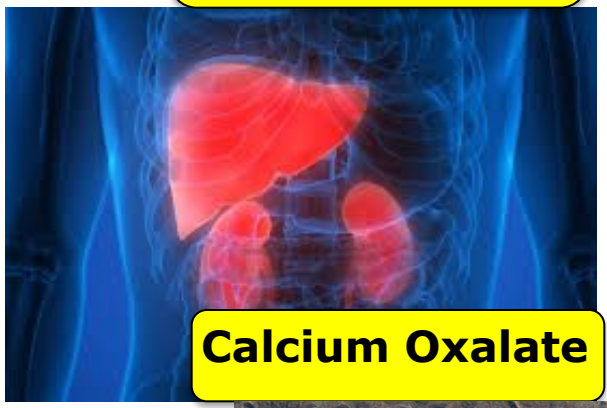
Hiperoxaluria Primaria

- trastorno congénito del metabolismo he
- producción excesiva de oxalato
- daño renal... ESRD
  - oxalosis infantil
  - nefrolitiasis pediátrica
  - nefrolitiasis severa del adulto
- Autosómica Recesiva
- Rara (prev.1-5/10^6 inc.1/120,000),
  1-2% ped.ESRD (EU), 10% ped.ESRD (NAf
- Infradiagnosticada: est. 1000genomes: inferred prevalence
  1:121,499 for PH1, 1:196,952 for PH2,
  and 1:79,499 for PH3
  PMID: 25644115



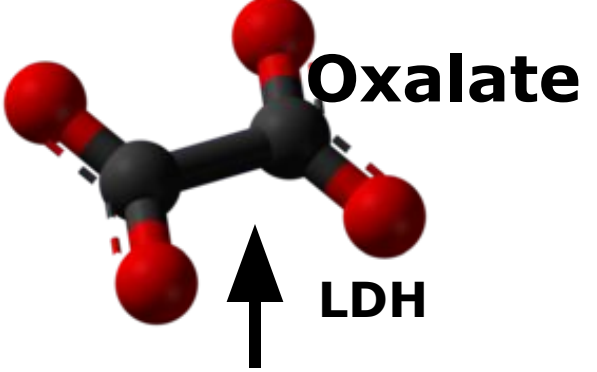
apCanarias

- PH type 1 (MIM #259900) is due to the defects in the gene that encodes the hepatic peroxisomal enzyme alanine:glyoxylate aminotransferase (AGT), a pyridoxal 5'-phosphate-dependent enzyme, which is involved in the transamination of glyoxylate to glycine [6]. It accounts for approximately 70 to 80 percent of PH cases [7,8]. (See 'Primary hyperoxaluria type 1' below.)

UpToDate®

- PH type 2 (MIM #260000) is due to defects in the gene that encodes the cytosolic enzyme glyoxylate reductase/hydroxypyruvate reductase (GRHPR), which is involved in the reduction of glyoxylate to glycolate [9]. It accounts for approximately 10 percent of PH cases [7,8]. (See 'Primary hyperoxaluria type 2' below.)

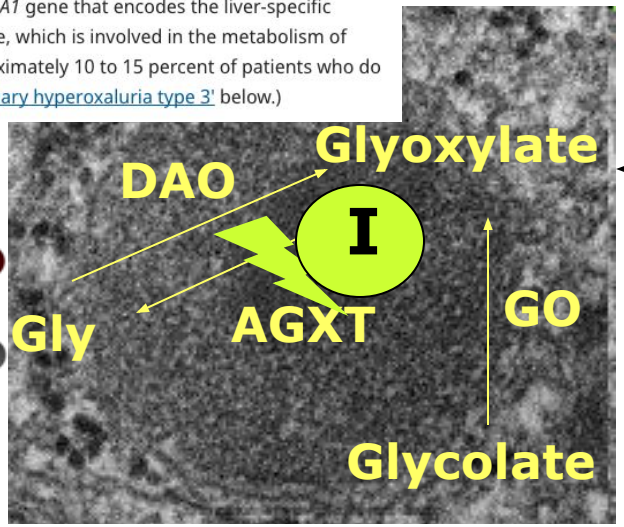
- PH type 3 (MIM #613616) is due to mutations in the *HOGA1* gene that encodes the liver-specific mitochondrial 4-hydroxy-2-oxoglutarate aldolase enzyme, which is involved in the metabolism of hydroxyproline. It appears PH type 3 accounts for approximately 10 to 15 percent of patients who do not have either type 1 or 2 disease [7,8,10,11]. (See 'Primary hyperoxaluria type 3' below.)

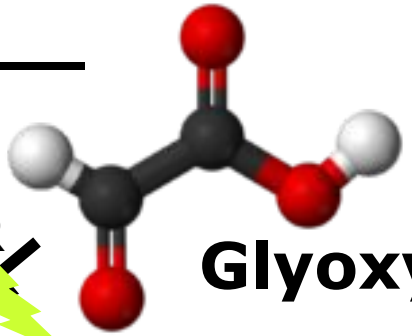


Peroxisomes

Glycine

Glycolate

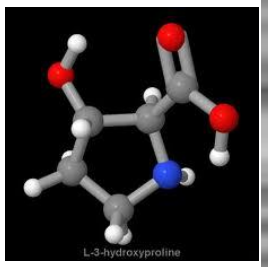


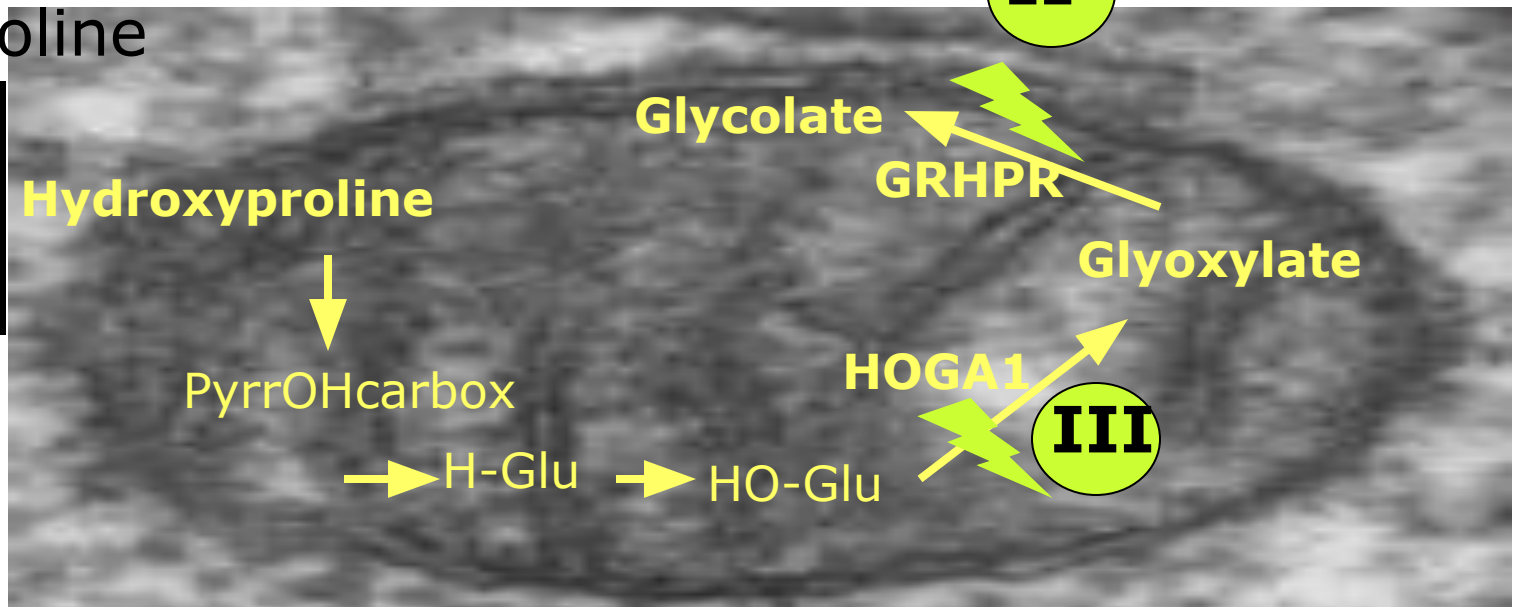


II

Mitochondria

Hydroxyproline





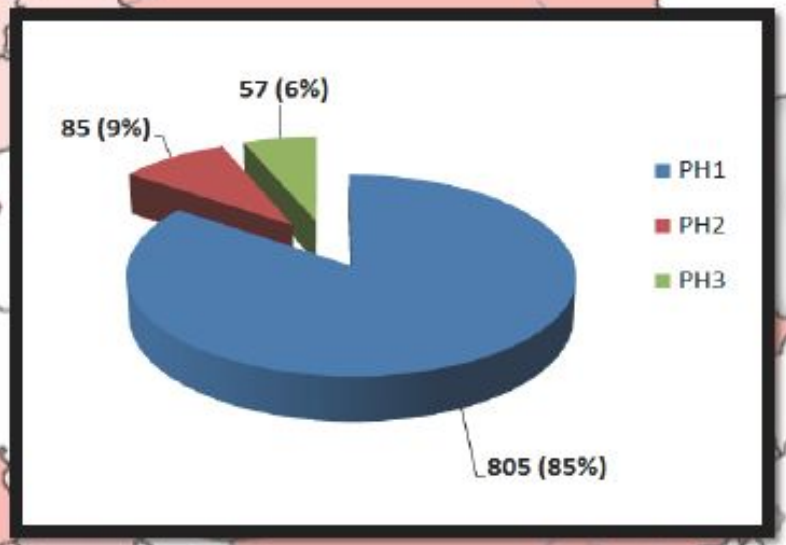
Estimated prevalence rate (per 10^6)

OXAL EUROPE

The Netherlands	- 5.42
UK	- 2.84
France	- 2.32
Germany	- 1.62
Italy	- 1.55

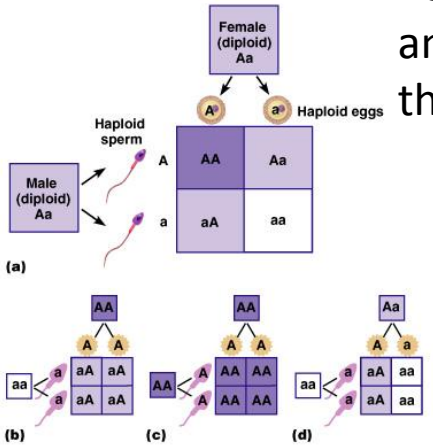
2018

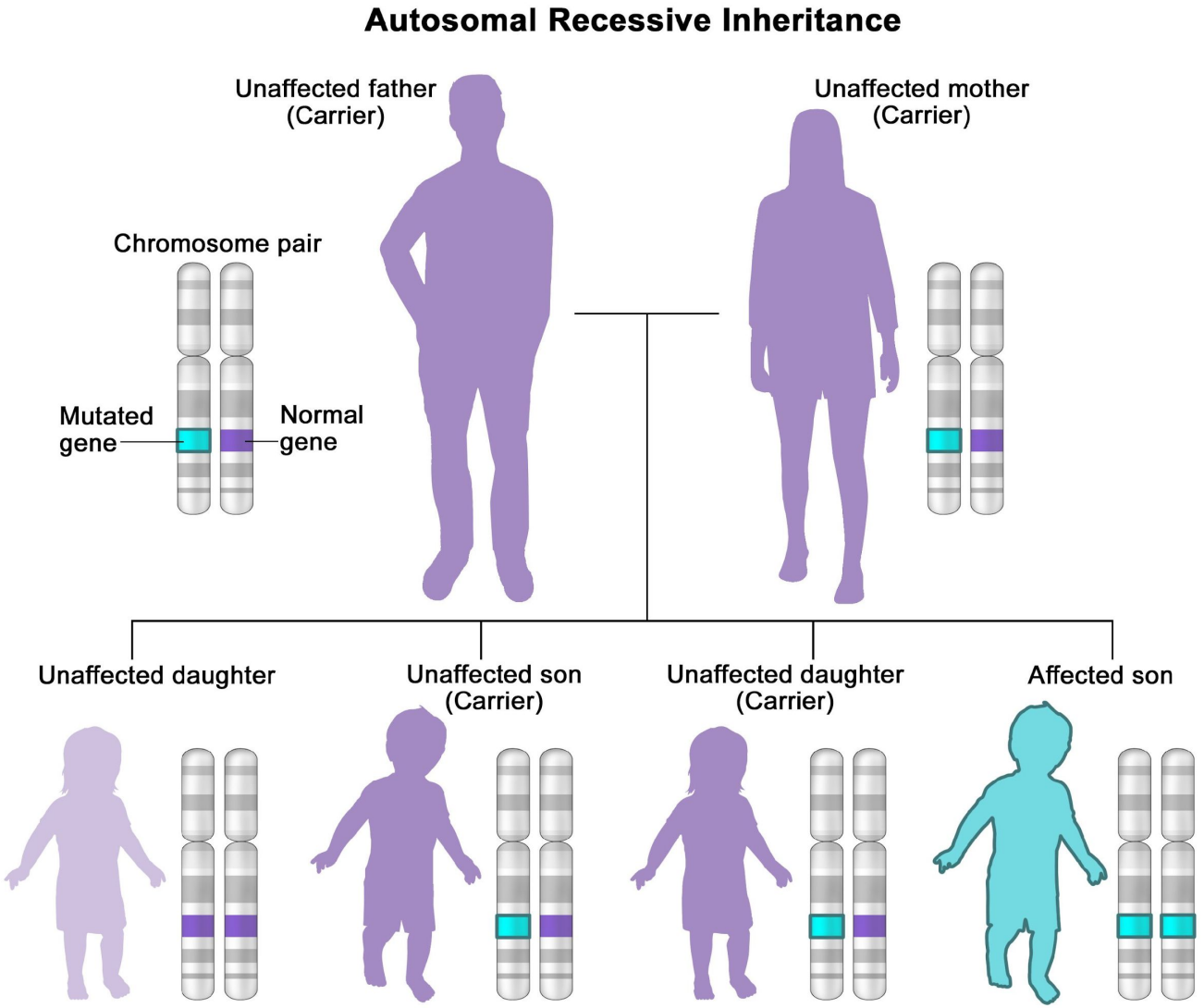
- >1200 PH Patients
- 21 Countries



Possible genotypes and their probabilities

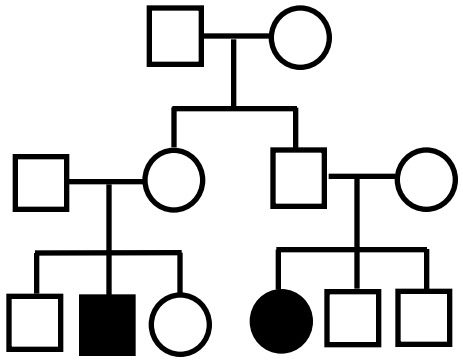
- Homozygous: AA and aa
- Heterozygous: Aa





Enf. Autosómicas Recesivas

-patrón HORIZONTAL
-riesgo RECURRENCIA 25%
-sanos transmiten, consanguinidad (>riesgo)
-hombres y mujeres afectados por igual



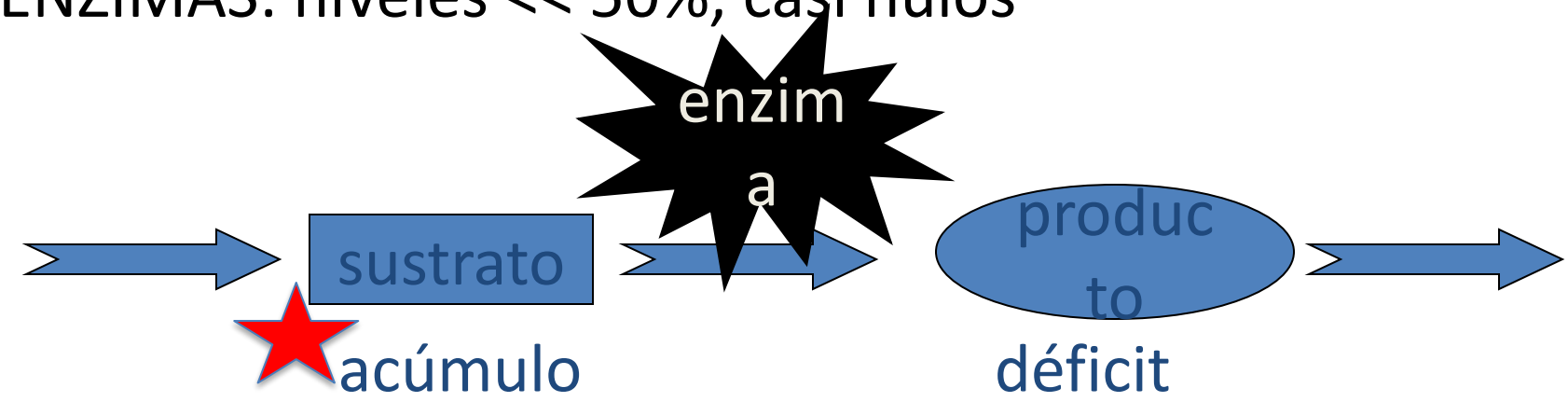
<u>Características clínicas generales:</u>

-familiares, muy raro ‘de novo’
-presentación temprana ‘errores congénitos mb’
-penetrancia completa
-expresividad bastante uniforme

Mecanismos moleculares

-pérdida Fx. (LoF): tipos mutaciones: SNV, indels

ENZIMAS: niveles << 50%, casi nulos



Heterogeneidad **genética**:
AGXT (2q37.3), GRHPR (9p13.2), HOGA1 (10q24.2)

Heterogeneidad **alélica**: cientos... ClinVar

NCBI Resources How To

Gene

Gene

Advanced

Full Report

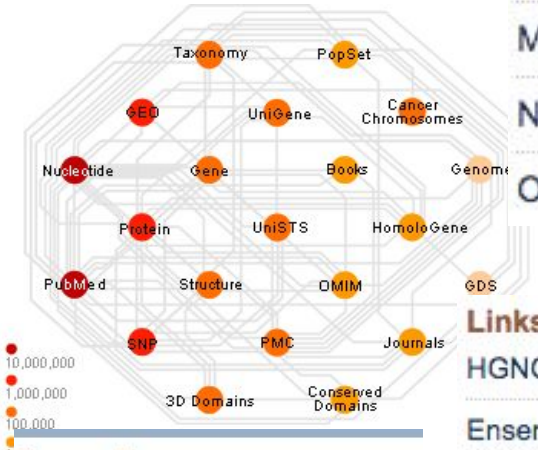
AGXT alanine--glyoxylate and serine--pyruvate aminotransferase [*Homo sapiens* (human)]

Gene ID: 189, updated on 26-Sep-2021

Dow

Summary

Official Symbol AGXT provided by HGNC
Official Full Name alanine--glyoxylate and serine--pyruvate aminotransferase provided by HGNC
Primary source HGNC:HGNC:341
See related Ensembl:ENSG00000172482 MIM:604285
Gene type protein coding
RefSeq status REVIEWED
Organism Homo sapiens
Lineage Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; P
Haplorrhini; Catarrhini; Hominidae; Homo
Also known as AGT; PH1; SPT; AGT1; SPAT; TLH6; AGXT1
Summary This gene is expressed only in the liver and the encoded protein is localized mostly in the peroxisomes, wher
glyoxylate detoxification. Mutations in this gene, some of which alter subcellular targetting, have been associ
primary hyperoxaluria. [provided by RefSeq, Jul 2008]
Expression Restricted expression toward liver (RPKM 387.9) See more
Orthologs mouse all



Genome Browsers

- Genome Data Viewer
- Variation Viewer (GRCh37.p13)
- Variation Viewer (GRCh38)
- 1000 Genomes Browser (GRCh37.p13)
- Ensembl
- UCSC

MedGen

Nucleotide

OMIM

Links to other resources

- HGNC
- Ensembl
- AceView
- AGXT database
- HuGE Navigator
- KEGG
- Reactome

ClinVar

ClinGen
Clinical Genome Resource

gnomAD
genome aggregation database

AGXT
View Gene Facts

Gene Facts

HGNC Symbol	AGXT (HGNC:341)
HGNC Name	alanine--glyoxylate and serine--pyruvate aminotransferase
Gene type	protein-coding gene
Locus type	gene with protein product
Previous symbols	SPAT
Alias symbols	AGXT1, PH1, AGT, SPT, AGT1
GenCC Classifications	Definitive
%HI	70.08
pLI	0
LOEUF	1.03
Cytoband	2q37.3
Genomic Coordinates	GRCh37/hg19: chr2:241808162-241818536
	GRCh38/hg38: chr2:240868824-240880500
MANE Select Transcript	NM_000030.3 ENST00000307503.4

AGXT

View Gene Facts

Curation Summaries | External Genomic Resources | ClinVar Variants

NCBI

MedGen: Genetics Summary

Organizes information related to human medical genetics, su

MedGen: Genetics Summary

NCBI

Genetic Practice Guidelines: Gene

As guidelines are identified that relate to a disorder, gene, or
This page provides an alphabetical list of the professional pra
have been identified.

