CALIFORNIA STATE UNIVERSITY SAN MARCOS

PROJECT SIGNATURE PAGE

PROJECT SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE

MASTER OF SCIENCE

IN

BIOTECHNOLOGY

PROJECT TITLE: Global Outreach-The Rare patient journey and regulatory obstacles in India; USP7 as a case study

AUTHOR: Kavita Chandrashekar

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THE PROJECT HAS BEEN ACCEPTED BY THE PROJECT COMMITTEE IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN BIOTECHNOLOGY.

Dr. Betsy Read PROJECT COMMITTEE CHAIR	Betsy A Read SIGNATURE	12/4/2018 DATE
Dr. Chandrasen Soans PROJECT COMMITTEE MEMBER	 SIGNATURE	12/5/18 DATE
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Global Outreach: The Rare Patient journey and regulatory obstacles in India; USP7 as a case study.

Kavita Chandrashekar

Committee

Dr. Betsy Read, Dr. Chandrasen Soans, Dr. Christina Waters

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ABSTRACT

Title	**Global Outreach: The Rare Patient journey and regulatory obstacles in India; USP7 as a case study**
Company	**Rare Science**
Author	**Kavita Chandrashekar**
Defense date	**10th August 2018**
Program	**Professional Science Masters Biotechnology**
School	**California State University San Marcos**

This project was conducted for Rare Science, a non-profit organization that works directly with patient families and foundations to accelerate therapeutic solutions for children with rare diseases.

Introduction

The famous philosopher once said, “Rare is the union of Purity and Beauty” - but this thought, however beautiful might not apply to diseases that are rare. In the United States, a rare disease is defined as a condition that affects fewer than 200,000 people at any given time [1]. When a disease occurrence is seldom, it is difficult for parents to seek answers to procure a quick diagnosis, find the root cause, and identify a treatment plan.

Rare Science aspires to connect patients, researchers, and physicians to accelerate discovery for therapeutic treatments. The Patient Outreach team focuses on a single rare genetic disease/condition each month. The overarching goal is to understand the disease, describe the common symptoms and identify closely related diseases (overlapping conditions). To accomplish this, physicians are interviewed, data is collected from the National Organization of Rare Disease (NORD), and a review of the literature is conducted. The information that is collected is uploaded through the RARE Hub which is a neutral common computational platform that links stakeholders including the patient family, foundation, research scientists and clinical entities. This then serves a valuable resource for any interested parties and may help with early diagnosis and intervention. Apart from the work of the patient outreach team, Rare Science aims to unite patient communities across the world by building registries rich in patient-reported information, clinical and research data.

Objective

For this project, the focus was on conditions associated with USP7 gene mutation with the goal of identifying children affected by that genetic disorder in India. The USP7 gene mutation was only recently discovered in 2013, with 34 cases reported around the world [1]. Collecting data from a wide pool, allows researchers to understand how genotype is related to phenotype and why a mutation manifests differently in each individual. But the challenge is that those affected are dispersed across different countries; they all have their own distinct regulations and reporting systems with varying access to genetic testing.

A rare disease has no geographic boundaries. Rare Science as a non-profit organization is interested in DNA sequencing as the means for identifying biological causes and solutions to rare diseases. Genome Sequencing information from individuals suffering from a rare disease is invaluable in terms of understanding the biological pathways and modeling drugs and other therapeutic modalities.

For USP7, India is an untapped resource. The aim of this project was to determine whether an individual with a USP7 gene mutation could be identified. Through this project, the key aim is to gain access to an untapped section of the population and provide a future of possibilities for children affected with rare diseases in India.

The specific objectives of the project include:

1) To comprehend the regulatory practices in India with respect to documenting the rare diseases.

2) To determine the challenges for rare disease patient families in India.

3) To trace the patient journey from realization to diagnosis, of a rare disease, by using USP7 as a case study.

