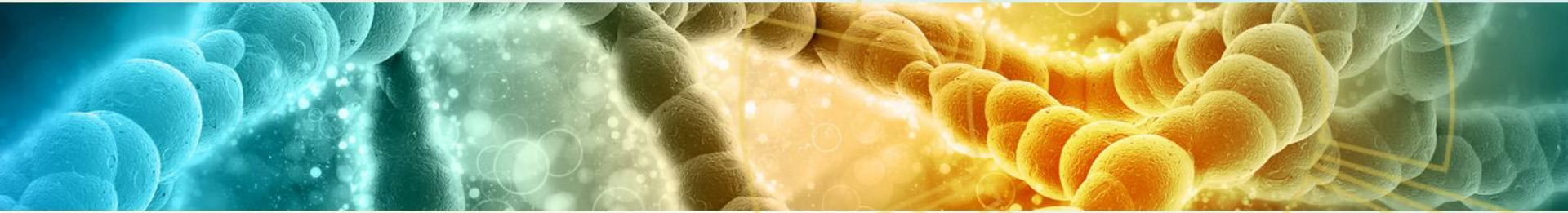


CENTRE DE REFERENCE DE LA MALADIE DE FABRY

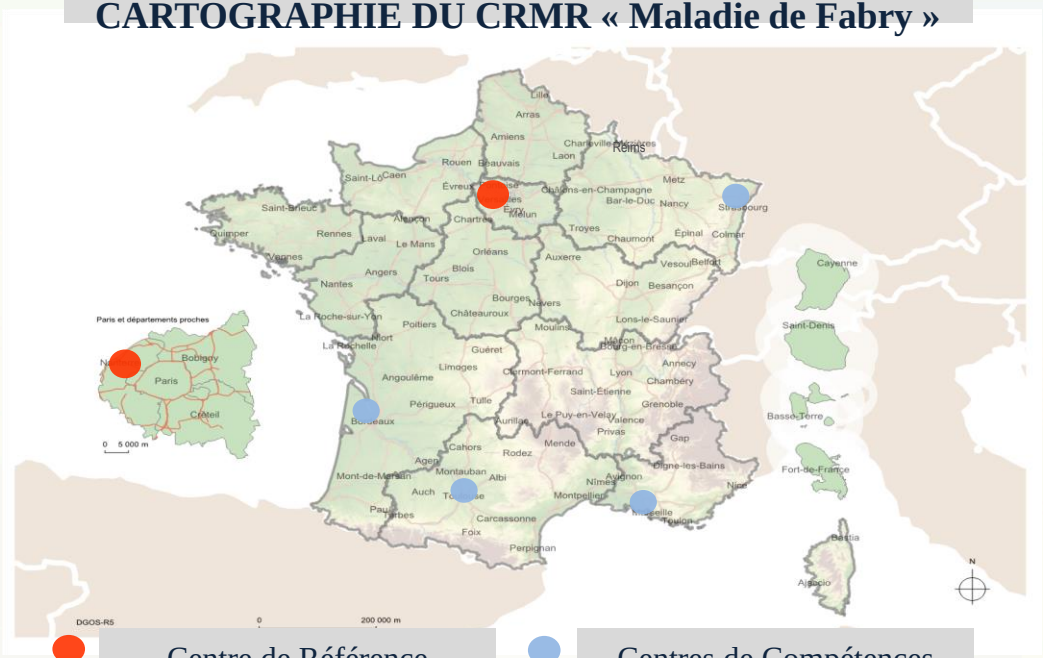
Prof. Dominique P. Germain, MD, PhD

Centre de Reference de la maladie de Fabry
Filière G2M (Prof. Pascale de Lonlay)
MetabERN

Journée Labellisation Filière G2M - Vendredi 18 Mars 2022

CARTOGRAPHIE

CARTOGRAPHIE DU CRMR « Maladie de Fabry »