Genetic Practice Guidelines: Gene

GTR: Gene Tests

A voluntary registry of genetic tests and laboratories, with de

AGXT (2q37.3)

Clinical significance

Conflicting interpretations (14)
Benign (59)
Likely benign (129)
Uncertain significance (75)
Likely pathogenic (59)
Pathogenic (253)
Risk factor (0)

Molecular consequence

Frameshift (39)
Missense (147)
Nonsense (33)
Splice site (29)
ncRNA (0)
Near gene (0)
UTR (12)

Variation type

Deletion (111)
Duplication (45)
Indel (8)
Insertion (27)
Single nucleotide (389)

GRHPR (9p13.2)

Clinical significance

Conflicting interpretations (13)
Benign (31)
Likely benign (81)
Uncertain significance (48)
Likely pathogenic (46)
Pathogenic (101)
Risk factor (0)

Molecular consequence

Frameshift (34)
Missense (50)
Nonsense (11)
Splice site (22)
ncRNA (0)
Near gene (0)
UTR (4)

Variation type

Deletion (44)
Duplication (76)
Indel (6)
Insertion (19)
Single nucleotide (183)

HOGA1 (10q24.2)

Clinical significance

Conflicting interpretations (14)
Benign (26)
Likely benign (74)
Uncertain significance (84)
Likely pathogenic (20)
Pathogenic (45)
Risk factor (0)

Molecular consequence

Frameshift (14)
Missense (63)
Nonsense (6)
Splice site (9)
ncRNA (0)
Near gene (0)
UTR (47)

Variation type

Deletion (21)
Duplication (16)
Indel (1)
Insertion (10)
Single nucleotide (213)

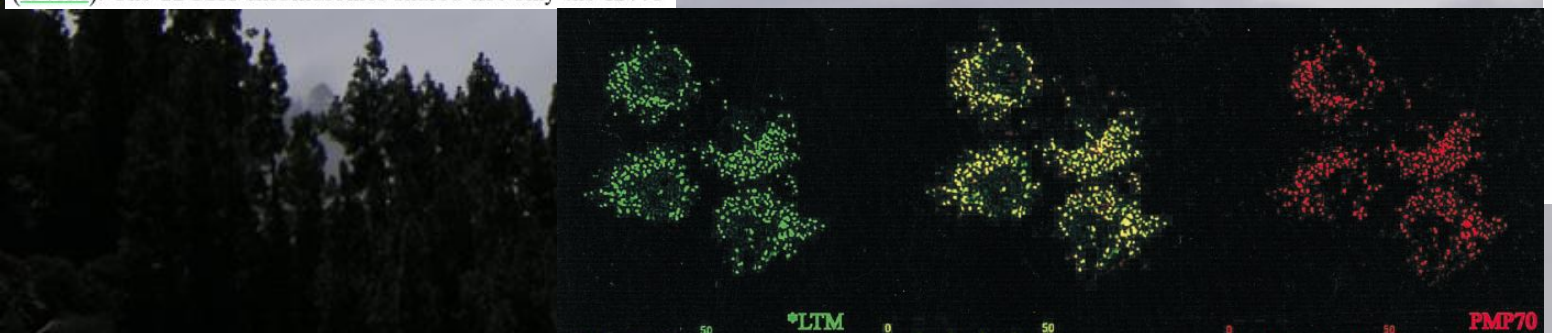
Primary hyperoxaluria type 1 in the Canary Islands: A conformational disease due to I244T mutation in the P11L-containing alanine:glyoxylate aminotransferase

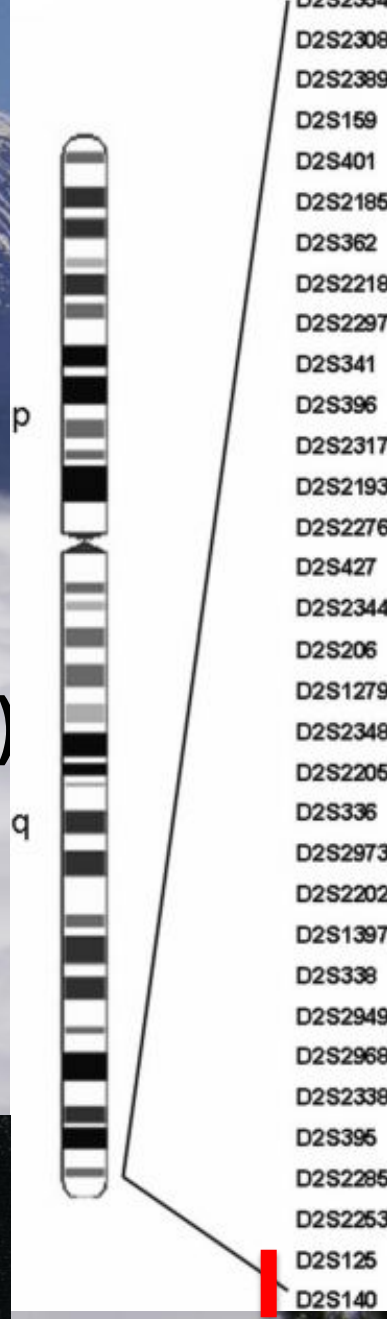
A. Santana[1,2], E. Salido[1,3,5], A. Torres[4], and L. J. Shapiro[5,6]

Synergistic Effect of P11L Polymorphism with I244T Is Crucial for Loss of Function. We expressed the wild-type *AGXT* cDNA and *AGXT*T* cDNA, carrying the change I244T in COS7 cells, by

- **mutations @ *AGXT***
- **->90% Ile244Thr (e7, T853C)**
- **Pro11Leu, i1ins., C386T, Ile340Met**
- **- " founder effect"**

I244T Is the Most Prevalent PH1 Mutation in the Canary Islands. The screening for *AGXT* mutations among our PH1 patients revealed that 22 of the 24 independent chromosomes studied (91.6%) had a T/C change at nucleotide 853 (exon 7), corresponding to a change of Ile to Thr at residue 244 in the AGXT protein. The other two PH1 chromosomes had a G/A change at nucleotide 630, a common mutation (11). Additional polymorphisms were detected in exon 1 (P11L), intron 1 (74-bp duplication), exon 2 (synonymous C/T change at nucleotide 386), and exon 10 (I340M). The 22 PH1 chromosomes shared not only the I244T





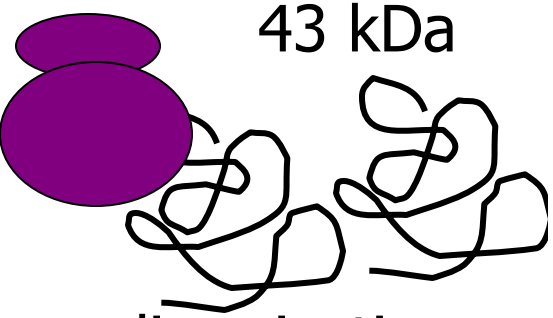
AGXT gene

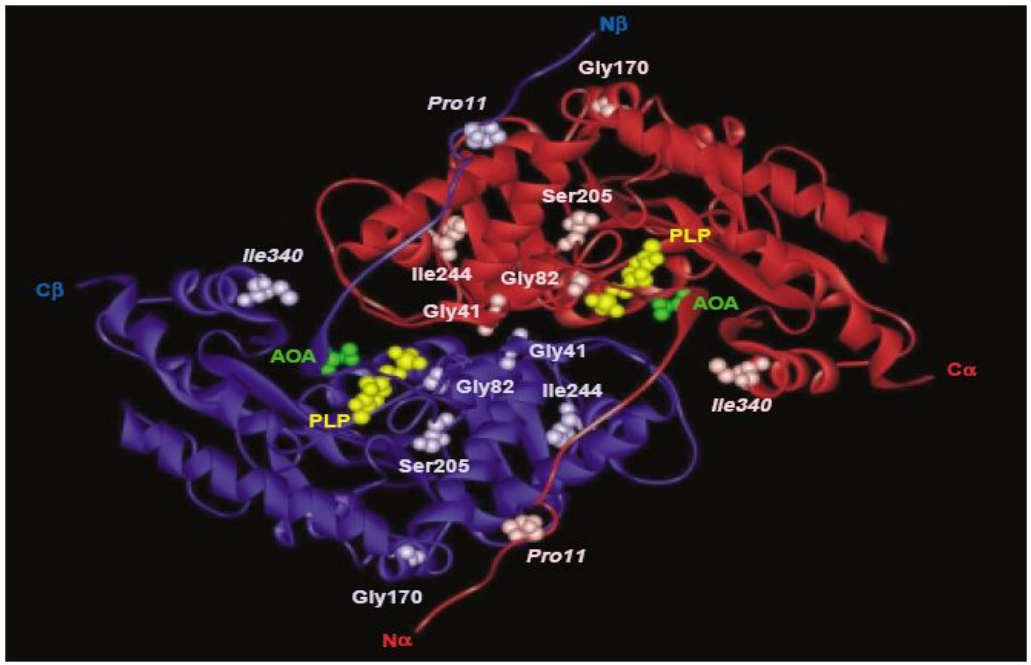
@ 2q37 ~ 10 kb 11 exons 1.6 kb mRNA

Major haplotype

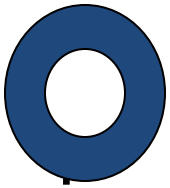
Minor haplotype

Pro11**Leu** **Ile**340**Met**





PTS

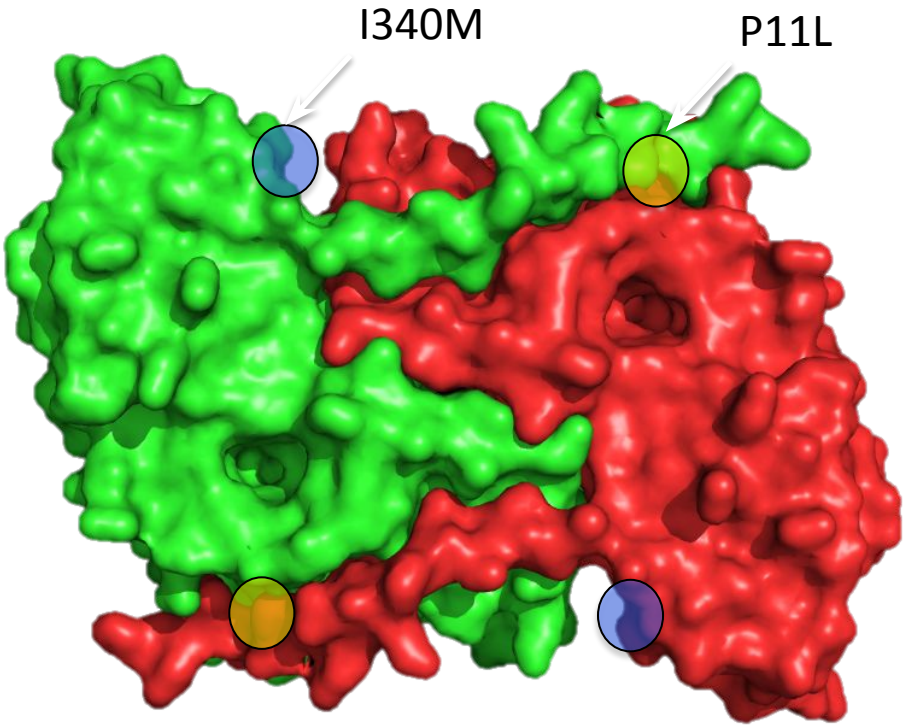


peroxisome

Two Main Alleles and More Than 150 Pathogenic Mutations

Two Main Alleles

- *Major* Allele or wild type: AGT-Ma
- *Minor* Allele: AGT-Mi P11L + I340M



Different Molecular Mechanisms

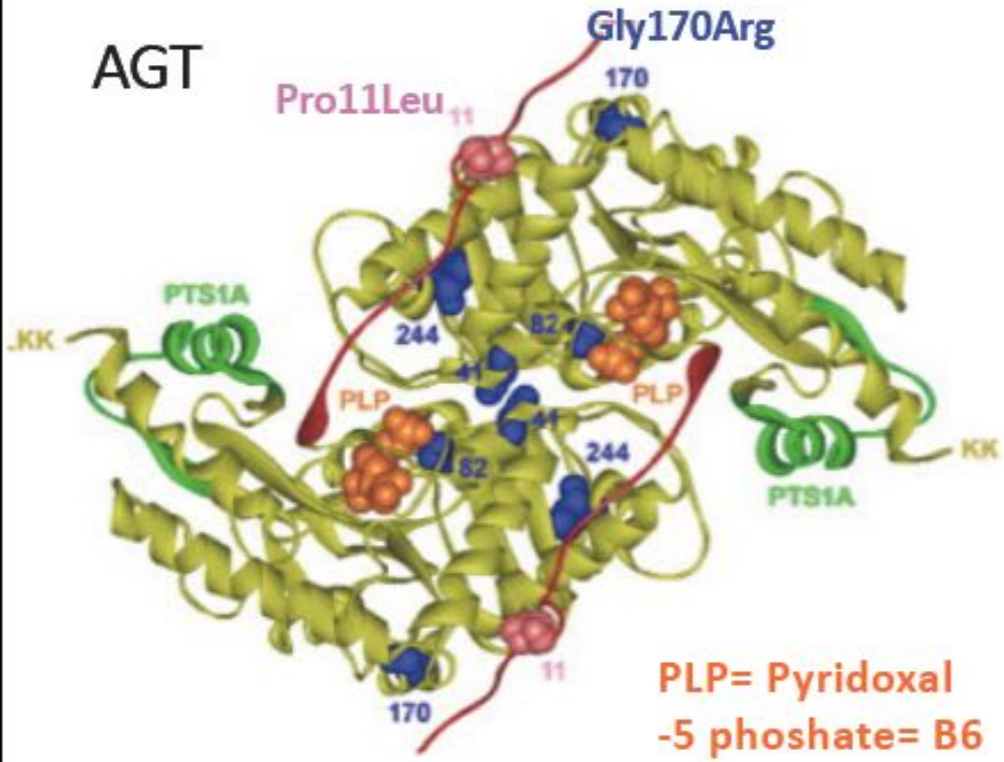
- Mistargeting to Mitochondria
- Aggregation
- Degradation
- Catalytic Defect

Mut.	Allele	Freq.*	Phenotype
G170R	Minor	30%	Mistargeting
I244T	Minor	9%	Aggregation
F152I	Minor	1-7%	Mistargeting
G41R	Both	1%	Aggregation
G82E	Major	<1%	Catalytic