Results

For this project, I interviewed 93 individuals including physicians, physical therapists, occupational therapists, Ayurvedic and Homeopathic health professionals, special health educators, and parents of children suffering from rare diseases using a 15-item questionnaire. The questionnaire helped to innumerate the challenges faced by the patient families in a country where healthcare regulations vary considerably.

Conclusion

Not a single USP7 patient in India could be equivocally identified. Although there is a large number of rare disease cases in India, there are no official patient registries to accurately document these conditions. In addition, lack of awareness of USP7 gene mutation was the biggest challenge in detecting potential cases. There are millions of children with Autism Spectrum Disorder who show the classic symptoms of USP7 including seizures, contractures or hip dysplasia. In a country where genome sequencing is not encouraged for medical diagnosis, makes it that much more difficult to identify patients suffering from USP7 gene mutations. India is also one of the 13 countries around the globe that is still in the Undiagnosed Diseases Network (UDN). “The UDN is a research study supported by National Institutes of Health Common Fund that seeks to provide answers for patients and families affected by rare conditions”. This paper focuses on the necessary tools and contributions needed by various organizations to bring the country into this network.

ACKNOWLEDGMENTS

This project would not have been possible without the kind support, valuable guidance and continuous encouragement from Dr. Betsy Read, Dr. Chandrasen Soans, and Dr. Christina Waters. I would like to extend my sincere gratitude to all of them. I am highly indebted to Dr. Betsy Read for providing me an opportunity to work with Rare Science for the SIR project. I would like to express my special gratitude to Dr. Christina Waters for letting me work on this enriching project and for her continuous support and guidance throughout my study and research. My thanks and appreciation also go to my colleagues for the stimulating discussions that provided useful insight. Last but not least, I would like to thank my spouse who has been my pillar of strength in this entire challenging journey.

Global Outreach-The Rare patient journey and regulatory obstacles in India; USP7 as a case study

-Committee Members:

Dr. Betsy Read

Dr. Chandrasen Soans

Dr. Christina Waters

Kavita Chandrashekar

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350 million people or 6 to 8% of the world's population is affected by a Rare disease

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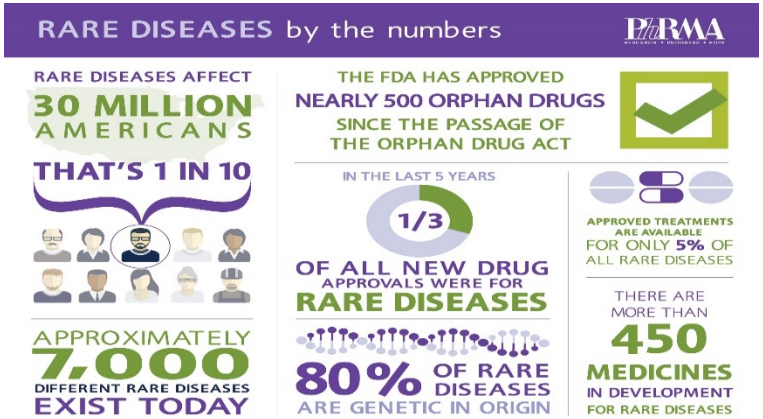
Most common challenges faced by parents across the world are desperation, lengthy years of diagnosis, and only few available treatment options



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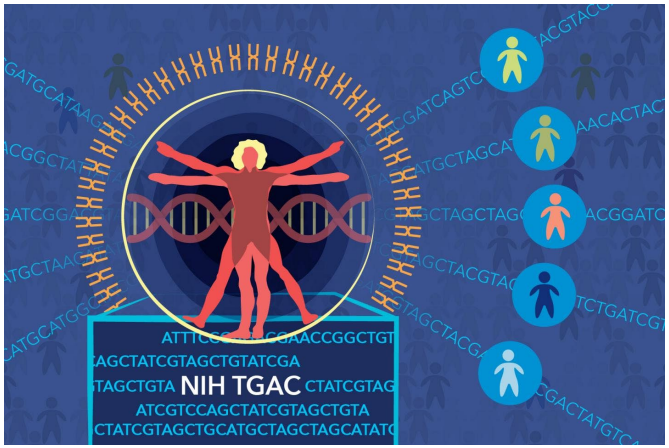
US and UK have made great advances in the field of Genomics

