRDD web portal provides computer resources related to drug discovery (www.osdd.net).

4.0 Outcomes

An example of an outcome from the OSDD is the drug discovery project for tuberculosis (TB). For life-style diseases, OSDD indicates that pharmaceutical companies actively scout advances in basic research in search of new and potentially lucrative drug targets. This is not the case with tuberculosis which is mainly a disease affecting developing and the poverty-stricken countries. Hence, this project initially leveraged the world's largest Mycobacterium tuberculosis (MTb) database (hosted by OSDD) to bring together 13 researchers across India to decode 400 of the 4,000 genes of MTb in less than 6 months; this constitutes years of work for a single

researcher (Menon, 2009). Dr. Anshu Bharadwaj, a scientist at the Institute of Genomics and Integrative Biology (IGIB), recently published results of the project having decoded 400 of the 4,000 genes of *Mycobacterium tuberculosis*. Another researcher has published the targets for several genes; and yet another project has shortlisted compounds that are to be tested against the biological targets (Menon, 2009).

The next big leap was to completely re-annotate the entire MTb genome for which OSDD has launched 'Connect to Decode' 2010. Within hours of its announcement, more than 500 researchers volunteered to join this new initiative. Connect to Decode is an ambitious initiative of the OSDD Consortium to (re)annotate the entire *Mycobacterium tuberculosis* genome involving a large number of students and faculty co-ordinators from around the world, and to create one of the most comprehensive datasets encompassing gene annotations, pathways and, immunome of the organism. All data that is generated as part of the Connect to Decode initiative will be made available on the OSDD portal under the OSDD license terms of use (c2d.osdd.net, 2009).

As is the case for the TB project, the OSDD platform brings together both public and private stakeholders with the goal of bringing down the cost of drug discovery for such neglected diseases via open knowledge sharing and constructive collaboration. Drug discovery in the context of a market greatly affected by TB should enable for a local understanding of the disease and product requirements. Furthermore, the training provided and lessons learned can then lend themselves to the discovery of other drugs for neglected diseases such as malaria and leishmaniasis. The associated knowledge production, knowledge dissemination, and IPR management rules specifically seek to ensure that multiple downstream product

development opportunities are exploited for affected markets.

5.0 The Future

Several new initiatives have been established by the CSIR including:

The establishment of an OSDD Chemistry laboratory at CSIR-IICT Hyderabad, exclusively dedicated to synthesis of potential anti TB compounds.

Large scale screening of molecules against TB to find novel molecules which may end up as new TB drugs. For this, CSIR laboratories will open up its small molecule libraries, from synthetic as well as natural sources. We welcome contributions of small molecules to the OSDD Open Access Repository.

Sequencing Mtb strains in large numbers to study variation in *Mycobacterium tuberculosis* (Mtb). This is an Open facility where all researchers who are having interesting TB strains are welcome to contribute them to the OSDD Open Access Repository. These strains will be sequenced and results will be available on OSDD open portal.

The initiation of a collaboration with the Indian Council for Medical Research (ICMR) to bring clinicians and researchers together for improving TB drug research.

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“In addition to the two molecules — developed by the companies — we have two leads of our own,” said OSDD project director Zakir Thomas (Times of India, 2011).

Finally, OSDD will extend its model to other neglected diseases such as Malaria. The early success of the Mtb OSDD programme has presented a model for the way drug discovery research for infectious diseases may move in the future.

(OSDD, 2011)

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