* Over Characterized Pathogenic Alleles

Williams *et al*. Hum Mutat, 30(6):910–7

AGT

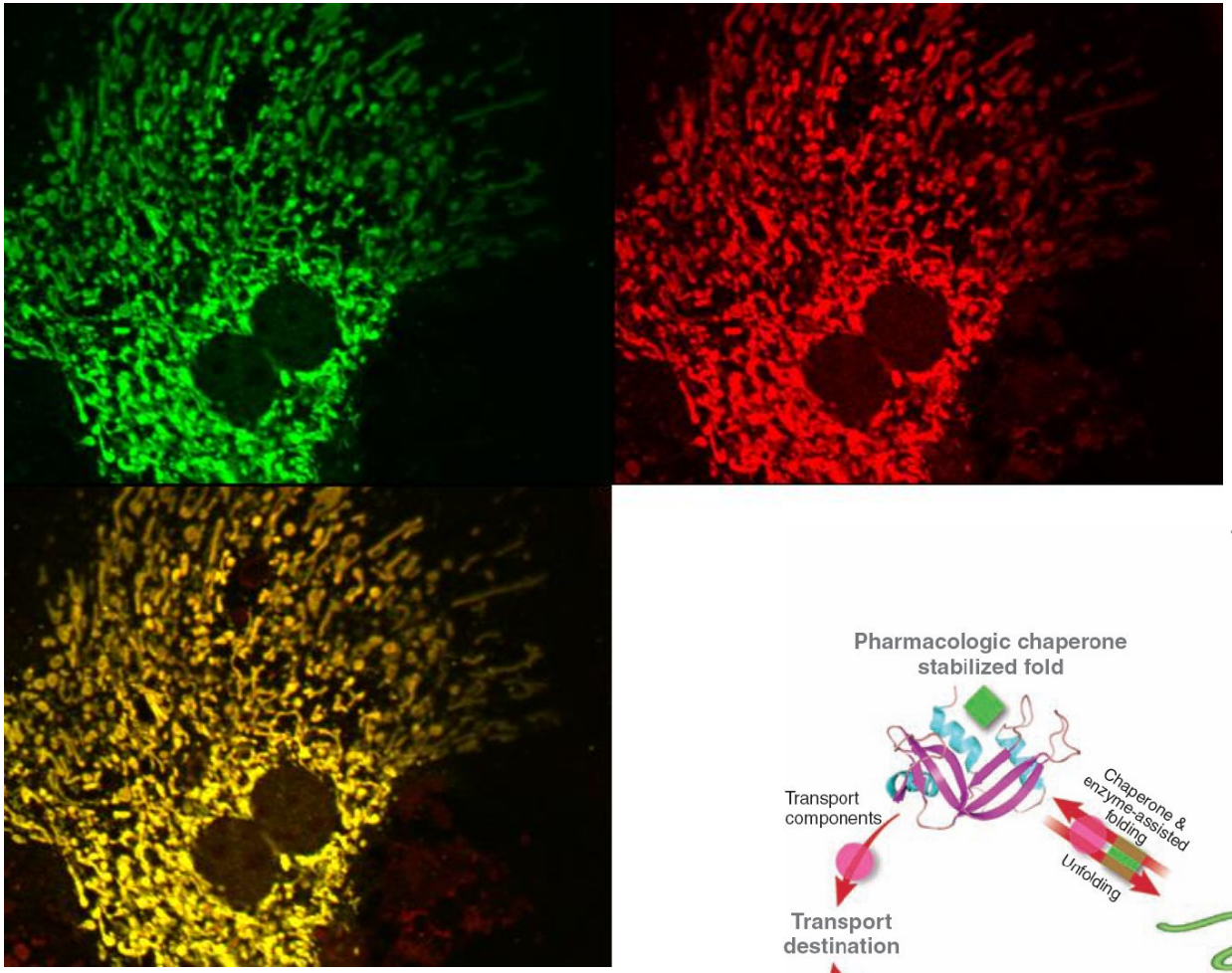


PLP= Pyridoxal
-5 phoshate= B6

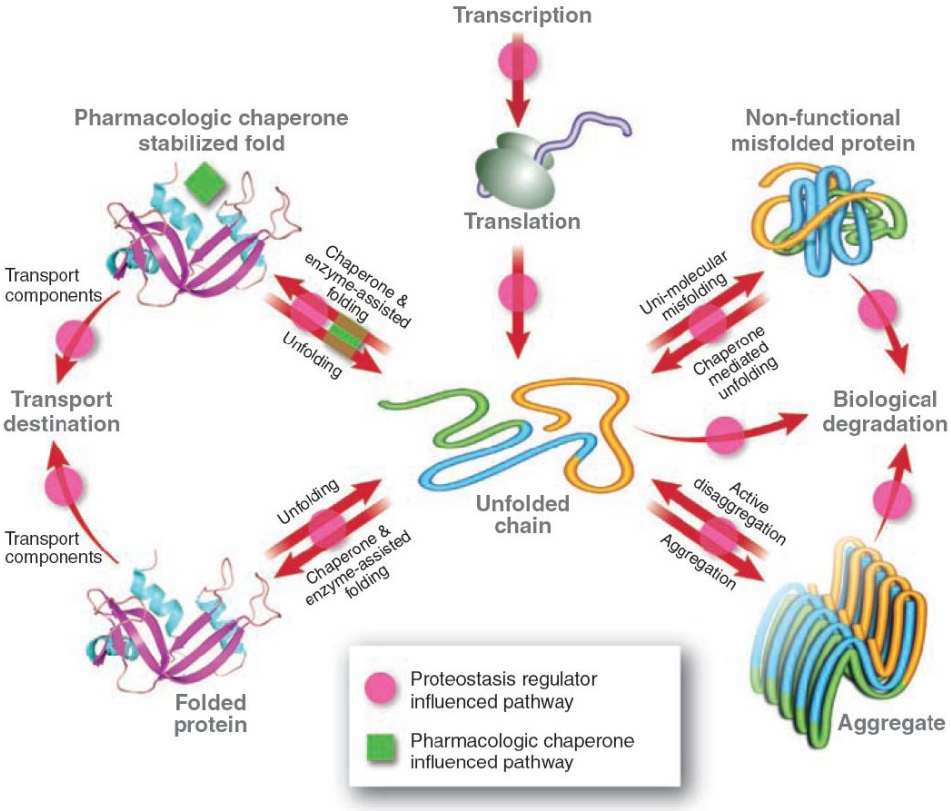
Gly170Arg (+Pro11Leu polymorphism)-> peroxisome-to-mitochondrion **mistargeting by unfolding -> impaired dimerization**:

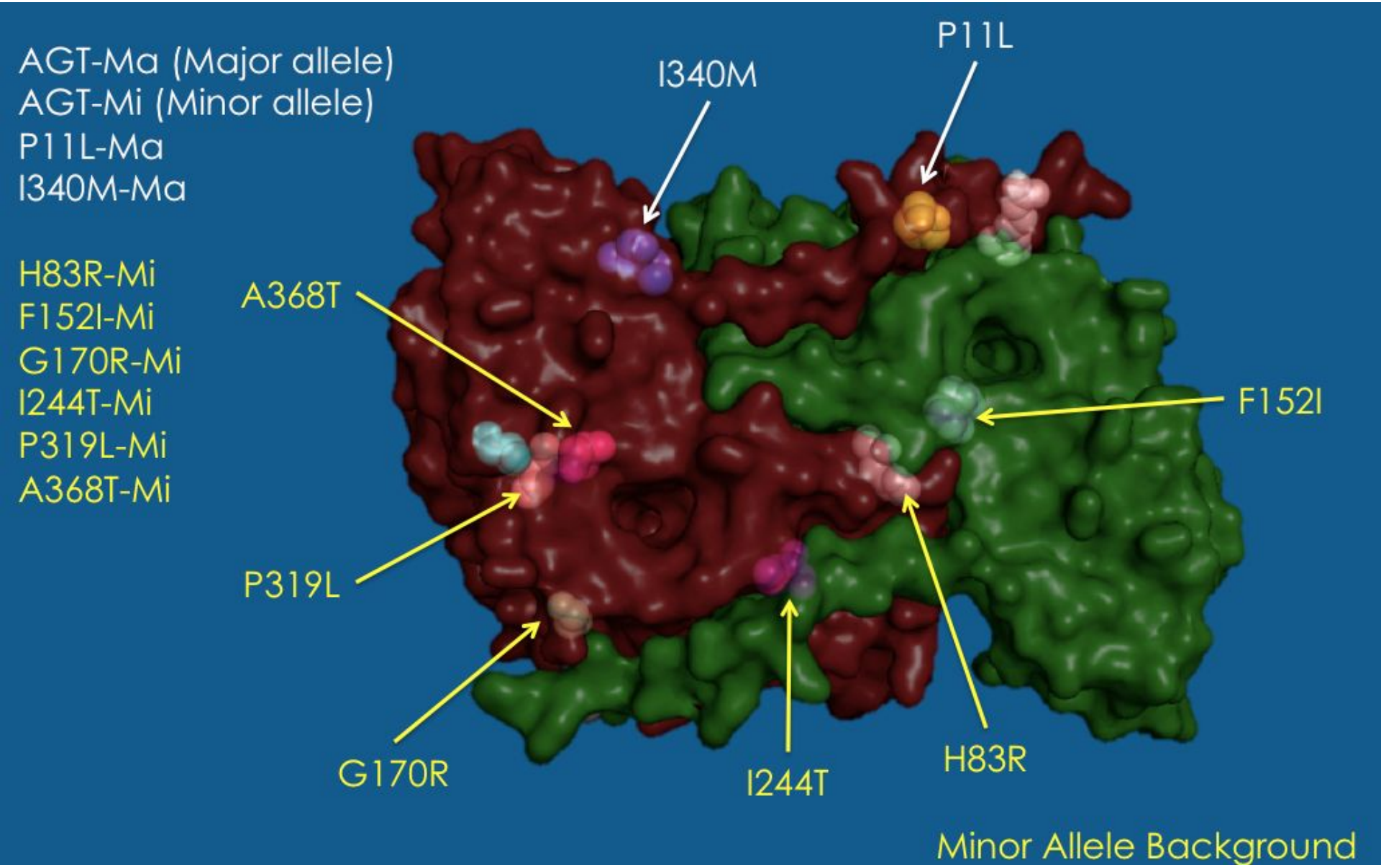
(partly) reversed by Vit B6 => lowering/normalisation oxalate on B6 therapy:

30% PH1 EU patients

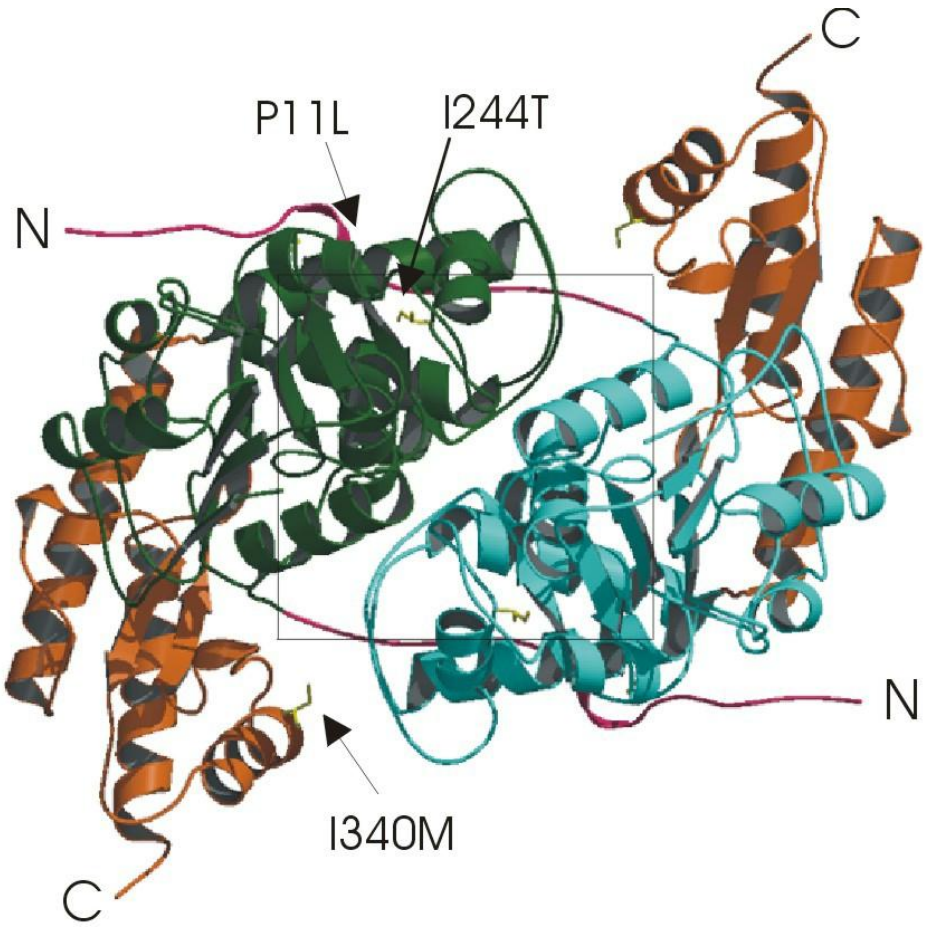


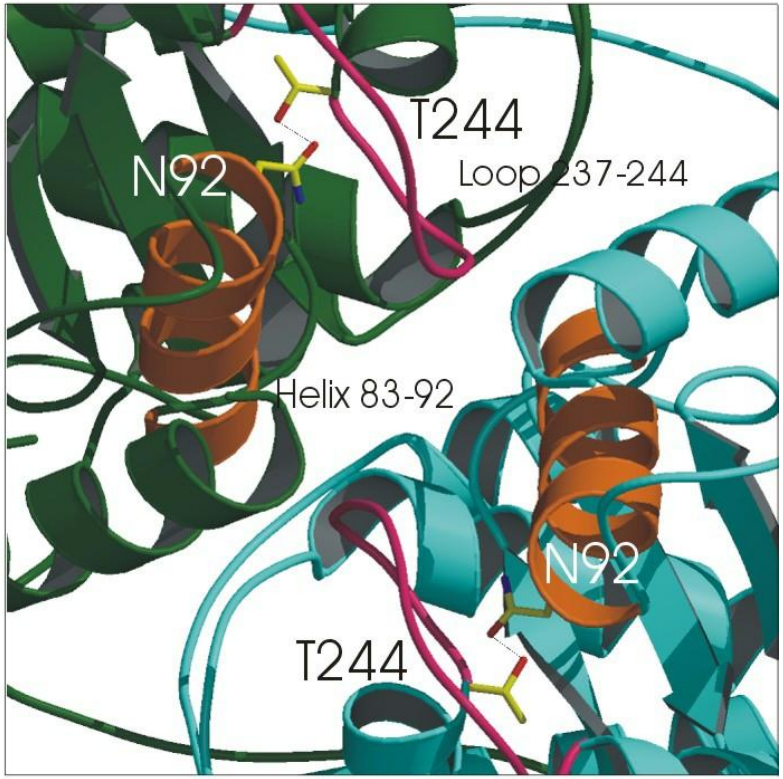
mitocondrial mistargeting



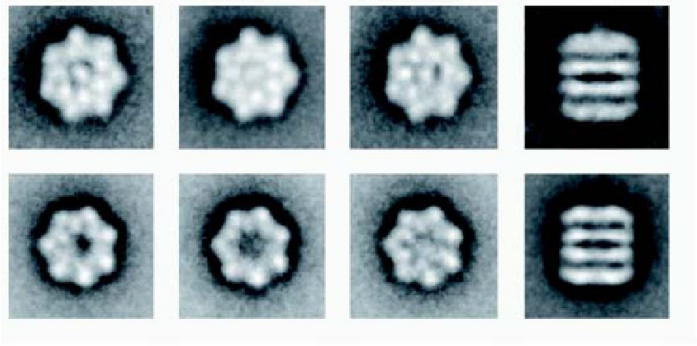

AGT-Ma (Major allele)
AGT-Mi (Minor allele)
P11L-Ma
I340M-Ma
H83R-Mi
F152I-Mi
G170R-Mi
I244T-Mi
P319L-Mi
A368T-Mi
I340M
P11L
A368T
F152I
P319L
G170R
I244T
H83R
Minor Allele Background

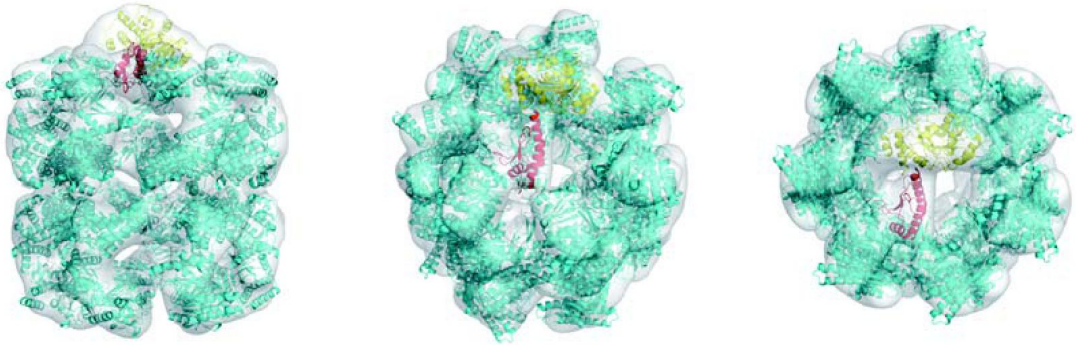
Ile244Thr
posibles implicaciones estructurales

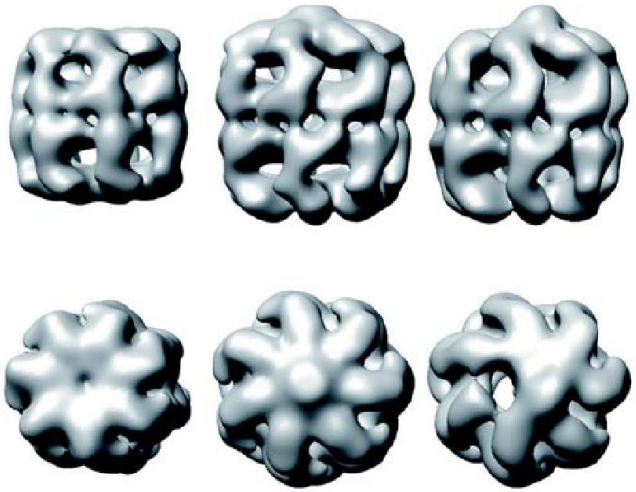




AGXT-GroE structure: direct observation of an early stage of the chaperone folding reaction cycle







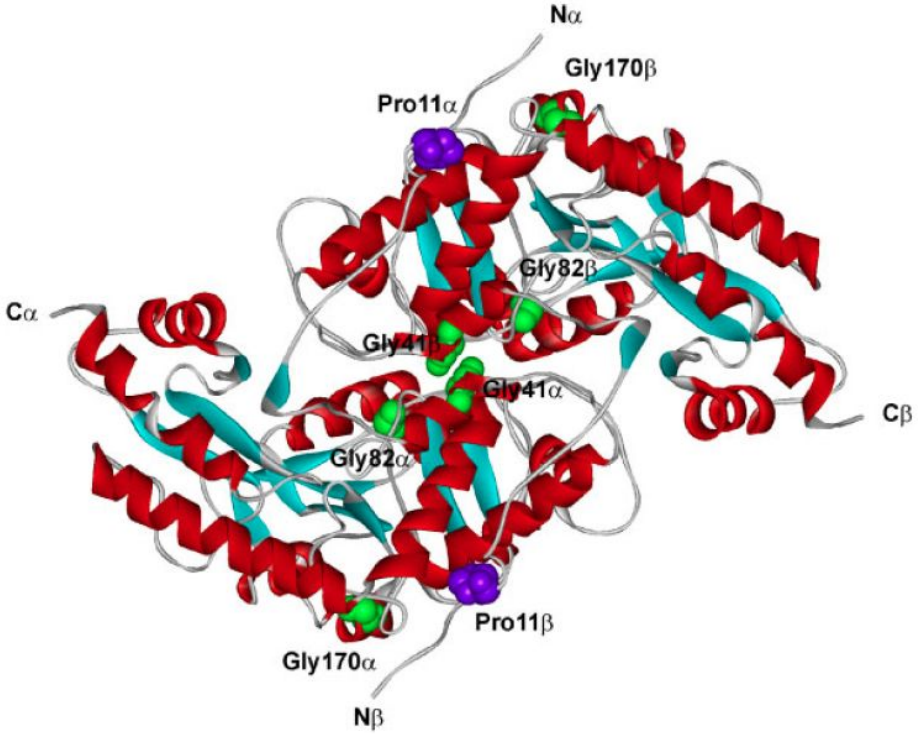
- AGXT-LTM forms non-native folding intermediates in an extended conformation accross the GroEL central cavity
- ATP induces conformational changes and internalization onto the folding cavity
- a 3D picture of an *in vivo* early step of the folding reaction cycle of the chaperonin
- supports a functional model in which the chaperonin promotes folding of the AGXT-LTM mutant protein through forced unfolding

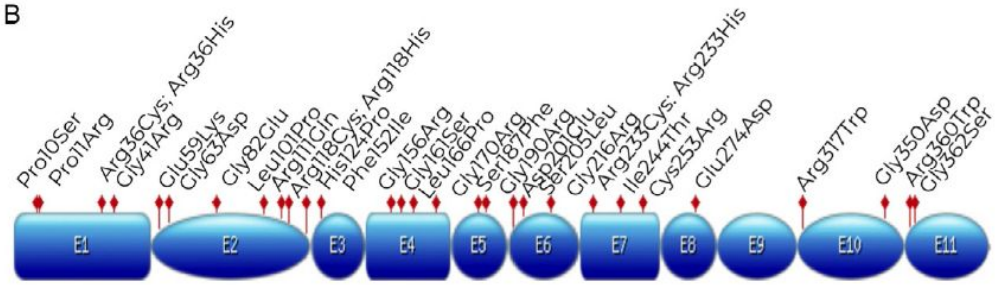
Structure of GroEL in Complex with an Early Folding Intermediate of Alanine Glyoxylate Aminotransferase[*]