The 100,000 Genomes Project

Genomics England & Partners

NHS

NHGRI



NIH- TGAC

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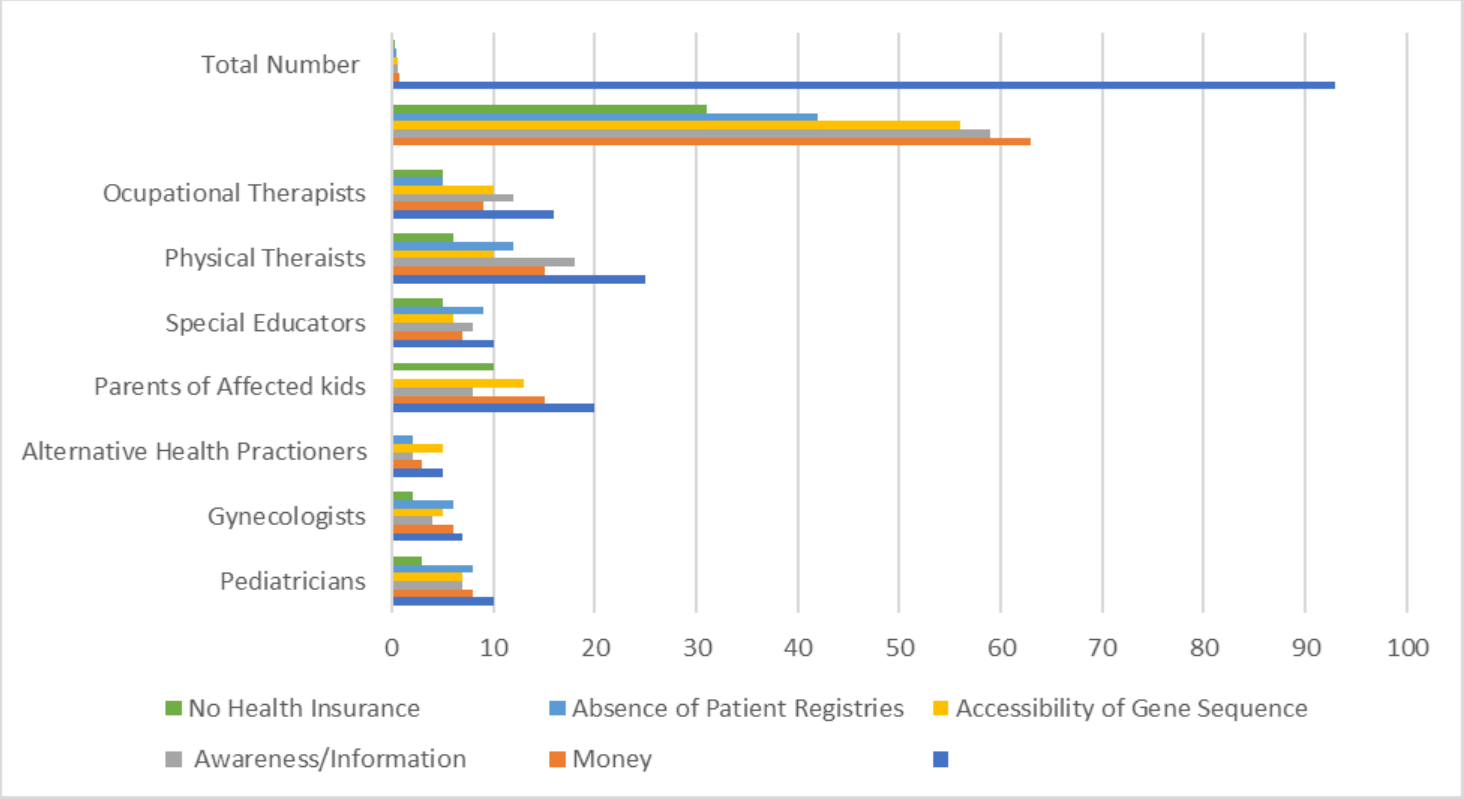
Insufficient Funds and Lack of Awareness account for the most common challenges faced by families with Rare disease patient families in India



