CURE SRD5A3

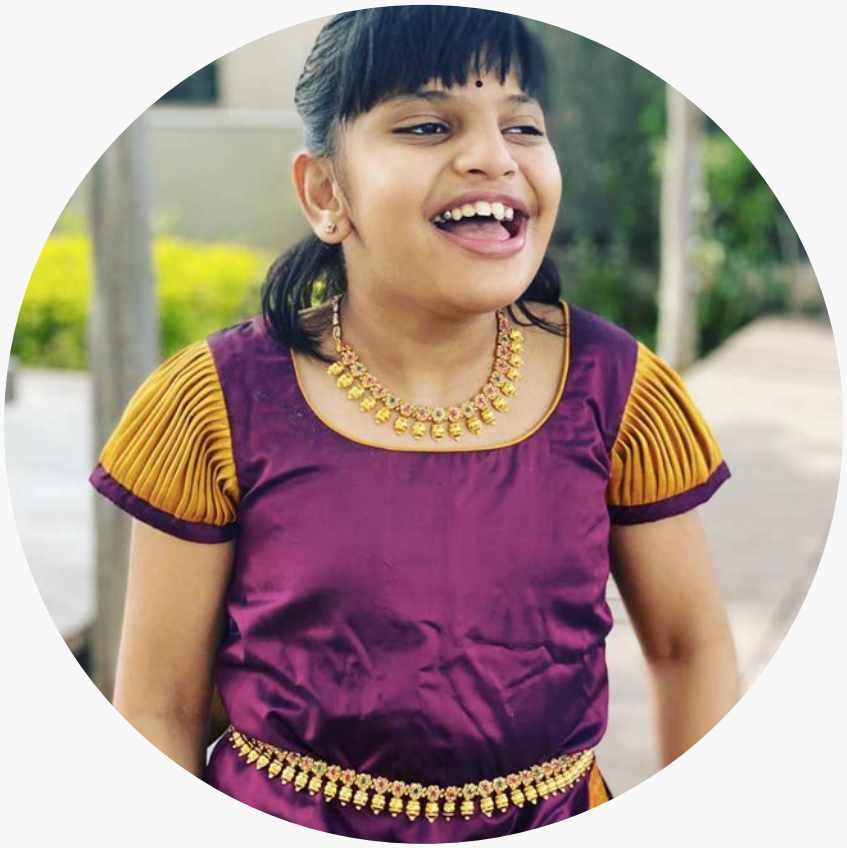
RESEARCH DECK

Vijay Sappani
Founder

ELA CAPITAL

SAPPANI FOUNDATION

OUR **STORY**



ELA SAPPANI

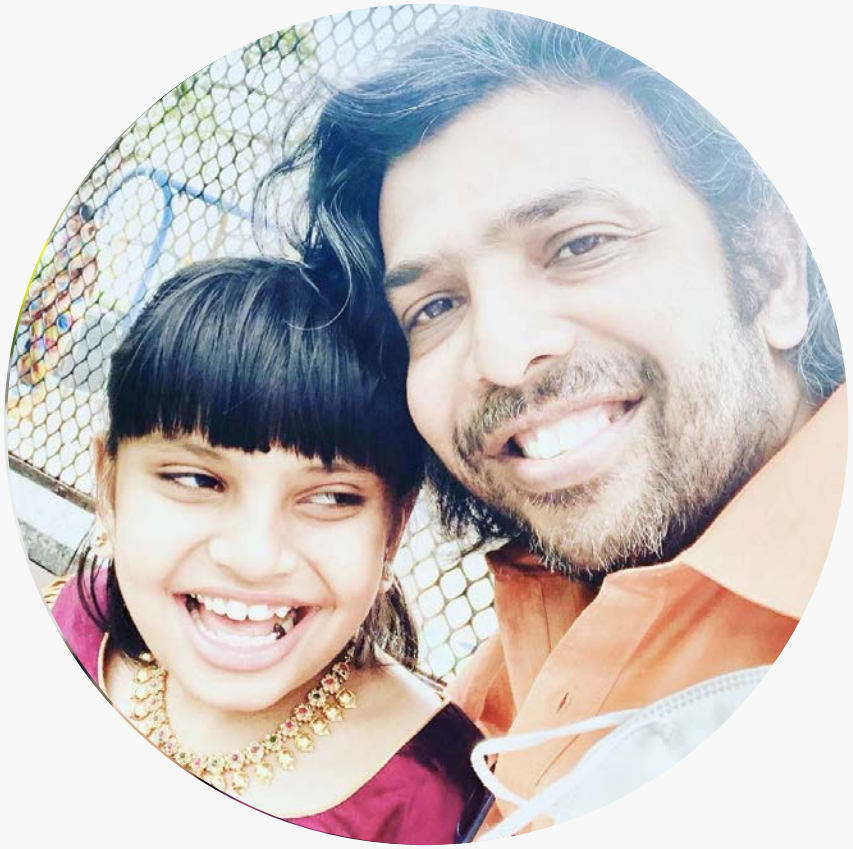
Cure SRD5A3 began in 2019 as a personal journey for Vijay Sappani when his daughter Ela was diagnosed with SRD5A3-CDG, an **ultra-rare congenital disorder of glycosylation** for which there are **no available treatments.**