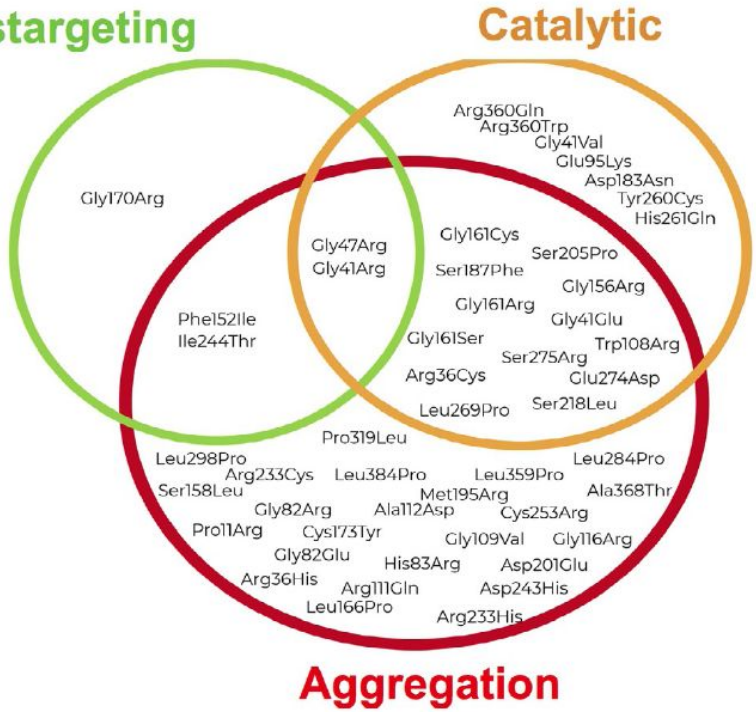
Received for publication, September 4, 2009, and in revised form, January 7, 2010 Published, JBC Papers in Press, January 7, 2010, DOI 10.1074/jbc.M109.062471

Armando Albert[‡1], Cristina Yunta[§], Rocío Arranz[¶], Álvaro Peña[¶], Eduardo Salido[§], José María Valpuesta[¶], and Jaime Martín-Benito[¶]

Advances in Protein Chemistry and Structural Biology, Volume 114
ISSN 1876-1623
https://doi.org/10.1016/bs.apcsb.2018.09.003

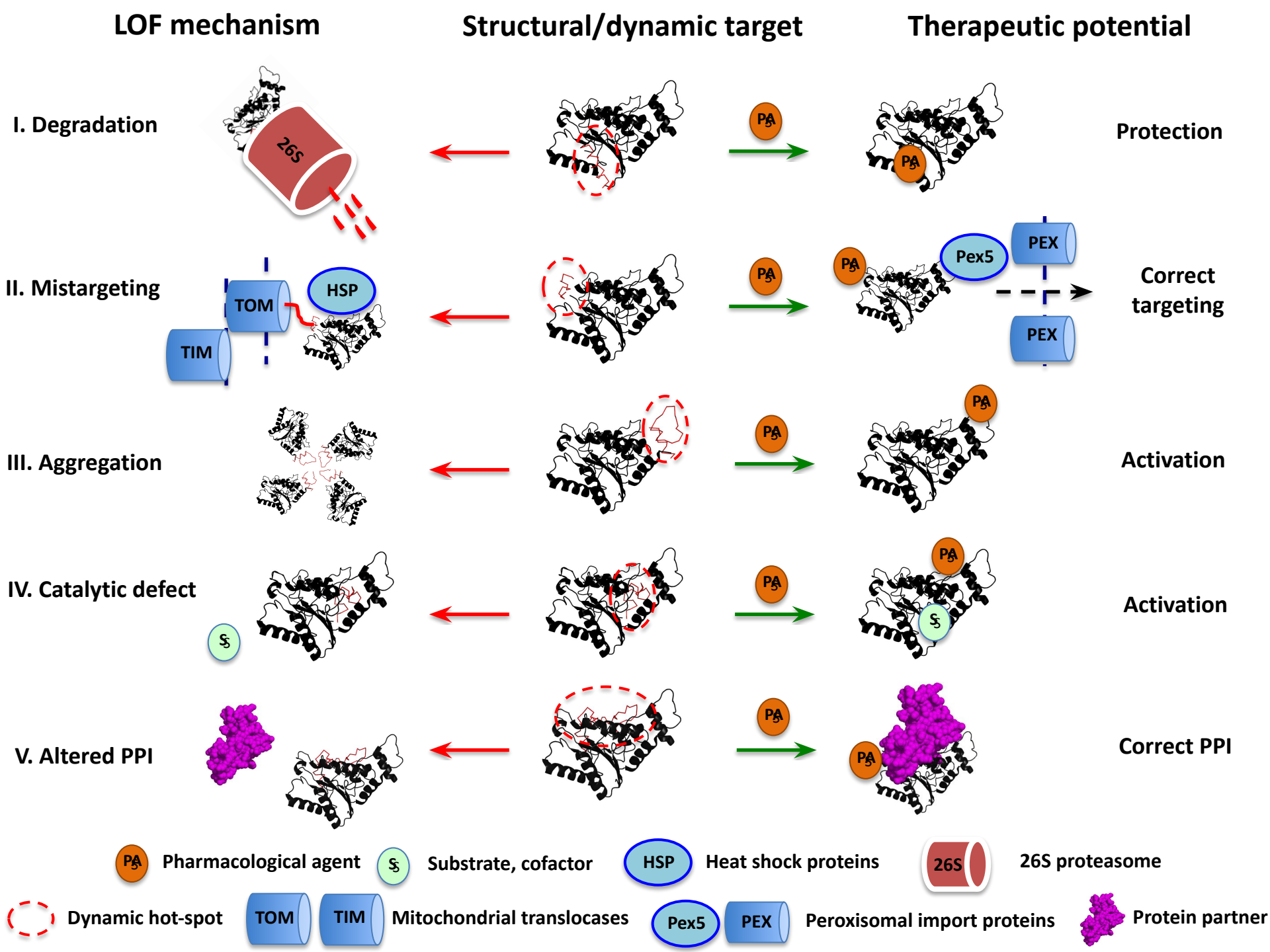






Structural and functional insights on the roles of molecular chaperones in the mistargeting and aggregation phenotypes associated with primary hyperoxaluria type I

José Ángel Fernández-Higuero[a,†], Isabel Betancor-Fernández[b,†], Noel Mesa-Torres[c,†], Arturo Muga[a], Eduardo Salido[b], Angel L. Pey[c,*]


LOF mechanism
Structural/dynamic target
Therapeutic potential
I. Degradation
26S
Protection
II. Mistargeting
TOM
HSP
TIM
Pex5
PEX
PEX
Correct targeting
III. Aggregation
Activation
IV. Catalytic defect
Activation
V. Altered PPI
Correct PPI
Pharmacological agent
Substrate, cofactor
Heat shock proteins
26S proteasome
Dynamic hot-spot
Mitochondrial translocases
Peroxisomal import proteins
Protein partner

Patients with primary hyperoxaluria type 2 have significant morbidity and require careful follow-up

Check for updates

OPEN

Sander F. Garrelfs[1], Gill Rumsby[2], Hessel Peters-Sengers[3], Florian Erger[4], Jaap W. Groothoff[1], Bodo B. Beck[4], Michiel J.S. Oosterveld[1], Alessandra Pelle[5], Thomas Neuhaus[6], Brigitte Adams[7], Pierre Cochat[8], Eduardo Salido[9], Graham W. Lipkin[10], Bernd Hoppe[11] and Sally-Anne Hulton[12]; on behalf of the OxalEurope Consortium

cases in the OxalEurope registry, a dataset containing 101 patients from eleven countries. Median follow up was 12.4 years. Median ages at first symptom and diagnosis for

(82.8% of patients). Genetic analysis revealed 18 novel mutations in the *GRHPR* gene. Of 238 spot-urine analys

45 (30.8) Exon 2 c.103delG p.Asp35Thrfs*11 Pathogenic

Molecular Analysis of the Glyoxylate Reductase (GRHPR) Gene and Description of Mutations Underlying Primary Hyperoxaluria Type 2

David P. Cregeen[1†], Emma L. Williams[2†], Sally Hulton[3], and Gill Rumsby[2*]

Table 2. Mutations Identified in GRHPR

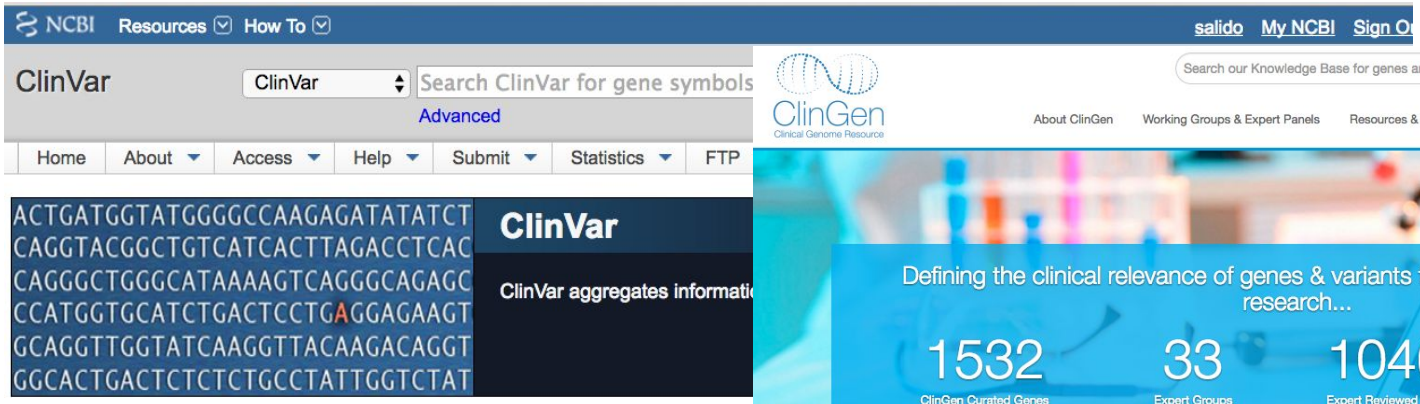
Sequence change	Description	Location	Restriction site affected (-loss; + gain of site)	Frequency (%)
		Mutations		
c.84-2A>G	missplicing	Intron 1	-*Pvu*II	3/38 (8%)
c.84-13_c.84-12del ; c.84-8_c.84-5del	? missplicing	Intron 1		1/38 (3%)
c.103delG	Frameshift, 44X	Exon 2	-BsmF1	14/38 (37%)[a]
c.295C>T	R99X	Exon 4	-*Bam*H1	2/38 (6%)
c.375delG	Frameshift, 133X	Exon 4	No	1/38 (3%)
c.403_405+2 delAAGT	missplicing	Exon 4/intron4	No	7/38 (18%)[b]
c.494G>A	G165N	Exon 6	+*Xba*I site	5/38 (13%)
c.540delT	Frameshift, 181X	Exon 6	+*Hin*fI	1/38 (3%)
c.608_609delCT	Frame shift, 210X	Exon 7	+*Ava*I site	3/38 (9%)
c.904C>T	R302C	Exon 9	-*Aci*I site	1/38 (3%)
		Polymorphisms		
c.579A>G	A193A	Exon 6	+*Aci*I site	
c.866-10_25(CT)8-9	CT repeat	Intron 7		

A report from the European Hyperoxaluria Consortium (OxalEurope) Registry on a large cohort of patients with primary hyperoxaluria type 3

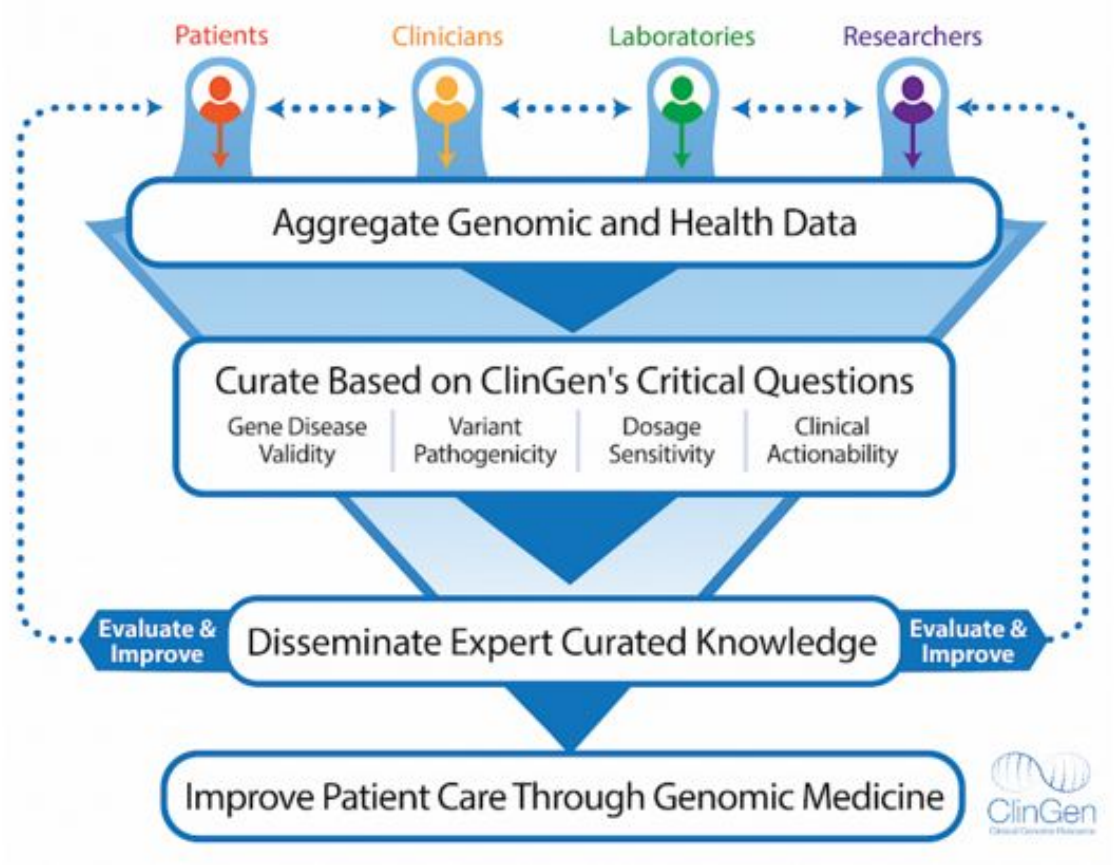
Cristina Martin-Higueras[1,11], Sander F. Garrelfs[2,11], Jaap W. Groothoff[2,11], Dorrit E. Jacob[3], Shabbir H. Moochhala[4], Justine Bacchetta[5], Cecile Acquaviva[5], Marcin Zaniew[6], Przymyslaw Sikora[7,11], Bodo B. Beck[8,9,10,11] and Bernd Hoppe[9]

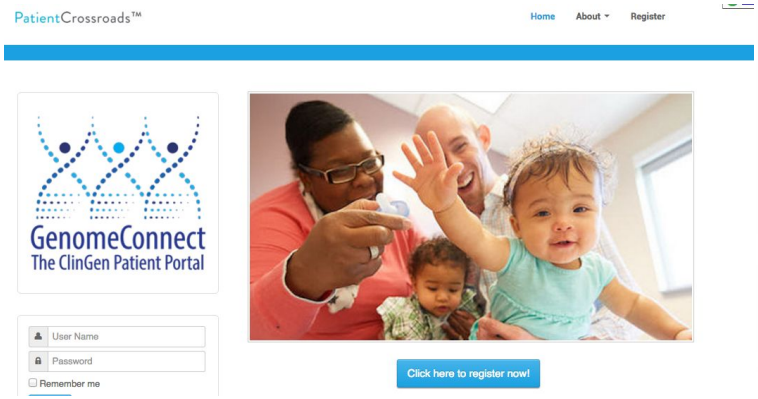
Outcome data in primary hyperoxaluria type 3 (PH3), described as a less severe form of the PH's with a low risk of chronic kidney disease, are scarce. To investigate this, we retrospectively analyzed the largest PH3 cohort reported so far. Of 95 patients, 74 were followed over a median of six years. Median age of first symptoms and diagnosis were 1.9

Genetics. Diagnosis was confirmed by genetic analysis in all cases. Six patients were diagnosed by family screening at ages 5.6, 8.1, 0.3, 1.2, 23, and 30 years. In total, we identified 37 different causative *HOGA1* variants. The most common mutation was the splice mutation c.700+5G>T, which occurred in 30 individuals in homozygous state and in 27 additional individuals in (compound) heterozygous state with other pathogenic variant(s) (allelic frequency [AF], 87 of 190 = 45.8%). The next most common variants were c.569C>T (AF, 8%) and c.944-46delAGG (AF, 5.3%). Eleven novel pathogenic variants were identified (Table 2[5,6,9–11,20–29]).



incorporando la medicina genómica en la atención médica



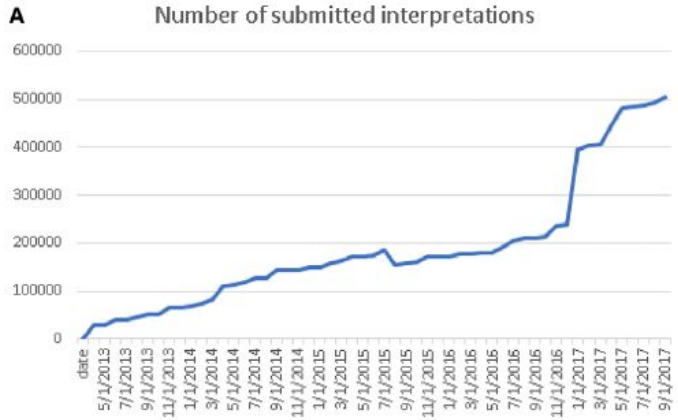


Nucleic Acids Research

Nucleic Acids Res. 2018 Jan 4; 46(Database issue): D1062–D1067. PMCID: PMC5753237
Published online 2017 Nov 20. doi: 10.1093/nar/gkx1153 PMID: 29165669

ClinVar: improving access to variant interpretations and supporting evidence

Melissa J Landrum,✉ Jennifer M Lee, Mark Benson, Garth R Brown, Chen Chao, Shanmuga Chitipiralla, Baoshan Gu, Jennifer Hart, Douglas Hoffman, Wonhee Jang, Karen Karapetyan, Kenneth Katz, Chunlei Liu, Zenith Maddipatla, Adriana Malheiro, Kurt McDaniel, Michael Ovetsky, George Riley, George Zhou, J Bradley Holmes, Brandi L Kattman, and Donna R Maglott



The ClinVar Variation ID represents the variant or set of variants that were interpreted (https://www.ncbi.nlm.nih.gov/clinvar/docs/identifiers/#variation). The set of variants that were interpreted may consist of a single variant; multiple variants as a haplotype (in *cis*); multiple variants as a genotype (in *trans*) when the individual variants are not interpreted independently; multiple variants where the phase is unknown or multiple variants in different genes. Since

Recommended types of search terms for ClinVar

Type of search term	Example
gene symbols	PTEN
HGVS expressions	NM_000314.4:c.395G>T
protein changes	G132V
rs numbers	rs121909241
diseases	PTEN hamartoma tumor syndrome
clinical features/phenotypes	short stature
submitters	NCBI
a location on a chromosome for an assembly	10[chr] AND 89623000:89730000[chrpos37] searches for variants on chromosome 10 between 89623000 and 89730000 based on GRCh37 (chrpos37)

A new INFO tag, MC, report the molecular consequence of the variant predicted by NCBI based on the sequence change, including the Sequence Ontology (9) identifier and the molecular consequence term.

tested. ClinVar aims to bridge this gap with submissions that are focused on patient-associated phenotypes. These submissions are distinguished by their collection method (MethodType in XML), either 'provider interpretation' or 'phenotyping only'. Phenotypes may be submitted as Human Phenotype Ontology (HPO) identifiers or terms; terms for clinical features not in HPO may be submitted and are assigned an identifier in MedGen (10).