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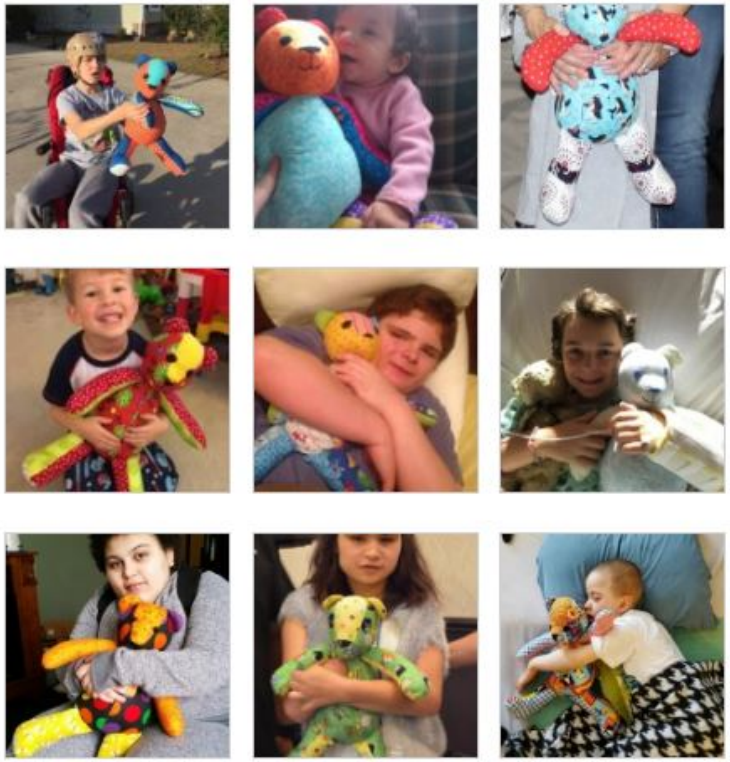
Rare Science is a San Diego based NGO that leverages rare disease research to connect families across the globe



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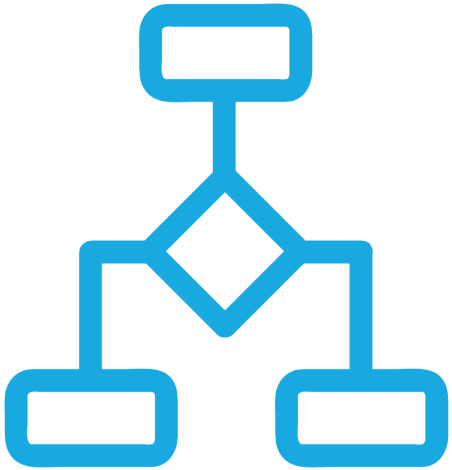
My project objectives were to identify a USP7 child from India and connect them to a support group

Assimilate patient challenges



Develop a flowchart

Understand regulatory practices in India

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USP7 is an ultra-rare gene mutation that was used as a case example for this study