Ela's journey has been difficult for her and her family, taking **7 specialists** and **3 years just to reach a diagnosis.** She continues to work with over **8 therapists regularly** as this disorder **affects every aspect of her daily life.**

Cure SRD5A3 is committed to improving the quality of life for this underserved patient population by **advancing research on and developing therapies for SRD5A3-CDG.**

CURE SRD5A3

OUR **STORY**



VIJAY & ELA

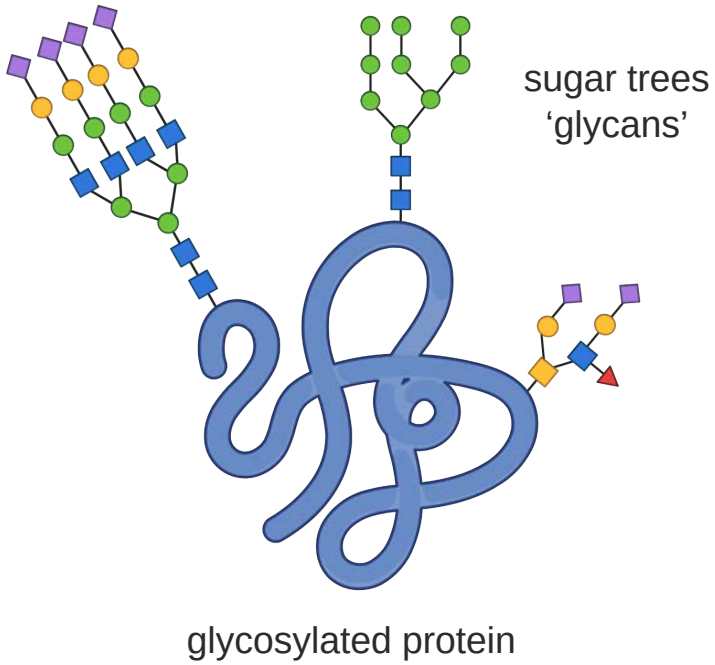
As a parent of a child with a rare disease and the founder of Cure SRD5A3, Vijay is a leading advocate in the rare disease and CDG communities globally.

Vijay does philanthropic work through the Sappani Foundation with a key focus on rare diseases and CDG. He also sits on the board of directors for the Canadian Organization for Rare Disorders (CORD) and CDG Canada.

CURE SRD5A3

CONGENITAL DISORDERS OF **GLYCOSYLATION (CDG)**

SRD5A3-CDG is one of over 170 rare CDG which are single-gene metabolic disorders caused by defects in glycosylation.



- Glycosylation is the complex process by which sugars are added to proteins and lipids.
- Most CDGs have a significant impact on quality of life and affect multiple organ systems, highlighting the critical importance of glycosylation.
- Common symptoms include developmental delays, intellectual disability, neurological abnormalities, clotting and endocrine problems.