The former AF INFO tag was split into three tags, one for each source of allele frequency data: AF_ESP for GO-ESP [https://esp.gs.washington.edu/drupal/]; AF_EXAC for the ExAC Consortium (6); and AF_TGP for the 1000 Genomes Project (7).

TABLE 1 Top ten genes for number of variants in ClinVar

Gene	Number of variants
TTN	10,615
BRCA2	9,372
BRCA1	6,614
ATM	5,304
APC	4,774
TSC2	3,607
NF1	3,398
MSH6	3,297
MSH2	2,771
LDLR	2,435

TABLE 2 Top ten genes from ACMG SF v2.0 for total number of variants and number of Pathogenic or Likely pathogenic variants in ClinVar

Gene	Total variants	P[a]/LP[b] variants
BRCA2	9,372	2,961
BRCA1	6,614	2,525
APC	4,774	711
TSC2	3,607	355
MSH6	3,297	619
MSH2	2,771	837
LDLR	2,435	1,721
MLH1	2,263	800
FBN1	2,081	1,034
RYR1	1,690	227

[a]P, Pathogenic.
[b]LP, Likely pathogenic.

TABLE 3 Genes in ClinVar with the most variants having f evidence

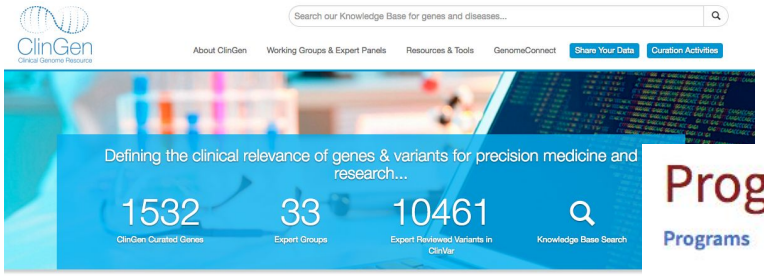
Gene	# variants with experimental results
LDLR	313
AGXT	102
APOB	28
ABCA4	23
GATM	15
GRHPR	15
PCSK9	12

Received: 8 May 2018 | Revised: 10 August 2018 | Accepted: 30 August 2018
DOI: 10.1002/humu.23641

SPECIAL ARTICLE

ClinVar at five years: Delivering on the promise

Melissa J. Landrum | Brandi L. Kattman



Sharing Data. Building Knowledge. Improving Care.

Program for Personalized and Genomic Medicine

Programs > Program for Personalized and Genomic Medicine > Implementation Projects > Genetic Variant Interpretation Tool

Home

Genetic Variant Interpretation Tool

Interpretation of sequence variants | RICHARDS *et al*

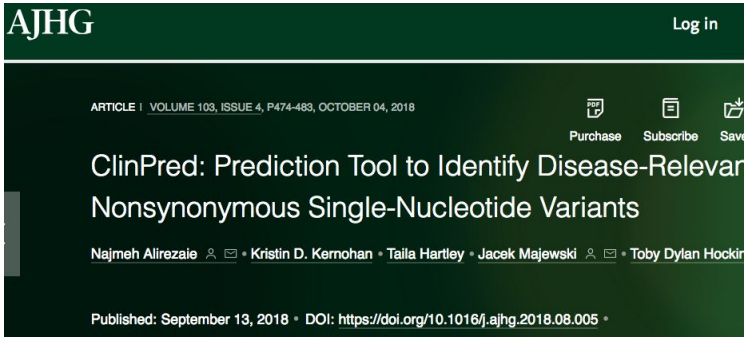
ACMG STANDARDS AND GUIDELINES

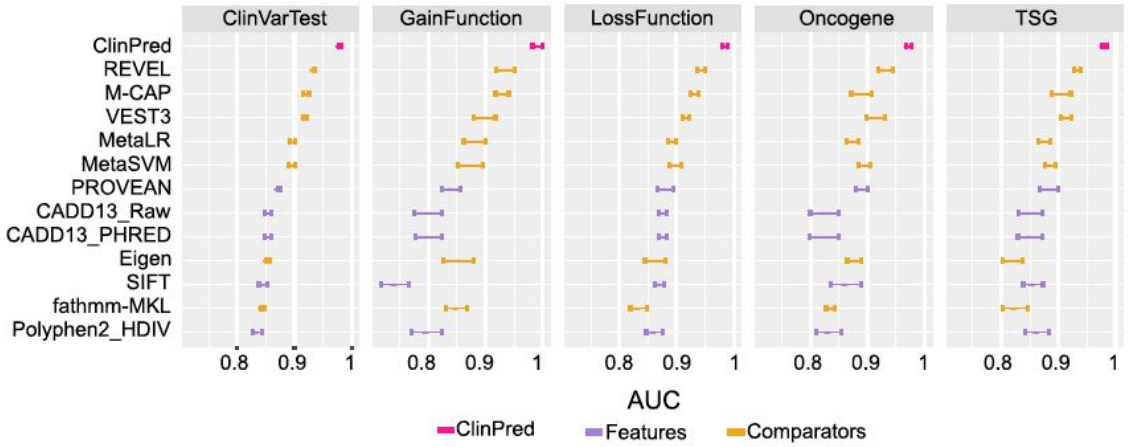
- **Patient registries**
- **Disease-expert**
- **Gene-expert**

WHAT IS THE CLINGEN PATHOGENICITY CALCULATOR?

The shift from genetic testing of individual genes to exome and genome sequencing has been accompanied by new challenges in genome interpretation. The American College of Medical Genetics and Genomics and the Association for Molecular Pathology (ACMG/AMP) have published **Standards and Guidelines for the Interpretation of Sequence Variants**. To enable wide application of the ACMG/AMP and similar guidelines and the development of collective knowledge by the community, ClinGen has developed the ClinGen Pathogenicity Calculator. By automating the formal reasoning, the Calculator

	Benign		Pathogenic			
	Strong	**Supporting**	**Supporting**	**Moderate**	**Strong**	**Very strong**
Population data	MAF is too high for disorder BA1/BS1 **OR** observation in controls inconsistent with disease penetrance BS2			Absent in population databases PM2	Prevalence in affecteds statistically increased over controls PS4	
Computational and predictive data		Multiple lines of computational evidence suggest no impact on gene /gene product BP4 Missense in gene where only truncating cause disease BP1 Silent variant with non predicted splice impact BP7 In-frame indels in repeat w/out known function BP3	Multiple lines of computational evidence support a deleterious effect on the gene /gene product PP3	Novel missense change at an amino acid residue where a different pathogenic missense change has been seen before PM5 Protein length changing variant PM4	Same amino acid change as an established pathogenic variant PS1	Predicted null variant in a gene where LOF is a known mechanism of disease PVS1
Functional data	Well-established functional studies show no deleterious effect BS3		Missense in gene with low rate of benign missense variants and path. missenses common PP2	Mutational hot spot or well-studied functional domain without benign variation PM1	Well-established functional studies show a deleterious effect PS3	
Segregation data	Nonsegregation with disease BS4		Cosegregation with disease in multiple affected family members PP1	Increased segregation data →		
De novo data				De novo (without paternity & maternity confirmed) PM6	De novo (paternity and maternity confirmed) PS2	
Allelic data		Observed in *trans* with a dominant variant BP2 Observed in *cis* with a pathogenic variant BP2		For recessive disorders, detected in trans with a pathogenic variant PM3		
Other database		Reputable source w/out shared data = benign BP6	Reputable source = pathogenic PP5			
Other data		Found in case with an alternate cause BP5	Patient's phenotype or FH highly specific for gene PP4			





Missense prediction	ConSurf	http://consurftest.tau.ac.il	Evolutionary conservation
	FATHMM	http://fathmm.biocompute.org.uk	Evolutionary conservation
	MutationAssessor	http://mutationassessor.org	Evolutionary conservation
	PANTHER	http://www.pantherdb.org/tools/csnpScoreForm.jsp	Evolutionary conservation
	PhD-SNP	http://snps.biofold.org/phd-snp/phd-snp.html	Evolutionary conservation
	SIFT	http://sift.jcvi.org	Evolutionary conservation
	SNPs&GO	http://snps-and-go.biocomp.unibo.it/snps-and-go	Protein structure/function
	Align GVGD	http://agvgd.iarc.fr/agvgd_input.php	Protein structure/function and evolutionary conservation
	MAPP	http://mendel.stanford.edu/SidowLab/downloads/MAPP/index.html	Protein structure/function and evolutionary conservation
	MutationTaster	http://www.mutationtaster.org	Protein structure/function and evolutionary conservation
	MutPred	http://mutpred.mutdb.org	Protein structure/function and evolutionary conservation
	PolyPhen-2	http://genetics.bwh.harvard.edu/pph2	Protein structure/function and evolutionary conservation
	PROVEAN	http://provean.jcvi.org/index.php	Alignment and measurement of similarity between variant sequence and protein sequence homolog
	nsSNPAnalyzer	http://snpanalyzer.uthsc.edu	Multiple sequence alignment and protein structure analysis
	Condel	http://bg.upf.edu/fannsdb/	Combines SIFT, PolyPhen-2, and MutationAssessor
	CADD	http://cadd.gs.washington.edu	Contrasts annotations of fixed/nearly fixed derived alleles in humans with simulated variants

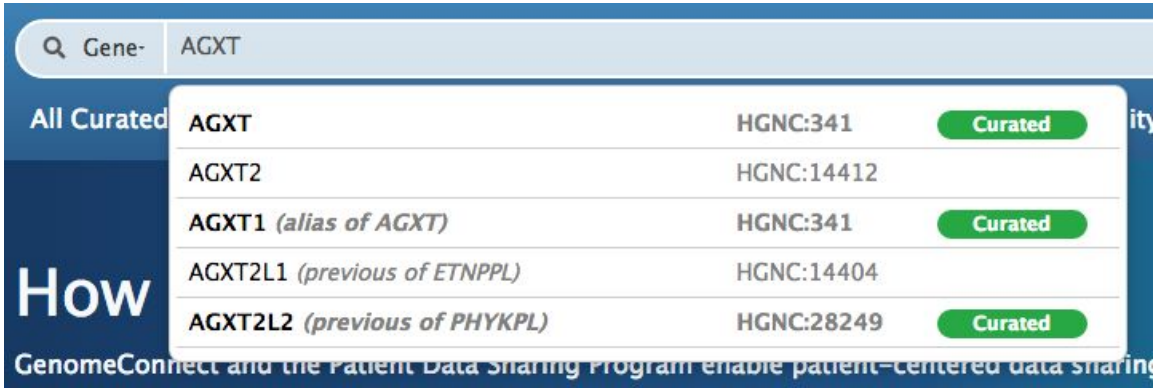
How do you read a ClinVar record?

GenomeConnect and the Patient Data Sharing Program enable patient-centered data sharing. The primary place where data are shared is NCBI's ClinVar. Learn more about what ClinVar is and how to read a ClinVar record below.

ClinGen
Clinical Genome Resource

About | For Individuals (GenomeConnect) | For Advocates & Groups | Staff | How To Use Data | Review a ClinVar Record | Registry List

https://www.clinicalgenome.org/genomeconnect/how-to-search-clinvar/



Curation Summaries | Status and Future Work (1) | External Genomic Resources | ClinVar Variants

Group By Activity | Group By Gene-Disease Pair

Gene-Disease Validity

Gene	Disease	MOI	Expert Panel	Classification	Report & Date
AGXT	alanine glyoxylate aminotransferase deficiency MONDO:0100278	AR	Peroxisomal Disorders GCEP	Definitive	02/07/2020

MedGen: Genetics Summary

Organizes information related to human medi

MedGen: Genetics Summary

Genetic Practice Guidelines: Gene

As guidelines are identified that relate to a dis
This page provides an alphabetical list of the
have been identified.

Genetic Practice Guidelines: Gene

GTR: Gene Tests

A voluntary registry of genetic tests and labor
analytic and clinical validity. GTR also is a nex
variety of resources, including practice guideli
single gene tests for Mendelian disorders, son

GTR: Gene Tests

CPIC Pharmacogenomics Prescribing Guidelines

The Clinical Pharmacogenetics Implementation Consortium (CPIC)
Pharmacogenomics Research Network (PGRN).

CPIC Pharmacogenomics Prescribing Guidelines

PharmGKB: Gene

PharmGKB is a comprehensive resource that curates knowledge ab
clinicians and researchers.

PharmGKB: Gene

OMIM: Gene

An Online Catalog of Human Genes and Genetic Disorders.

OMIM: Gene

Gene Reviews

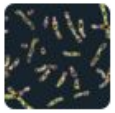
An international point-of-care resource for busy clinicians, provic
inherited conditions in a standardized journal-style format, cover
and their families.

Gene Reviews

ClinVar - Gene

ClinGen and ClinVar are close partners and have esta
ClinGen. ClinVar aggregates information about geno

ClinVar - Gene



1000 Genomes

An interactive graphical viewer that allows users to e
sequence reads) that have been produced by the 10(

1000 Genomes

NCBI Browser

The 1000 Genomes Browser allows users to explore
have been produced by the 1000 Genomes project.

NCBI Browser

Disease characteristics

Go to:

Excerpted from the *GeneReview:* Primary Hyperoxaluria Type 1

Primary hyperoxaluria type 1 (PH1) is caused by a deficiency of the liver peroxisomal enzyme alanine:glyoxylate-aminotransferase (AGT), which catalyzes the conversion of glyoxylate to glycine. When AGT activity is absent, glyoxylate is converted to oxalate, which forms insoluble calcium oxalate crystals that accumulate in the kidney and other organs. Individuals with PH1 are at risk for recurrent nephrolithiasis (deposition of calcium oxalate in the renal pelvis / urinary tract), nephrocalcinosis (deposition of calcium oxalate in the renal parenchyma), or end-stage renal disease (ESRD). Age at onset of symptoms ranges from infancy to the sixth decade. Approximately 10% of affected individuals present in infancy or early childhood with nephrocalcinosis, with or without nephrolithiasis, and failure to thrive related to renal failure. The majority of individuals with PH1 present in childhood or early adolescence, usually with symptomatic nephrolithiasis and normal or reduced kidney function. The remainder of affected individuals present in adulthood with recurrent renal stones and a mild-to-moderate reduction in kidney function. The natural history of untreated PH1 is one of progressive decline in renal function as a result of calcium oxalate deposits in kidney tissue and complications of nephrolithiasis (e.g., obstruction and infection) with eventual progression to oxalosis (widespread tissue deposition of calcium oxalate) and death from ESRD and/or complications of oxalosis. [from GeneReviews]

Full text of *GeneReview* (by section):

Summary | Diagnosis | Clinical Characteristics | Genetically Related (Allelic) Disorders | Differential Diagnosis | Management | Genetic Counseling | Resources | Molecular Genetics | Chapter Notes | References

Authors:

Dawn S Milliner | Peter C Harris | David J Sas, *et. al.* view full author information

Additional descriptions

Go to:

From OMIM

Primary hyperoxaluria type I is an autosomal recessive disorder characterized by an accumulation of calcium oxalate in various bodily tissues, especially the kidney, resulting in renal failure. Affected individuals have decreased or absent AGXT activity and a failure to transaminate glyoxylate, which causes the accumulated glyoxylate to be oxidized to oxalate. This overproduction of oxalate results in the accumulation of nonsoluble calcium oxalate in various body tissues, with pathologic sequelae (Takada et al., 1990; Danpure et al., 1989; Williams et al., 2009) Genetic Heterogeneity of Primary Hyperoxaluria Type II primary hyperoxaluria (HP2; 260000) is caused by mutation in the glyoxylate reductase/hydroxypyruvate reductase gene (GRHPR; 604296) on chromosome 9. Type III primary hyperoxaluria (HP3; 613616) is caused by mutation in the mitochondrial dihydrodipicolinate synthase-like gene (DHDPSL; 613597) on chromosome 10q24. http://www.omim.org/entry/259900

From MedlinePlus Genetics

Primary hyperoxaluria is a rare condition characterized by recurrent kidney and bladder stones. The condition often results in end stage renal disease (ESRD), which is a life-threatening condition that prevents the kidneys from filtering fluids and waste products from the body effectively.\n\nPrimary hyperoxaluria results from the overproduction of a substance called oxalate. Oxalate is filtered through the kidneys and excreted as a waste product in urine, leading to abnormally high levels of this substance in urine (hyperoxaluria). During its excretion, oxalate can combine with calcium to form

kidney and bladder stones. Deposits of calcium oxalate can damage the kidneys and

Professional guidelines

Go to:

PubMed

Primary hyperoxaluria Type 1: indications for screening and guidance for diagnosis and treatment.

Cochat P, Hulton SA, Acquaviva C, Danpure CJ, Daudon M, De Marchi M, Fargue S, Groothoff J, Harambat J, Hoppe B, Jamieson NV, Kemper MJ, Mandrile G, Marangella M, Picca S, Rumsby G, Salido E, Straub M, van Woerden CS; OxalEurope.
Nephrol Dial Transplant 2012 May;27(5):1729-36. doi: 10.1093/ndt/gfs078. PMID: 22547750

Recent clinical studies

Go to:

Etiology

Preemptive liver transplant in two patients with primary hyperoxaluria type 1: Clinical significance of nephrolithiasis and nephrocalcinosis.

Uchida H, Sakamoto S, Kodama T, Nakao T, Yanagi Y, Shimizu S, Fukuda A, Sato M, Kamei K, Kasahara M
Pediatr Transplant 2022 Dec;26(8):e14380. Epub 2022 Aug 18 doi: 10.1111/petr.14380. PMID: 35979862

Extended genetic analysis of exome sequencing for primary hyperoxaluria in pediatric urolithiasis patients with hyperoxaluria.

Zhao Y, Li Y, Fang X, He L, Fan Y, Geng H, Wu J
Gene 2022 Mar 20;815:146155. Epub 2022 Jan 5 doi: 10.1016/j.gene.2021.146155. PMID: 34995728

Primary Hyperoxaluria Type 3 Can Also Result in Kidney Failure: A Case Report.

Singh P, Granberg CF, Harris PC, Lieske JC, Licht JH, Weiss A, Milliner DS
Am J Kidney Dis 2022 Jan;79(1):125-128. Epub 2021 Jul 7 doi: 10.1053/j.ajkd.2021.05.016. PMID: 34245816 **Free PMC Article**

Phase 1/2 Study of Lumasiran for Treatment of Primary Hyperoxaluria Type 1: A Placebo-Controlled Randomized Clinical Trial.

Frishberg Y, Deschênes G, Groothoff JW, Hulton SA, Magen D, Harambat J, Van't Hoff WG, Lorch U, Milliner DS, Lieske JC, Haslett P, Garg PP, Vaishnaw AK, Talamudupula S, Lu J, Habtemariam BA, Erbe DV, McGregor TL, Cochat P; study collaborators.
Clin J Am Soc Nephrol 2021 Jul;16(7):1025-1036. Epub 2021 May 13 doi: 10.2215/CJN.14730920. PMID: 33985991 **Free PMC Article**

Diagnosis

PHYOX2: a pivotal randomized study of nedosiran in primary hyperoxaluria type 1 or 2.

