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Patient-driven initiatives for prioritizing drug discovery for rare diseases

India has made great strides in pharmaceuticals with a market size of about $40 billion in this sector. However, our success mostly lies in generics and biosimilars for common disorders[1,2]. There has been little effort to take on the challenge of new drug discovery, especially for rare and neglected diseases where treatments are either not available or are forbiddingly expensive[3]. For many rare genetic disorders, the emerging technologies of gene therapy, gene editing and stem cells are being harnessed in advanced countries to develop novel treatments. With the Indian economic growth on an upward trend, and with the coming-of-age of our pharmaceutical industry, it is reasonable to expect much greater indigenous efforts in new drug discovery taking place within India. While we are amply endowed with intellectual resources, we need to evolve the culture of collaborative problem-solving if we are to succeed in the complex endeavour of new drug discovery. Not only do the clinicians, scientists, funding agencies and pharmaceutical companies require to synergize but the patients cannot be mute spectators and must join these efforts. Highly organized patient groups in some rare diseases have provided the momentum and driven the research, through resource generation, lobbying with regulatory bodies and keeping track of new technologies applicable to their diseases[4].

Patients can best articulate the special concerns of rare diseases

Due to their low frequency, rare diseases are almost invisible to people who matter - doctors, scientists and policymakers. Lack of awareness, even among doctors, results in little effort to study these diseases and find treatments. This is where patient advocacy can play crucial roles[4]. A highly successful patient group in the U.S. 'Parent Project Muscular Dystrophy' (PPMD) demonstrated how the best interests of patients could be served through organized efforts of parents and caregivers of children suffering from Duchenne muscular dystrophy (DMD)[5,6]. In response to a draft guidelines issued for public comment in March 2013, by the European Medicines Agency on clinical investigation of medicinal products for the treatment of DMD, PPMD prepared a white paper, 'Putting Patients First,' to communicate the concerns of the stakeholders who believed that the draft guidelines did not adequately address the patients' needs[7]. As a result, the U.S. federal regulatory body, Food and Drug Administration (FDA) invited PPMD to submit a proposed draft guidance document for the industry. With help from a bevy of scientific experts, industry representatives and healthcare and policy consultants, PPMD crafted a set of guidelines in 2014 for developing drugs for DMD[4]. The FDA used the group's regulatory guidance the first-ever from a rare disease patient organization as a blueprint for its own draft recommendations[8]. In April 2016, Sarepta Therapeutics was denied clearance for the drug Exondys 51 for DMD by the U.S. FDA, on the ground of insufficient data to show the drug's benefit. The clinical trial had been done with only 12 patients. However, patients and their families felt that the drug was beneficial and should not be denied to them. Patient advocacy groups including the Muscular Dystrophy Association and PPMD pressed their case with FDA and succeeded in reversing the decision in September 2016. FDA reversed its decision as the patient groups convinced them that a rare disease with no good treatment options warranted listening to the patient community[9]. Sarepta was asked to conduct a larger two-year clinical trial to confirm that the drug increases dystrophin levels and improves motor function in patients[9]. Accelerated approval made this drug available to patients based on initial data. FDA has been working to incorporate patient opinion in regulatory review processes as it recognizes that patients are perhaps better placed to weigh the benefits with the potential risks that they may undertake with a new drug[10].

Patients can contribute to prioritizing drug targets and planning clinical trials

It is recognized that patient involvement can help in planning clinical trials in multiple ways, especially in fixing end points and treatment outcome[11]. Patient-reported outcome (PRO) is being used in the assessment of clinical trials. Carrillo from the National Institutes of Health, USA, recently reported that 'Incorporation of disease-specific PRO endpoints is of growing importance in drug development. Detecting a clinically meaningful treatment effect that also results in a meaningful effect on quality of life is necessary to allow for adequate review of promising drug therapies'[12]. Use of PRO in clinical trials has also been stressed by the FDA in their guidelines for industry[13]. Moreover, patient groups can help in the efficient and cost-effective recruitment of participants in trials, which can effectively lower the cost of drug development.

Patients have also supported drug development by contributing to fundraising required for drug development. In both Europe and the USA, there are many success stories. Muscular Dystrophy Association of America has helped to carry out the development of a gene therapy system in spite of scepticism from industry[14]. Development of therapy for Limb Girdle Muscular Dystrophy is being mainly supported by patient groups, such as Jain Foundation[15]. A recent study carried out by EURODIS (Rare Diseases Europe) showed that 37 per cent of the rare diseases patient groups in Europe supported research towards therapy to different extent[16]. The Dystrophy Annihilation Research Trust (DART) has completed preclinical studies for an exon-skipping therapy and The Dystrophy Annihilation Research Trust (DART) in India has completed preclinical studies for an exon-skipping therapy and has got permission to treat a DMD patient.

India with its large population size needs to replicate the success of DART by incentivizing and promoting patient groups and including them in the entire process of drug development pipeline starting with identification of drug targets to planning and execution of clinical trials. None could have greater motivation to find rapid treatment for a rare disease than the parents of a suffering child. Including patients and their loved ones as participants in the rare disease drug discovery endeavour is, thus, the need of the hour.

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Alok Bhattacharya[1,*] & Sudha Bhattacharya[2]

[1]Department of Biology, Ashoka University, National Capital Region, Sonepat 131 029, Haryana & [2]School of Environmental Sciences, Jawaharlal Nehru University, New Delhi 110 067, India

[*]*For correspondence*: alok.bhattacharya@gmail.com

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