CURE SRD5A3

STEROID 5A-REDUCTASE TYPE 3 **(SRD5A3-CDG)**

- SRD5A3-CDG is an ultra-rare (60+ patients) autosomal recessive disease caused by mutations in the *SRD5A3* gene.
- The homozygous nonsense mutation c.57G>A, p. (W19X) is the most common mutation, reported in ~50% of patients.
- W19X is associated with early-onset retinal dystrophy.

CLINICAL PRESENTATION

SRD5A3-CDG is a multisystemic disorder present at birth. Symptoms include:

Neurological: intellectual disability, developmental delay, ataxia, poor muscle tone

Ophthalmological: visual loss, early-onset retinal dystrophy, retinitis pigmentosa, nystagmus

Skin: dry skin, ichthyosis, skin rash

Skeletal: scoliosis, kyphosis

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STEROID 5A-REDUCTASE TYPE 3 **(SRD5A3-CDG)**

DIAGNOSIS & BIOMARKERS

Diagnosis is achieved through analysis of serum transferrin glycans and genetic testing.

There are no established therapeutic biomarkers for SRD5A3-CDG.

DISEASE MODELS

Existing disease models include patient fibroblast lines, patient-specific mutation KO worms, cerebellum-specific conditional KO and conditional ready floxed mouse models.

TREATMENTS

There are no available therapies for SRD5A3-CDG.

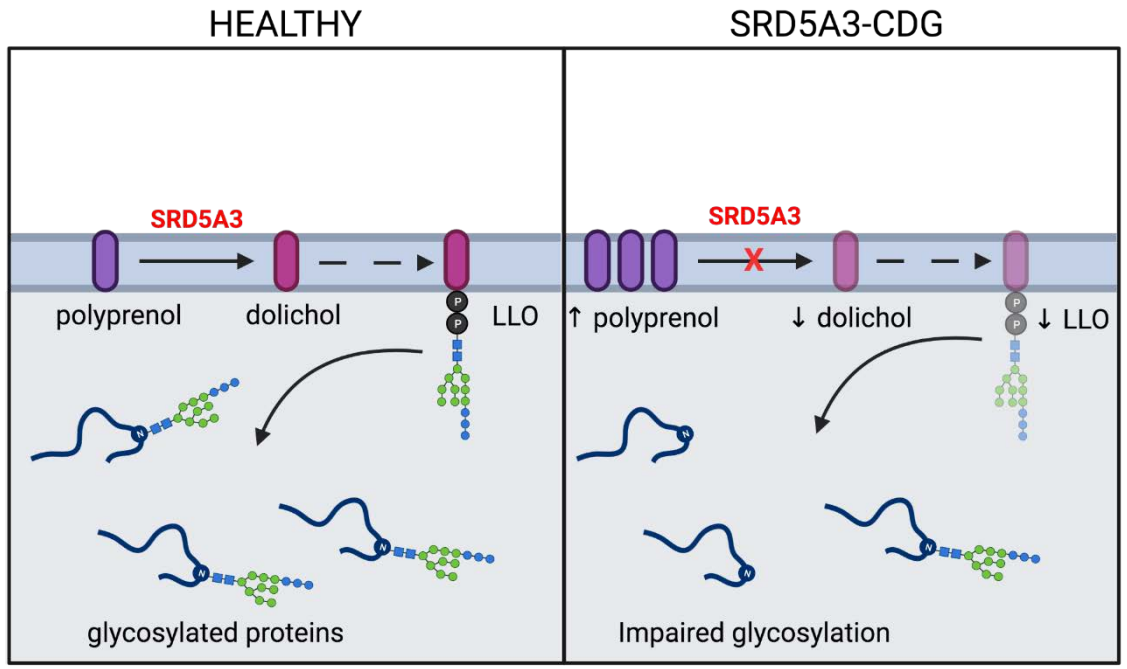
24 variants have been reported, most of which likely result in a null protein. SRD5A3-CDG is a good candidate for gene therapy.