Baum MA, Langman C, Cochat P, Lieske JC, Moochhala SH, Hamamoto S, Satoh H, Mourani C, Ariceta G, Torres A, Wolley M, Belostotsky V, Forbes TA, Groothoff J, Hayes W, Tönshoff B, Takayama T, Rosskamp R, Russell K, Zhou J, Amrite A, Hoppe B; PHYOX2 study investigators.
Kidney Int 2023 Jan;103(1):207-217. Epub 2022 Aug 22 doi: 10.1016/j.kint.2022.07.025. PMID: 36007597

Preemptive liver transplant in two patients with primary hyperoxaluria type 1: Clinical significance of nephrolithiasis and nephrocalcinosis.

Uchida H, Sakamoto S, Kodama T, Nakao T, Yanagi Y, Shimizu S, Fukuda A, Sato M, Kamei K, Kasahara M
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Primary Hyperoxaluria Type 3 Can Also Result in Kidney Failure: A Case Report.

Singh P, Granberg CF, Harris PC, Lieske JC, Licht JH, Weiss A, Milliner DS
Am J Kidney Dis 2022 Jan;79(1):125-128. Epub 2021 Jul 7 doi: 10.1053/j.ajkd.2021.05.016. PMID: 34245816 **Free PMC Article**

Clinical characterization of primary hyperoxaluria type 3 in comparison with types 1 and 2.

Singh P, Viehman JK, Mehta RA, Cogal AG, Hasadsri L, Oglesbee D, Olson JB, Seide BM, Sas DJ, Harris PC, Lieske JC, Milliner DS
Nephrol Dial Transplant 2022 Apr 25;37(5):869-875. doi: 10.1093/ndt/gfab027. PMID: 33543760 **Free PMC Article**

A report from the European Hyperoxaluria Consortium (OxalEurope) Registry on a large cohort of patients with primary hyperoxaluria type 3.

Martin-Higueras C, Garrelfs SF, Groothoff JW, Jacob DE, Moochhala SH, Bacchetta J, Acquaviva C, Zaniew M, Sikora P, Beck BB, Hoppe B
Kidney Int 2021 Sep;100(3):621-635. Epub 2021 Apr 16 doi: 10.1016/j.kint.2021.03.031. PMID: 33865885

See all (290)

Therapy

PHYOX2: a pivotal randomized study of nedosiran in primary hyperoxaluria type 1 or 2.

Baum MA, Langman C, Cochat P, Lieske JC, Moochhala SH, Hamamoto S, Satoh H, Mourani C, Ariceta G, Torres A, Wolley M, Belostotsky V, Forbes TA, Groothoff J, Hayes W, Tönshoff B, Takayama T, Rosskamp R, Russell K, Zhou J, Amrite A, Hoppe B; PHYOX2 study investigators.
Kidney Int 2023 Jan;103(1):207-217. Epub 2022 Aug 22 doi: 10.1016/j.kint.2022.07.025. PMID: 36007597

Lumasiran for Advanced Primary Hyperoxaluria Type 1: Phase 3 ILLUMINATE-C Trial.

Michael M, Groothoff JW, Shasha-Lavsky H, Lieske JC, Frishberg Y, Simkova E, Sellier-Leclerc AL, Devresse A, Guebre-Egziabher F, Bakkaloglu SA, Mourani C, Saqan R, Singer R, Willey R, Habtemariam B, Gansner JM, Bhan I, McGregor T, Magen D
Am J Kidney Dis 2023 Feb;81(2):145-155.e1. Epub 2022 Jul 14 doi: 10.1053/j.ajkd.2022.05.012. PMID: 35843439

Prognosis

Genetic assessment in primary hyperoxaluria: why it matters.

Mandrile G, Beck B, Acquaviva C, Rumsby G, Deesker L, Garrelfs S, Gupta A, Bacchetta J, Groothoff J; OxalEurope Consortium/Erknet Guideline Workgroup On Hyperoxaluria.
Pediatr Nephrol 2023 Mar;38(3):625-634. Epub 2022 Jun 13 doi: 10.1007/s00467-022-05613-2. PMID: 35695965 **Free PMC Article**

HOGA1 gene pathogenic variants in primary hyperoxaluria type III: Spectrum of pathogenic sequence variants, and phenotypic association.

Abid A, Raza A, Aziz T, Khaliq S
Hum Mutat 2022 Dec;43(12):1757-1779. Epub 2022 Nov 2 doi: 10.1002/humu.24490. PMID: 36259736

Preemptive liver transplant in two patients with primary hyperoxaluria type 1: Clinical significance of nephrolithiasis and nephrocalcinosis.

Uchida H, Sakamoto S, Kodama T, Nakao T, Yanagi Y, Shimizu S, Fukuda A, Sato M, Kamei K, Kasahara M
Pediatr Transplant 2022 Dec;26(8):e14380. Epub 2022 Aug 18 doi: 10.1111/petr.14380. PMID: 35979862

End Points for Clinical Trials in Primary Hyperoxaluria.

Milliner DS, McGregor TL, Thompson A, Dehmel B, Knight J, Rosskamp R, Blank M, Yang S, Fargue S, Rumsby G, Groothoff J, Allain M, West M, Hollander K, Lowther WT, Lieske JC
Clin J Am Soc Nephrol 2020 Jul 1;15(7):1056-1065. Epub 2020 Mar 12 doi: 10.2215/CJN.13821119. PMID: 32165440 **Free PMC Article**

Patients with primary hyperoxaluria type 2 have significant morbidity and require careful follow-up.

Garrelfs SF, Rumsby G, Peters-Sengers H, Erger F, Groothoff JW, Beck BB, Oosterveld MJS, Pelle A, Neuhaus T, Adams B, Cochat P, Salido E, Lipkin GW, Hoppe B, Hulton SA; OxalEurope Consortium.
Kidney Int 2019 Dec;96(6):1389-1399. Epub 2019 Sep 3 doi: 10.1016/j.kint.2019.08.018. PMID: 31685312

See all (162)

Clinical prediction guides

Lumasiran for Advanced Primary Hyperoxaluria Type 1: Phase 3 ILLUMINATE-C Trial.

Michael M, Groothoff JW, Shasha-Lavsky H, Lieske JC, Frishberg Y, Simkova E, Sellier-Leclerc AL, Devresse A, Guebre-Egziabher F, Bakkaloglu SA, Mourani C, Saqan R, Singer R, Willey R, Habtemariam B, Gansner JM, Bhan I, McGregor T, Magen D
Am J Kidney Dis 2023 Feb;81(2):145-155.e1. Epub 2022 Jul 14 doi: 10.1053/j.ajkd.2022.05.012. PMID: 35843439

Primary Hyperoxaluria Type 3 Can Also Result in Kidney Failure: A Case Report.

Singh P, Granberg CF, Harris PC, Lieske JC, Licht JH, Weiss A, Milliner DS
Am J Kidney Dis 2022 Jan;79(1):125-128. Epub 2021 Jul 7 doi: 10.1053/j.ajkd.2021.05.016. PMID: 34245816 **Free PMC Article**

Recent systematic reviews

Go to:

Transplantation outcomes in patients with primary hyperoxaluria: a systematic review.

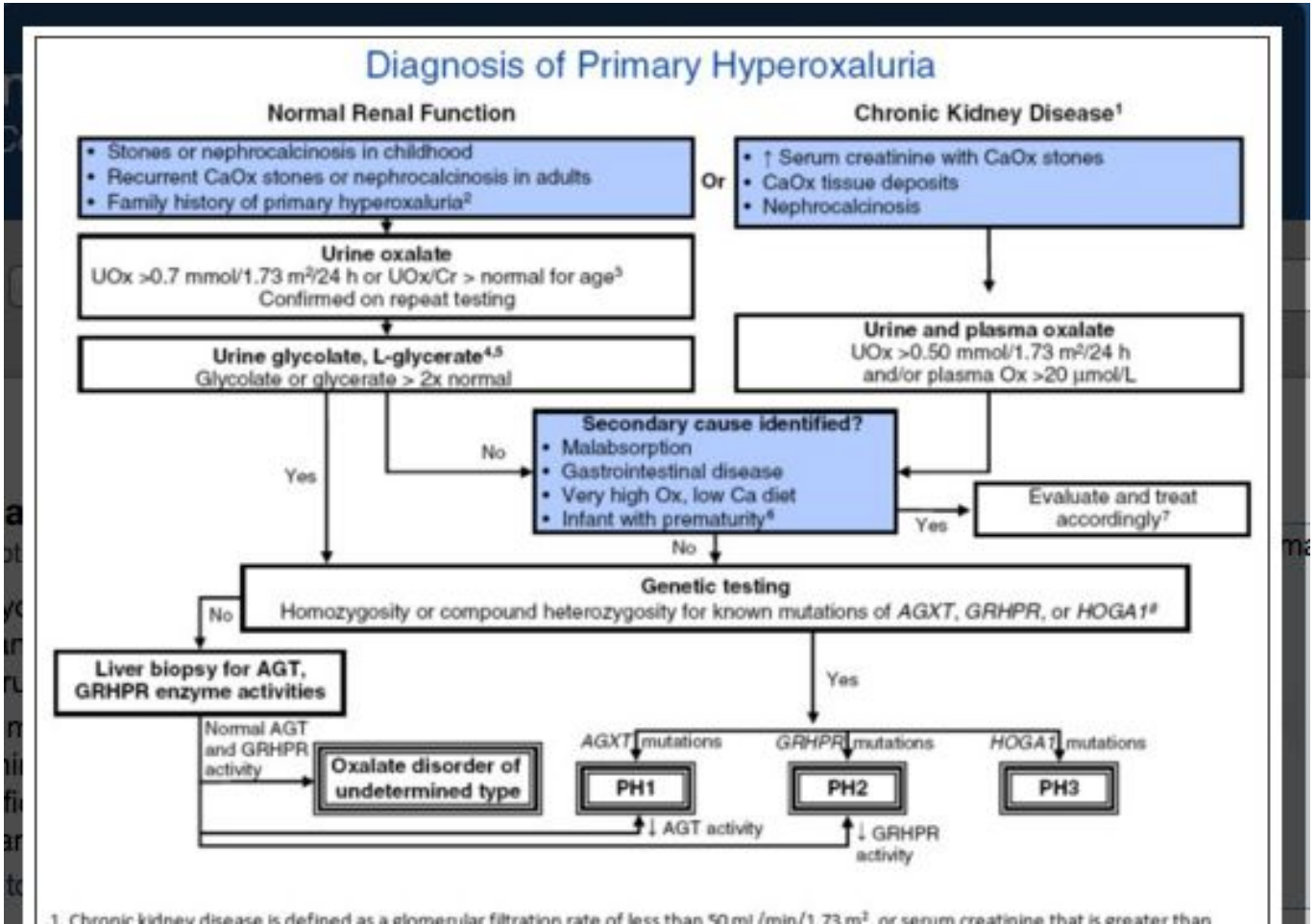
Metry EL, van Dijk LMM, Peters-Sengers H, Oosterveld MJS, Groothoff JW, Ploeg RJ, Stel VS, Garrelfs SF

Pediatr Nephrol 2021 Aug;36(8):2217-2226. Epub 2021 Apr 8 doi: 10.1007/s00467-021-05043-6. PMID: 33830344 **Free PMC Article**

Updated Genetic Testing of Primary Hyperoxaluria Type 1 in a Chinese Population: Results from a Single Center Study and a Systematic Review.

Du DF, Li QQ, Chen C, Shi SM, Zhao YY, Jiang JP, Wang DW, Guo H, Zhang WJ, Chen ZS

Curr Med Sci 2018 Oct;38(5):749-757. Epub 2018 Oct 20 doi: 10.1007/s11596-018-1941-y. PMID: 30341509



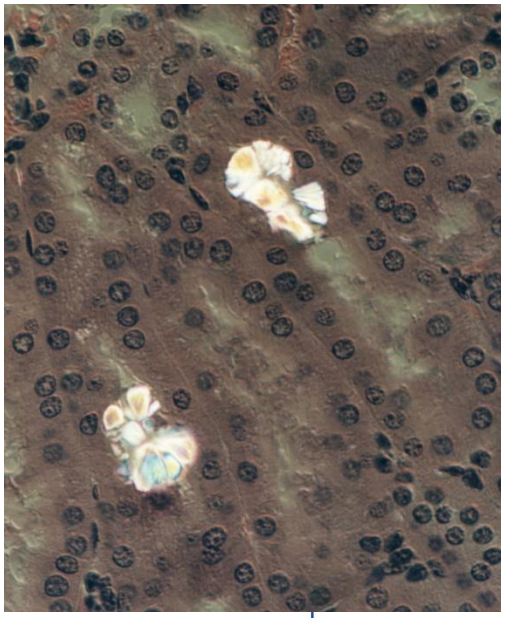
Molecular therapies

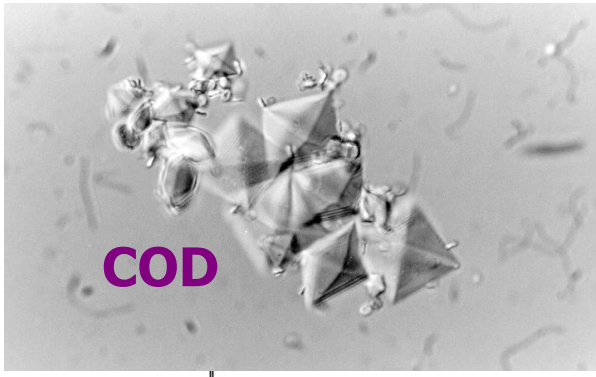
- Enzyme Replacement Therapy (ERT)
- Substrate Reduction Therapy (SRT) (& Ox Degr.)
- Chaperone-Proteostasis Regulator Therapy (CPRT)
- Gene Therapy (GT)
- Cell Therapy (CT)
- Kidney protection Therapy

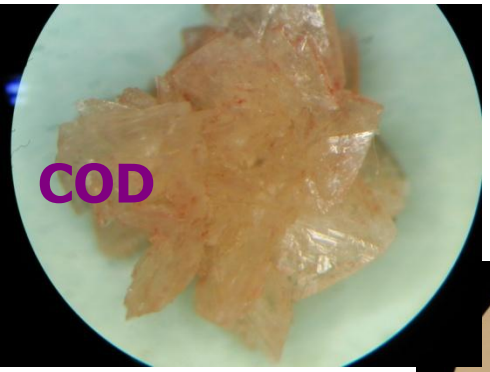
explored in cellular and animal models:
CHO cells
mouse KOs: hepatocytes & organism

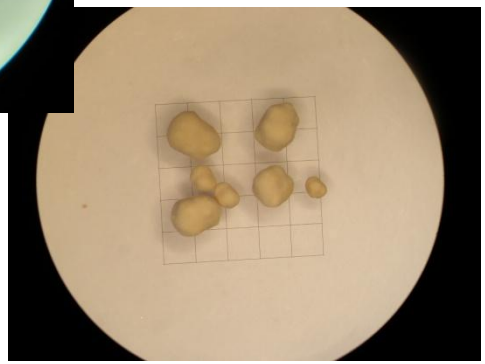
Genetically modified mouse models of hyperoxaluria

-*Agxt*KO
-*Grhpr*KO
-*Hoga1*KO
-*Hao1*KO



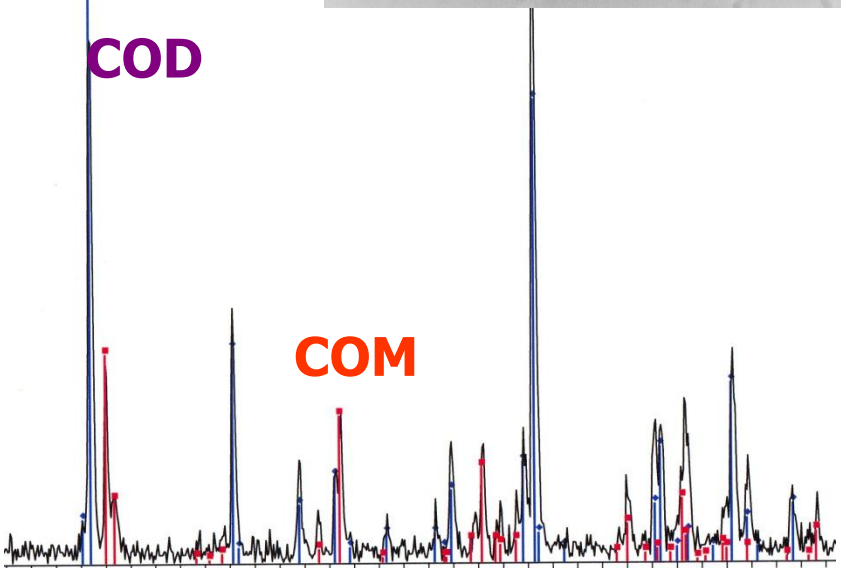






COM

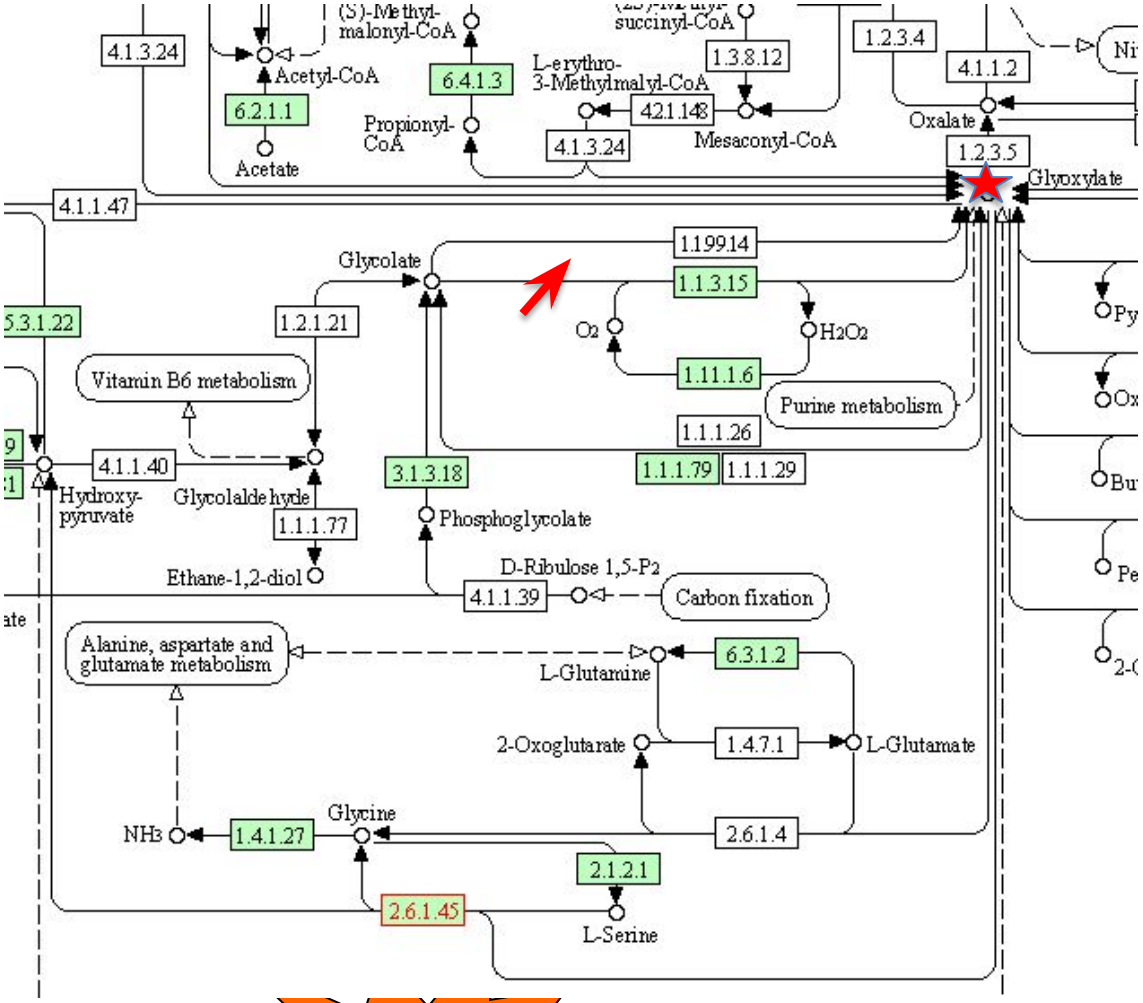
COD



Substrate Reduction Therapy (SRT)

- Targets identified: - **Glycolate Oxidase (GO)**
  - **LDH**
    - PRDH2
      - *GRHPR enhancement*
- Advances: - **GO siRNA**
  - **LDH siRNA**
    - **GO inhibitors** (small molecule)

- *Related: Oxalate Degradation Therapy*
  - Gut sink: Probiotics (Oxthera)
    Protein crystals (Altus)
  - RBC sink (B.Cellini, personal comm.)