FOUNDATION USP7 DELETION OR MUTATION

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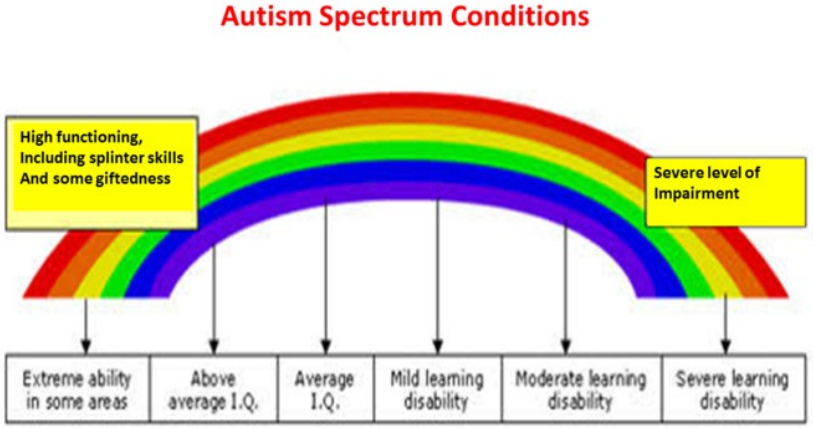
USP7 is often confused and misdiagnosed as Prader-Willi or Schaaf-Yang syndrome



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Health professionals from across India were targeted for this study to provide insight into the state of Rare diseases in the country

93 people interviewed
Included:

Pediatricians
Gynecologists
Physical Therapists
Occupational Therapists
Alternative health
Practioners
Special Educators
Parents of affected
children

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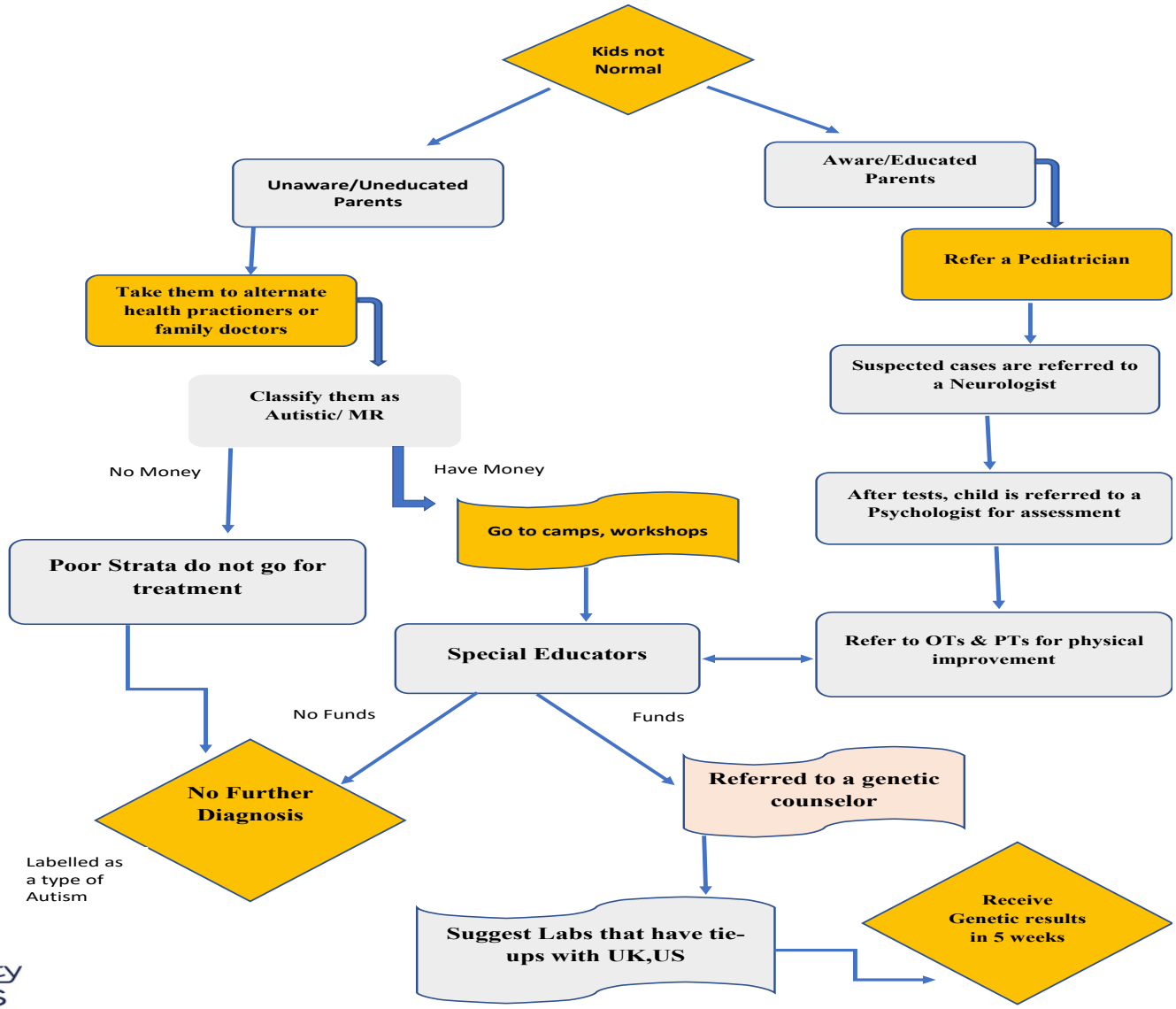
The flowchart depicts the potential journey of patients from disclosure to diagnosis in India