CURE SRD5A3

SRD5A3 IS A CRITICAL ENZYME IN **DOLICHOL PRODUCTION**

- SRD5A3, also known as the enzyme polyprenol reductase, catalyzes the conversion of polyprenol to dolichol in the ER membrane.
- The synthesis of the lipid dolichol is one of the first steps in glycosylation.
- Dolichol acts as a lipid carrier for glycans (LLO) that are transferred onto proteins and as a sugar donor in multiple glycosylation pathways.
- Losing SRD5A3 function impairs glycosylation, resulting in insufficient glycosylation of proteins.

It is unknown whether SRD5A3-CDG pathology is driven by polyprenol accumulation, dolichol deficiency and/or insufficient glycosylation of proteins.



LLO: lipid-linked oligosaccharide

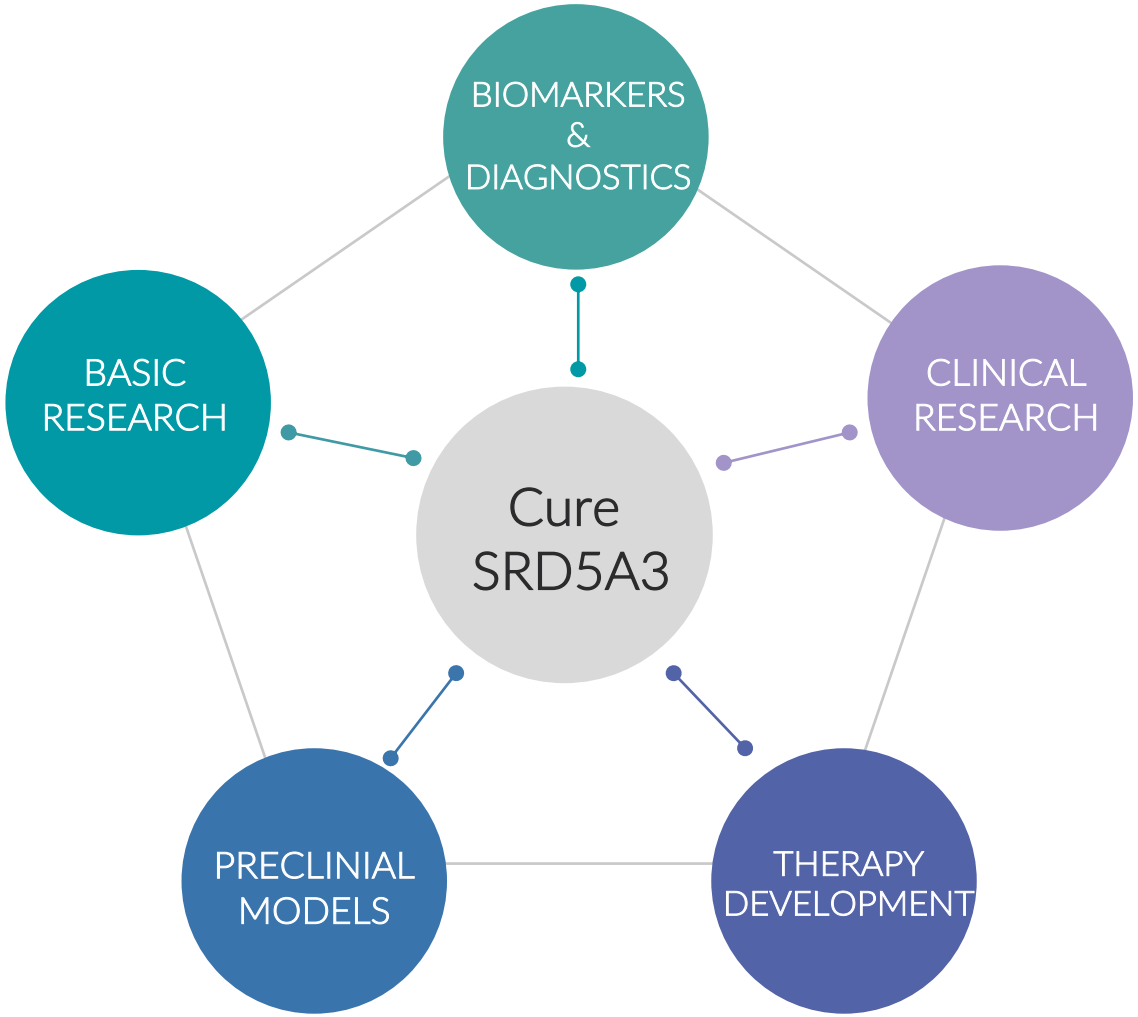
CURE SRD5A3

OUR **STRATEGIC APPROACH**

At Cure SRD5A3, we are focused on SPEED TO A CURE. With speed in mind, we are taking a strategic approach to our R&D program:

- Hub and spoke model: Design R&D projects executed by CRO/academic partners
- Parallel pursuit of basic/clinical research and therapeutic development
- Maintain ownership over IP developed
- Growing engagement of the patient community and expert advisors through our research activities

Wherever possible, we seek to harness scientific discoveries on SRD5A3-CDG to advance research on other CDGs.



CURE SRD5A3

THE **CURE SRD5A3 LEADERSHIP TEAM**

Vijay Sappani

FOUNDER

Vijay is an angel investor and diversified entrepreneur with a focus on life sciences and emerging technology start-ups. He is the founder and CEO of Ela Capital Inc. and the Chairman of the Sappani Foundation.

Dr. Kristin Kantautas

RESEARCH DIRECTOR

Kristin has worked in the life sciences industry as a consultant specializing in rare diseases. She holds a PhD in Molecular Genetics from the University of Toronto and is an expert on congenital disorders of glycosylation.

Dr. Abhi Pushparaj

SCIENTIFIC ADVISOR

Abhi obtained his PhD in Neuropharmacology from the University of Toronto and has extensive experience in designing clinical trials to obtain global regulatory approvals for medical devices and biopharmaceuticals.

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OUR **SCIENTIFIC ADVISORS**

Dr. Hudson Freeze

Sanford Burnham Prebys

Dr. Eva Morava-Kozicz

Mayo Clinic

Dr. Christina Lam

Seattle Children's Hospital

Dr. Ethan Perlstein

Perlara

Dr. Andrew Edmondson

Children's Hospital of Philadelphia

Dr. Yin Dong

University of Oxford

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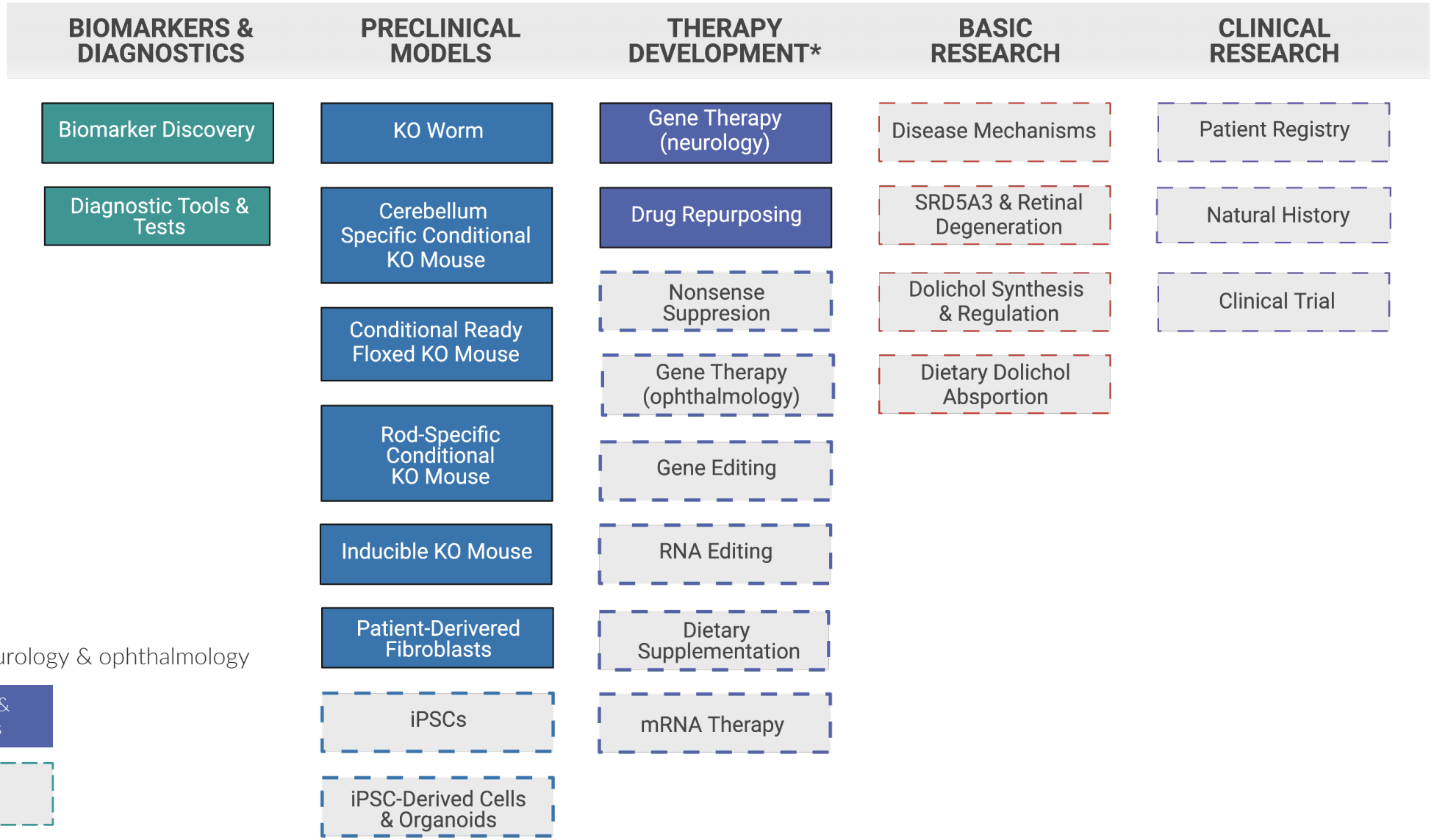
OUR **RESEARCH PROGRAM**