AGXT

Glyoxylate

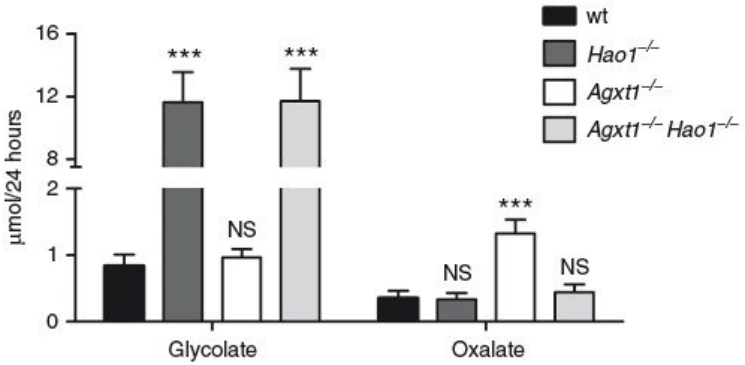
build-up

Glycine

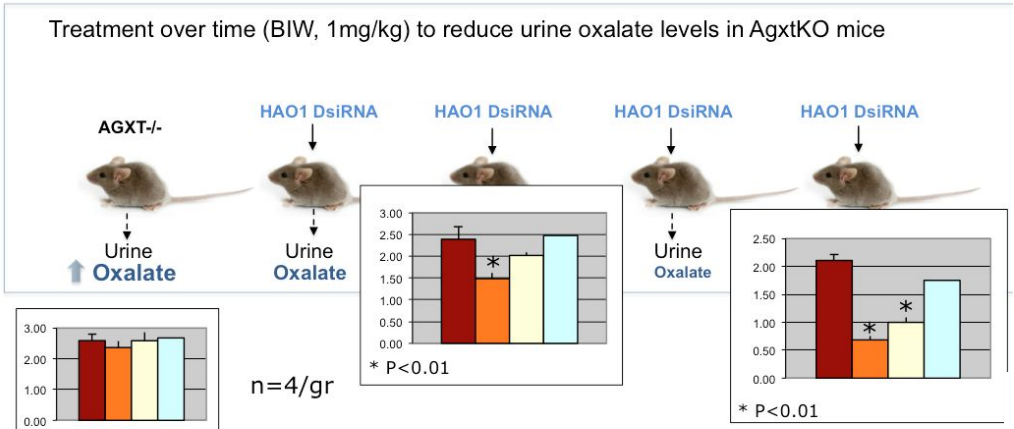
deficit

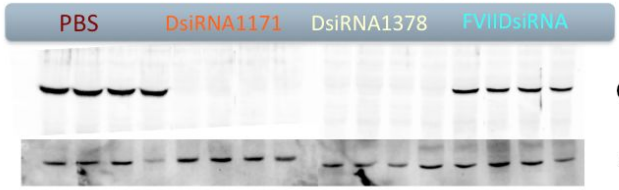
Glycolate Oxidase Is a Safe and Efficient Target for Substrate Reduction Therapy in a Mouse Model of Primary Hyperoxaluria Type I

Cristina Martin-Higueras[1], Sergio Luis-Lima[2] and Eduardo Salido[1,2]

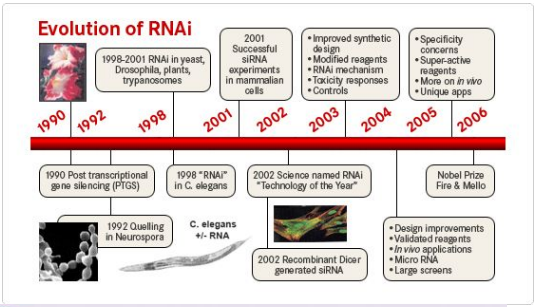


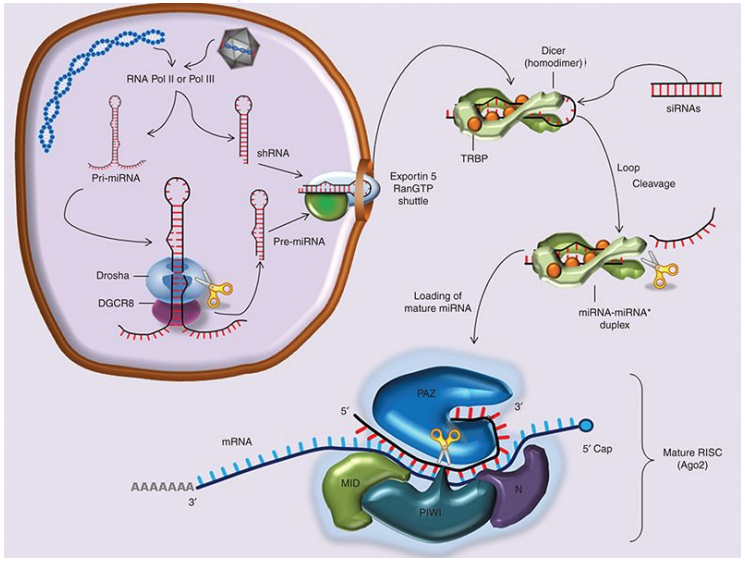
In vivo HAO1 DsiRNA administration to PH1 mice





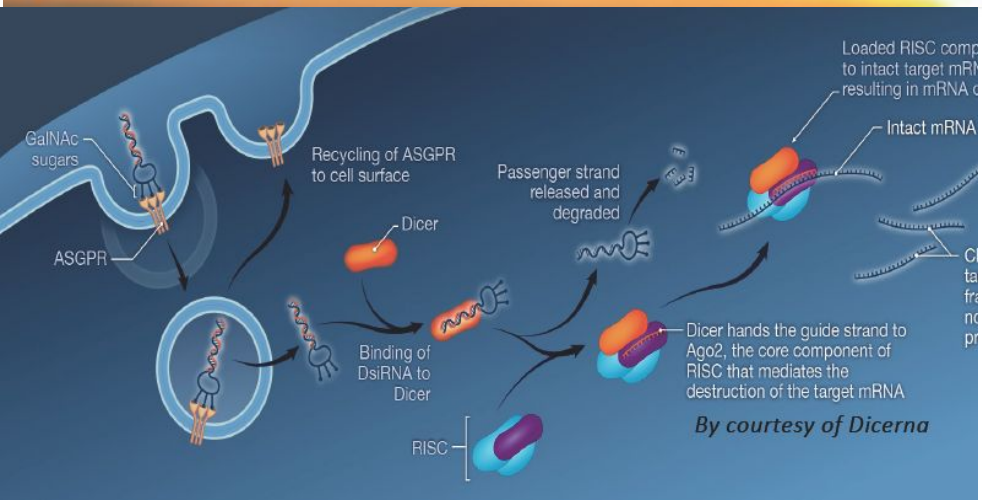
PBS
DsiRNA1171
DsiRNA1378
F VII DsiRNA





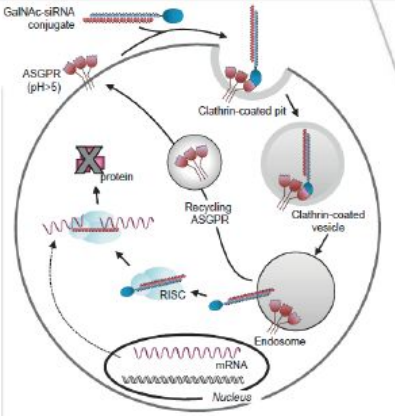
Inhibition of Glycolate Oxidase With Dicer-substrate siRNA Reduces Calcium Oxalate Deposition in a Mouse Model of Primary Hyperoxaluria Type 1

Chaitali Dutta[1], Nicole Avitahl-Curtis[1], Natalie Pursell[1], Marita Larsson Cohen[1], Benjamin Holmes[1], Rohan Diwanji[1], Wei Zhou[1], Luciano Apponi[1], Martin Koser[1], Bo Ying[1], Dongyu Chen[1], Xue Shui[1], Utsav Saxena[1], Wendy A Cyr[1], Anee Shah[1], Naim Nazef[1], Weimin Wang[1], Marc Abrams[1], Henryk Dudek[1], Eduardo Salido[2], Bob D Brown[1] and Chengjung Lai[1]



Asialoglycoprotein Receptor (ASAGPR)

- Highly expressed in hepatocytes
- High uptake
- Efficient delivery to hepatocytes by **s.c. Injection**
- **Liver specific**
- Proof of principle other iRNA drugs



By courtesy of Alnylam

phase 3 clinical trials
FDA approval

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FDA NEWS RELEASE

FDA Approves First Drug to Treat Rare Metabolic Disorder

Approval is for primary hyperoxaluria type 1, which causes recurrent kidney stones and loss of kidney function

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For Immediate Release:
November 23, 2020

Lumasiran

although preclinical studies were good for GO siRNA, in face of Alnylam competition, Dicerna decided to pursue LDH siRNA with clinical trials instead, also hoping to cast a wider net: PH1, PH2, PH3….. ***Nedosiran***

KI REPORTS
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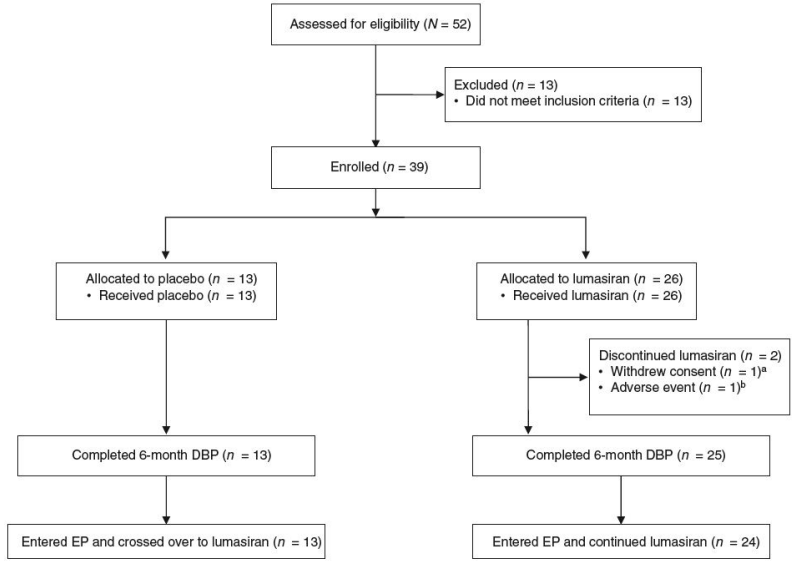
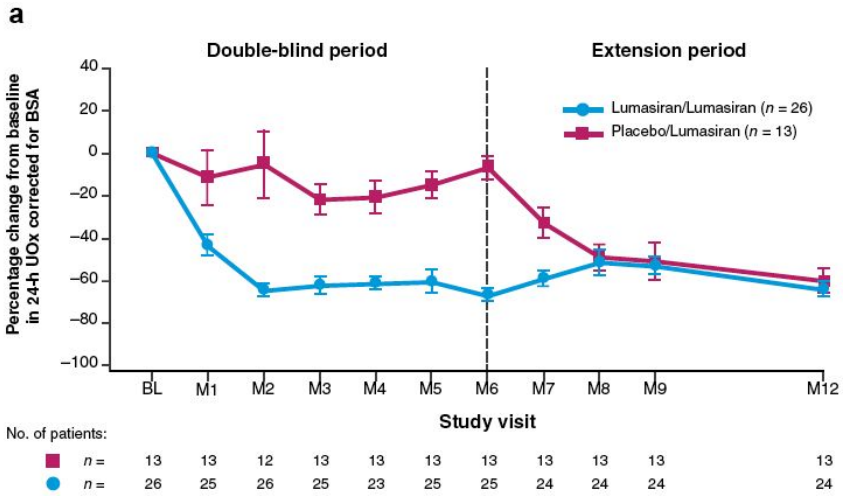
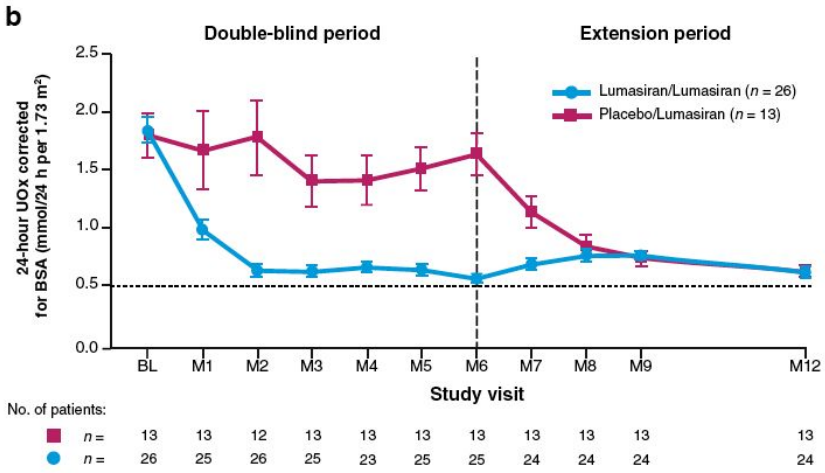
CLINICAL RESEARCH

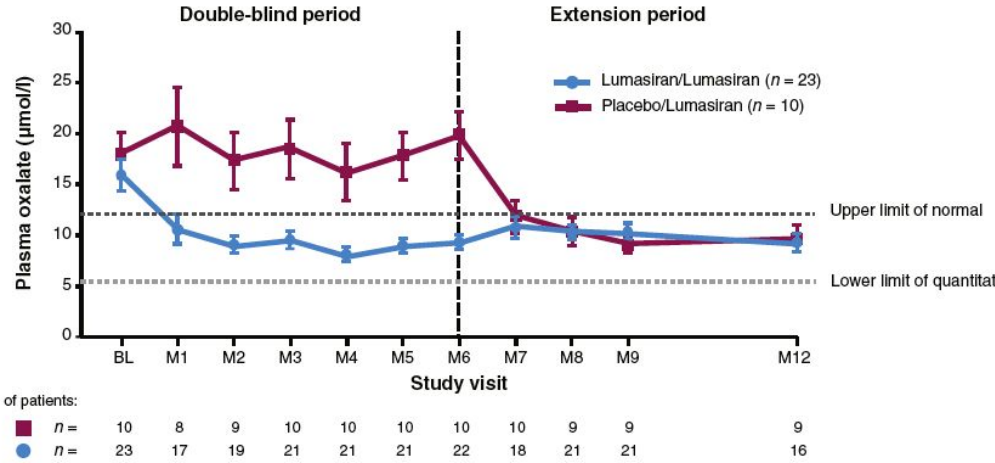
Randomized Clinical Trial on the Long-Term Efficacy and Safety of Lumasiran in Patients With Primary Hyperoxaluria Type 1

Sally A. Hulton[1], Jaap W. Groothoff[2], Yaacov Frishberg[3], Michael J. Koren[4], J. Scott Overcash[5], Anne-Laure Sellier-Leclerc[6], Hadas Shasha-Lavsky[7], Jeffrey M. Saland[8], Wesley Hayes[9], Daniella Magen[10], Shabbir H. Moochhala[11], Martin Coenen[12], Eva Simkova[13], Sander F. Garrelfs[2], David J. Sas[14], Kristin A. Meliambro[8], Taylor Ngo[15], Marianne T. Sweetser[15], Bahru A. Habtemariam[15], John M. Gansner[15], Tracy L. McGregor[15] and John C. Lieske[16]





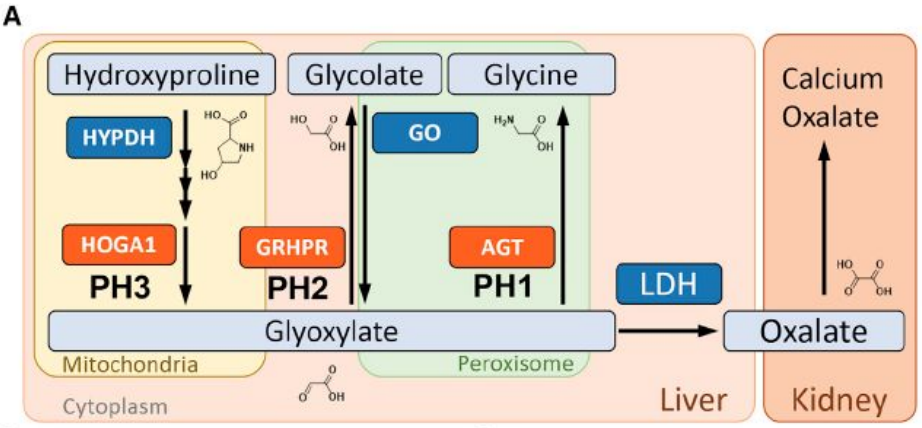


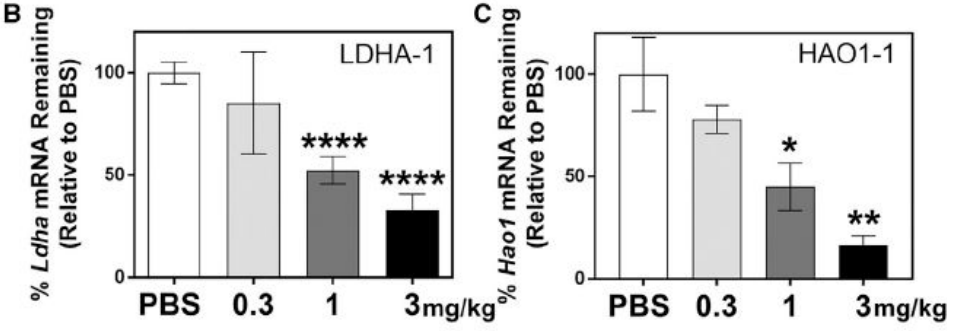


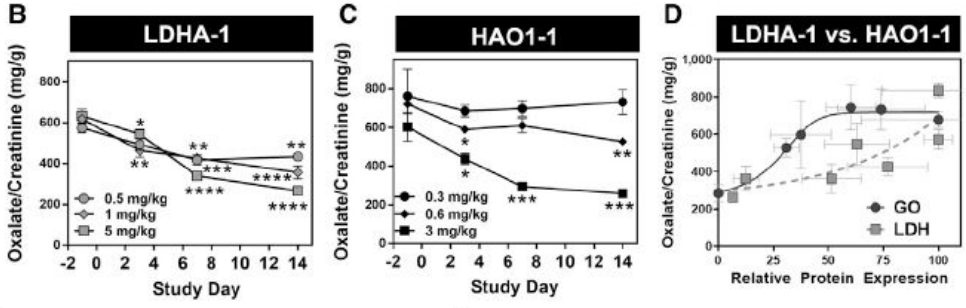
LDHa siRNA

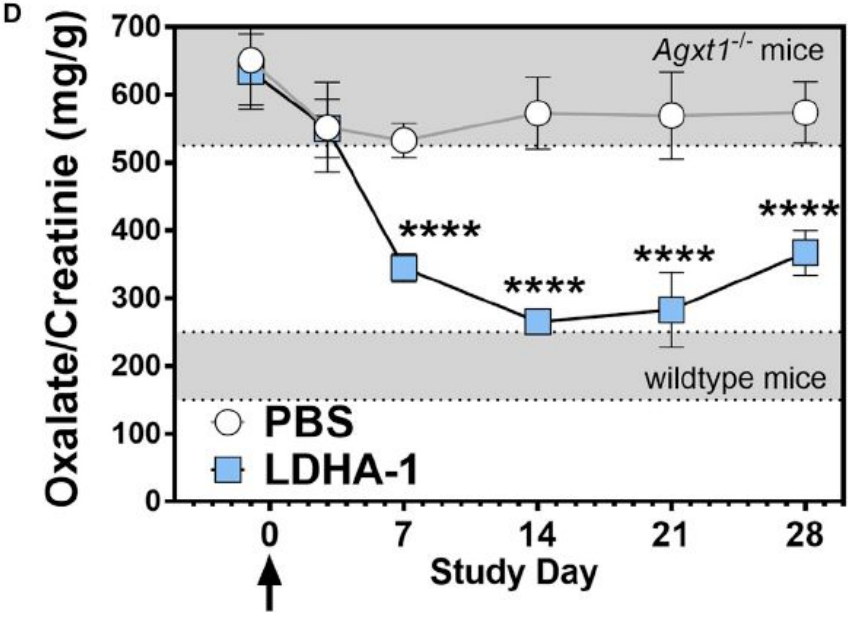
Specific Inhibition of Hepatic Lactate Dehydrogenase Reduces Oxalate Production in Mouse Models of Primary Hyperoxaluria