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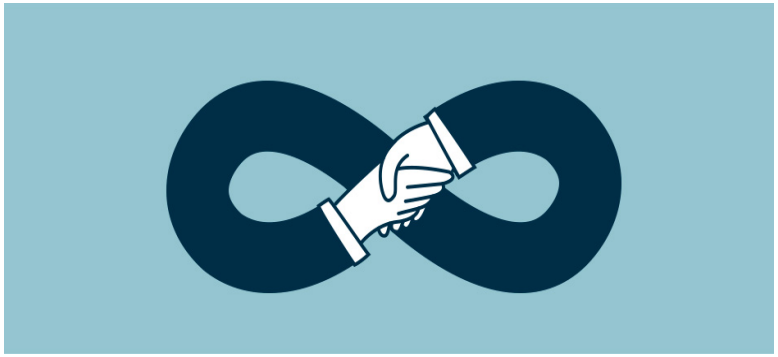
Established contact with Organization of Rare disease India (ORDI) with possible collaboration efforts between Rare Science and ORDI



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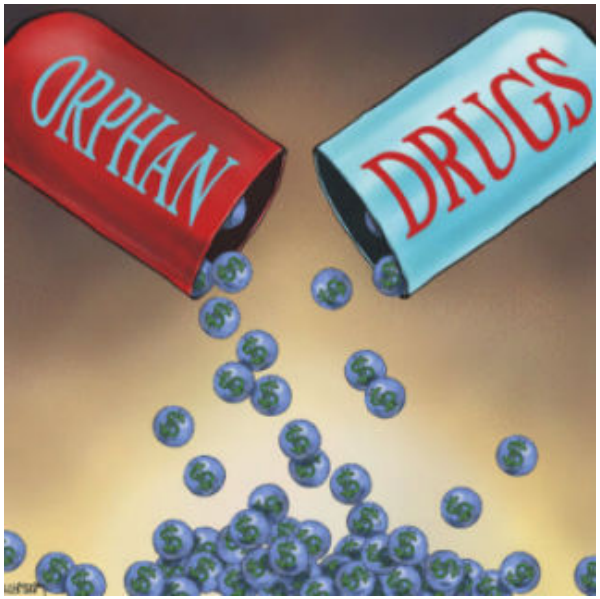
International partnerships



Future Scope for India to address the Rare disease landscape

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Conclusion

- **This study provided an overview of the challenges encountered by Rare disease patient families in India, based on the interview data.**
- **Of the 93 people interviewed, not one USP7 individual was identified.**
- **However, despite this setback, the major outcome for this study was identifying ORDI as a potential collaborator for Rare science.**

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Future Direction

- **Most of the genome sequencing in India focuses on agriculture**

To tackle the dearth in human genome sequencing India can:

- **Partner with international genomic corporations**
- **Increase funding options for genetic studies**
- **Implement information campaigns for Rare diseases**

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