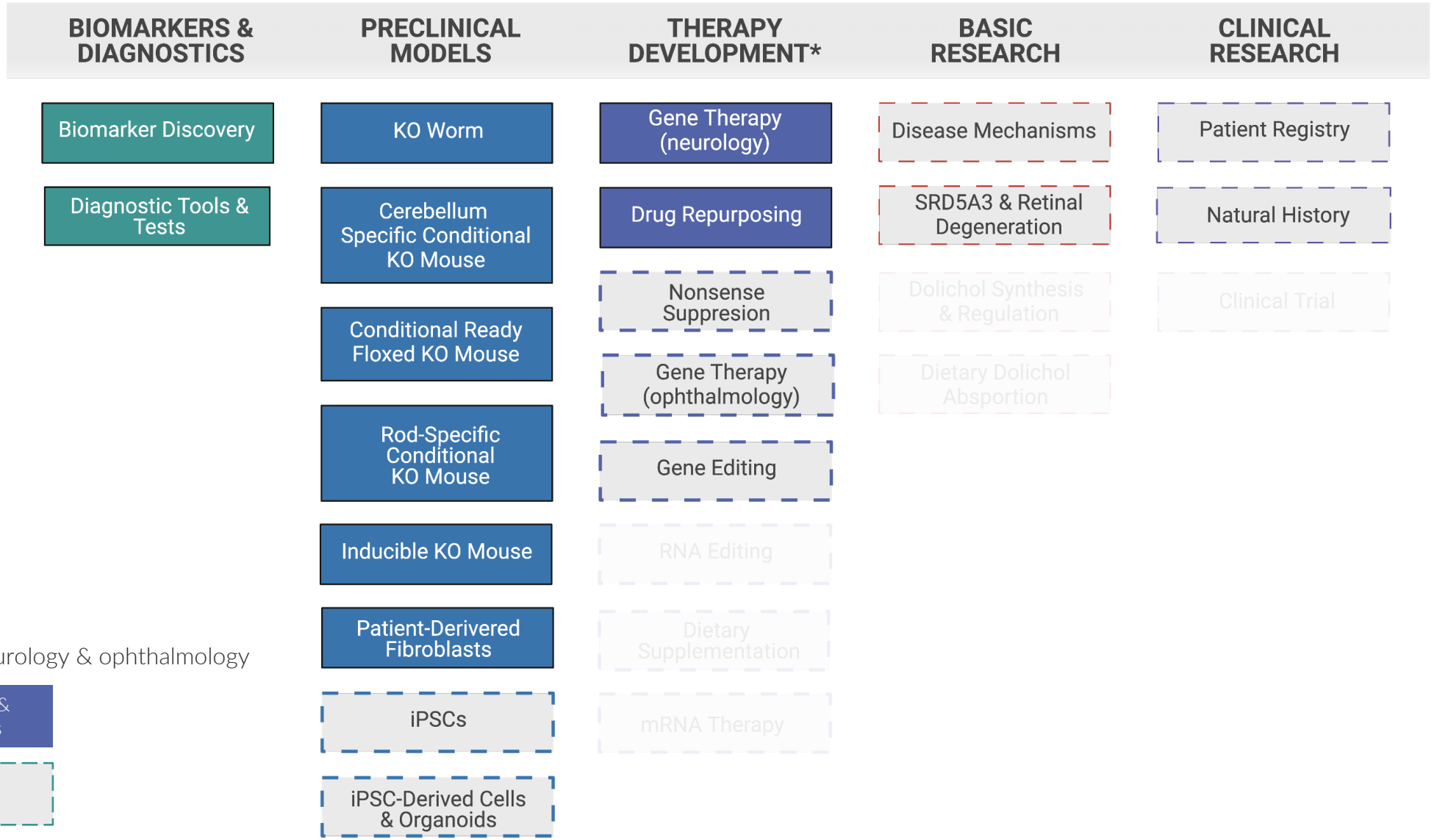
* Focus on neurology & ophthalmology

active research & available models

Future research projects

CURE SRD5A3

OUR **2-YR PRIORITY AREAS**



* Focus on neurology & ophthalmology

active research & available models

Future research projects

CURE SRD5A3

OUR **RESEARCH PARTNERS**

BIOMARKERS & DIAGNOSTICS

Dr. Eva Morava-Kozicz
Mayo Clinic

Dr. Akhilesh Pandey
Mayo Clinic

Dr. Dirk Lefeber
Radboud UMC

FDNA

Khure Health

PRECLINICAL MODELS

Dr. Steven Fliesler
University at Buffalo

The Jackson Laboratory

THERAPY DEVELOPMENT

Dr. Steven Grey
UT Southwestern

Dr. Eva Morava-Kozicz
Mayo Clinic

Dr. James Doyle
Modelis

BASIC RESEARCH

CLINICAL RESEARCH

Dr. Kimberly Goodspeed
UT Southwestern Medical Center

CURE SRD5A3

KEY **ACCOMPLISHMENTS**

01 **Natural History:** Conducted a natural history study in a new patient cohort.

02 **Model Generation**: Generated *SRD5A3* KO worms, zebrafish and a conditional-ready mouse model. Generating a rod-specific KO mouse to support ocular gene therapy development.

03 **CNS Gene Therapy**: Ongoing evaluation of gene therapy in a cerebellum-specific *Srd5a3* KO mouse model.

04 **Drug Repurposing**: Ongoing evaluation of drug repurposing hits in patient-derived cellular models.

05 **AI Diagnostic Platforms:** Collaborations with digital health companies, Khure Health and FDNA, to improve diagnosis for SRD5A3-CDG and all CDG types.

CURE SRD5A3

PARTNER WITH US

Cure SRD5A3 is seeking industry and academic partners to accelerate our path to a cure.

Industry Partners

Cure SRD5A3 is interested licensing and sharing in the benefits of an FDA approval, specifically a Rare Pediatric Disease Priority Review Voucher with industry partners

Academic Partners

Cure SRD5A3 will provide labs conducting research on SRD5A3-CDG in one of our priority areas with funding and access to biological assets

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CONTACT US

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