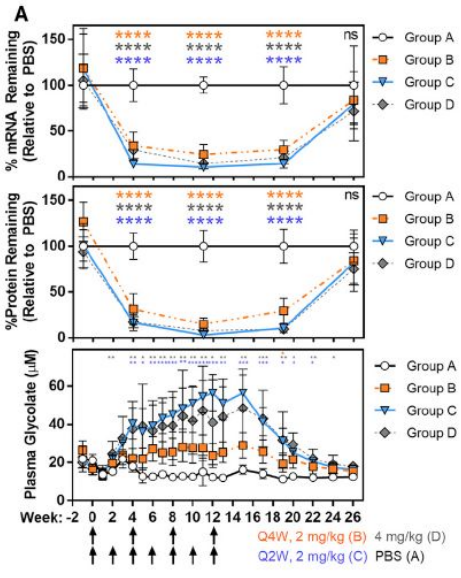
Chengjung Lai,[1] Natalie Pursell,[1] Jessica Gierut,[1] Utsav Saxena,[1] Wei Zhou,[1] Michael Dills,[1] Rohan Diwanji,[1] Chaitali Dutta,[1] Martin Koser,[1] Naim Nazef,[1] Rachel Storr,[1] Boyoung Kim,[1] Cristina Martin-Higueras,[2] Eduardo Salido,[2] Weimin Wang,[1] Marc Abrams,[1] Henryk Dudek,[1] and Bob D. Brown[1]

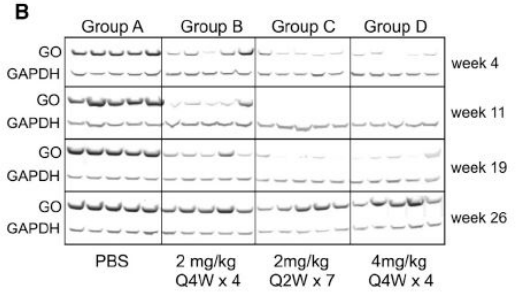


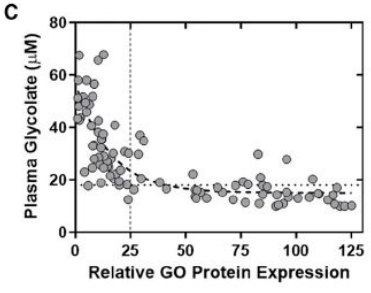












Non-linear Relationship between GO Enzyme Reduction and Glycolate Elevation in NHPs

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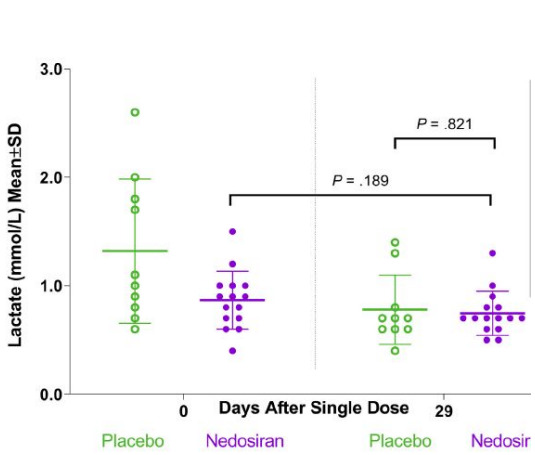
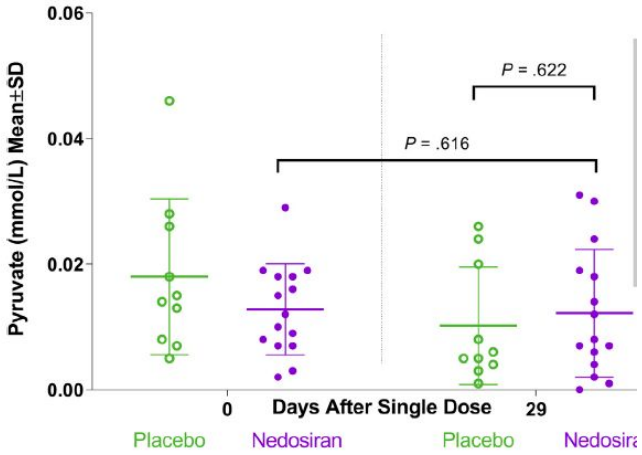
CLINICAL RESEARCH

Hepatic Lactate Dehydrogenase A: An RNA Interference Target for the Treatment of All Known Types of Primary Hyperoxaluria

Gema Ariceta[1,2], Kelly Barrios[3], Bob D. Brown[3], Bernd Hoppe[3,4], Ralf Rosskamp[3] and Craig B. Langman[5,6]

Conclusion: Phase I clinical data on nedosiran and published nonclinical data together provide substantial evidence that *LDHA* inhibition is a safe therapeutic mechanism for the treatment of all known types of PH.





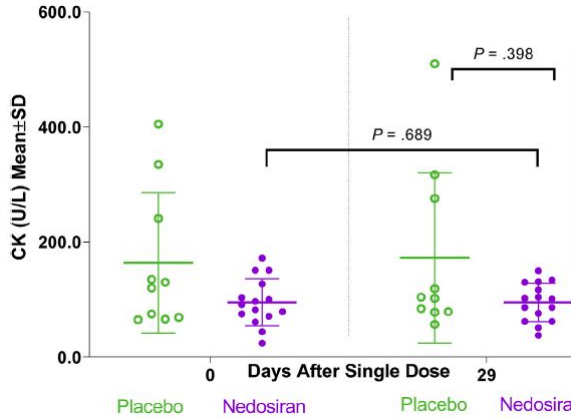
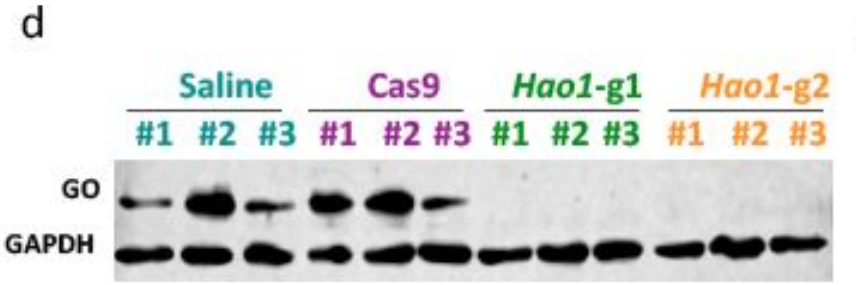
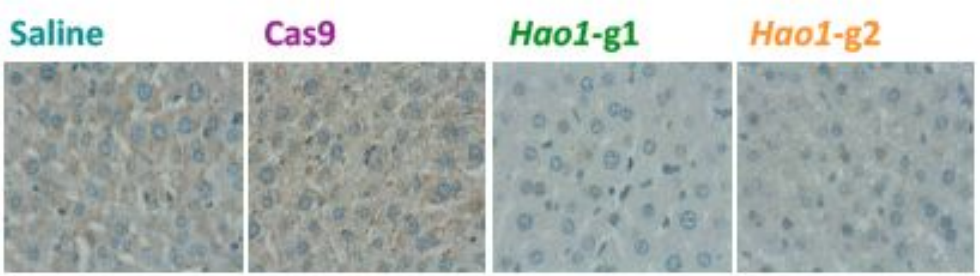


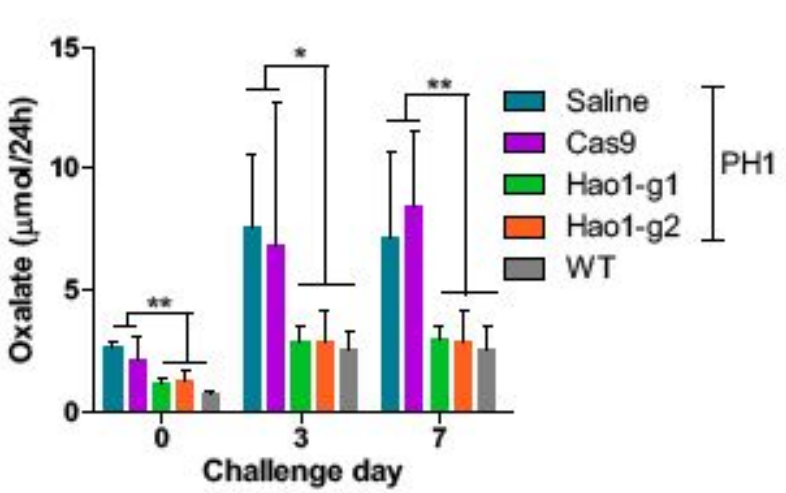
Table 4. Musculoskeletal adverse events in healthy volunteers

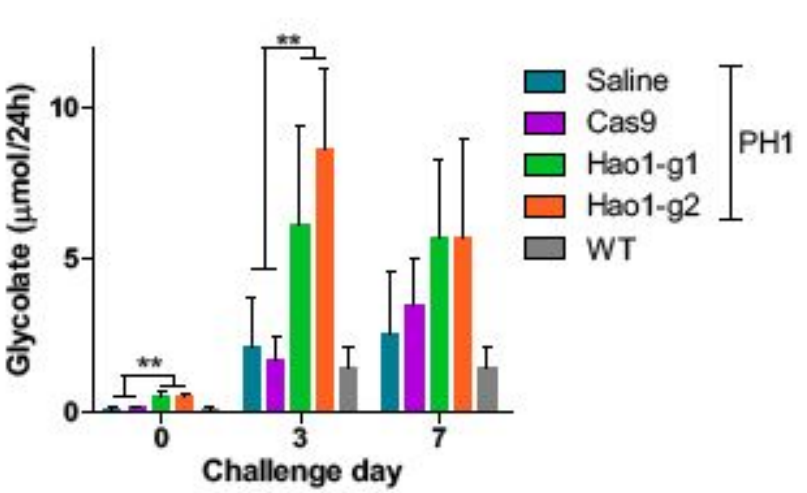
		Nedosiran, mg/kg					
System organ class and preferred term	Placebo ($N = 10$)	0.3 ($n = 3$)	1. 5 ($n = 3$)	3.0 ($n = 3$)	6.0 ($n = 3$)	12.0 ($n = 3$)	Overall ($n = 15$)
Participants with ≥1 TEAE, n (%), no. of TEAEs	3 (30.0), 4	0	0	1 (33.3), 1	2 (66.7), 3	1 (33.3), 2	4 (26.7), 6
Musculoskeletal and connective tissue disorders	0	0	0	0	1 (33.3), 1	1 (33.3), 1	2 (13.3), 2
Back pain	0	0	0	0	1 (33.3), 1	0	1 (6.7), 1
Myalgia	0	0	0	0	0	1 (33.3), 1	1 (6.7), 1

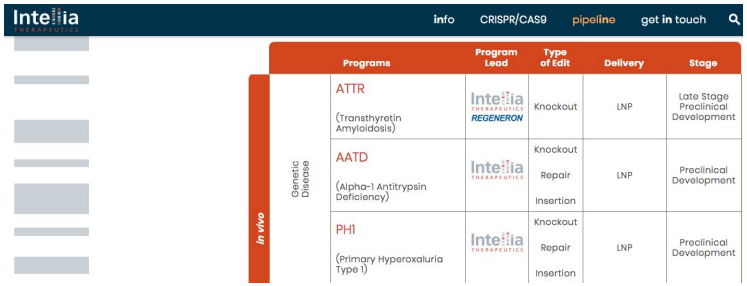
GO knock-out by *in vivo* CRISPR



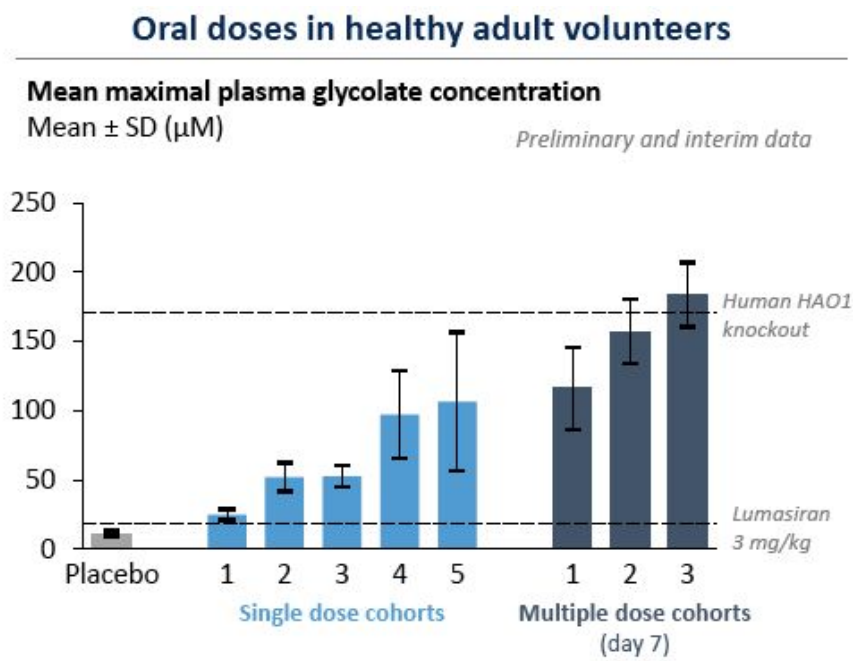








Glycolate Oxidase inhibitors

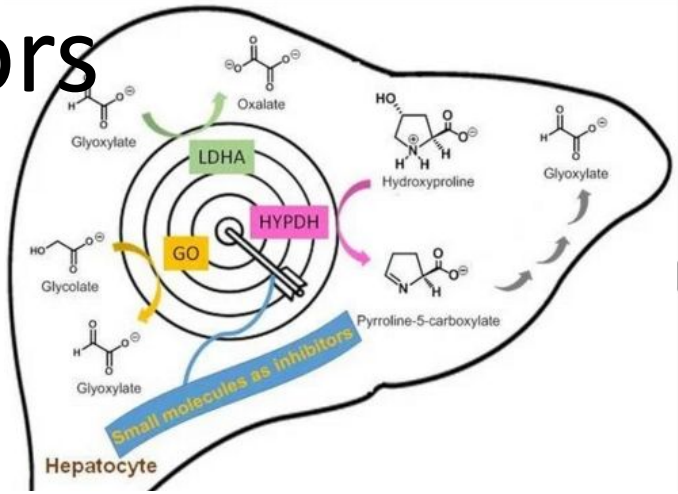


Well tolerated

- No safety signals of clinical concern
- All AEs were mild or moderate

Favorable PK/PD profile

- Potential to maximally inhibit GO with once-daily dosing
- Largest glycolate response observed to date by targeting GO



Review

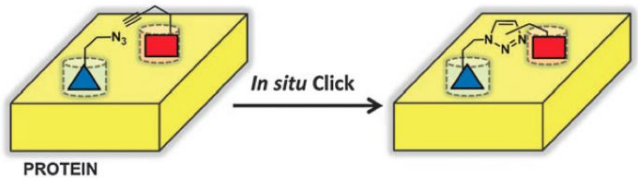
Small Molecule-Based Enzyme Inhibitors in the Treatment of Primary Hyperoxalurias

Maria Dolores Moya-Garzon [1,2,3], Jose Antonio Gomez-Vidal [1], Alfonso Alejo-Armijo [4], Joaquin Altarejos [4], Juan Roberto Rodriguez-Madoz [5,6], Miguel Xavier Fernandes [7], Eduardo Salido [8], Sofia Salido [4,*] and Monica Diaz-Gavilan [1,*]

bridgebio

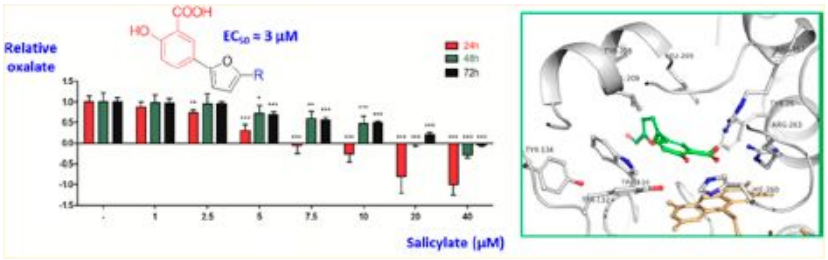
Orfan Biotech

Dr. M.Fernandes



Dra. M.Gavilan, Univ.Granada

Dra. S.Salido, Univ.Jaén



Salicylic Acid Derivatives Inhibit Oxalate Production in Mouse Hepatocytes with Primary Hyperoxaluria Type 1

María Dolores Moya-Garzón,[†,§] Cristina Martín Higueras,[‡,§] Pablo Peñalver,[†,∥] Manuela Romera,[†] Miguel X. Fernandes,[‡,⊥] Francisco Franco-Montalbán,[†] José A. Gómez-Vidal,[†] Eduardo Salido,[*,‡] and Mónica Díaz-Gavilán[*,†]