Centre de Référence Coordonnateur

Centres de Compétences

PRESENTATION DE LA STRUCTURE

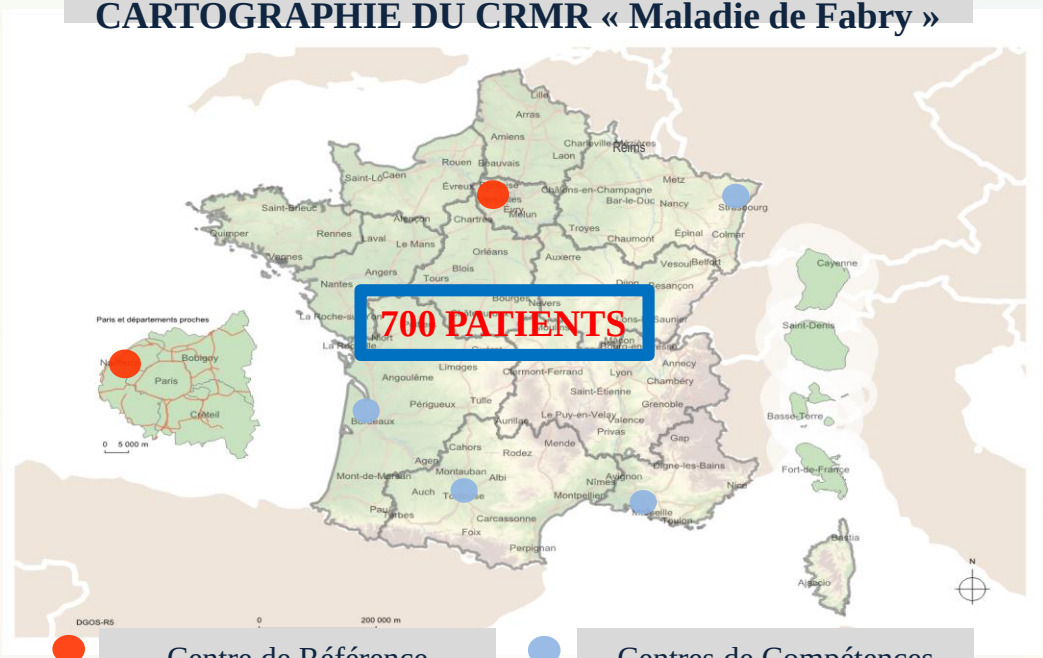
q17. Présentation de la structure

Centre de Référence de la maladie de Fabry
Centre de Référence Coordonnateur : Service de Génétique Médicale GHU Paris Saclay Raymond POINCARE (Assistance Publique - Hôpitaux de Paris) 104,Boulevard Raymond Poincaré 92380 Garches
en réseau avec 4 Centres de Compétences de Maladies Rares (CCMR)
- CCMR 1 Service de Génétique Médicale (Professeur Didier LACOMBE) CHRU de Bordeaux, 33000 Bordeaux
- CCMR 2 Service de Néphrologie (Professeur Bertrand DUSSOL) Assistance Publique – Hôpitaux de Marseille, 13000 Marseille
- CCMR 3 Service de Médecine Interne (Docteur Esther NOEL) CHRU de Strasbourg, 67000 Strasbourg
- CCMR 4 Service de Néphrologie pédiatrique - CHRU de Toulouse - coordonnateur en attente de confirmation, 31000 Toulouse

Association des Patients de la maladie de Fabry (APMF)

CARTOGRAPHIE

CARTOGRAPHIE DU CRMR « Maladie de Fabry »

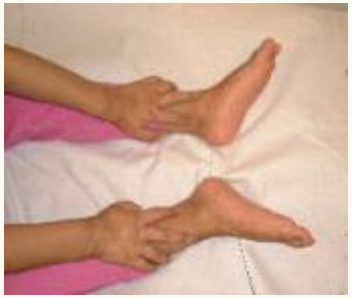


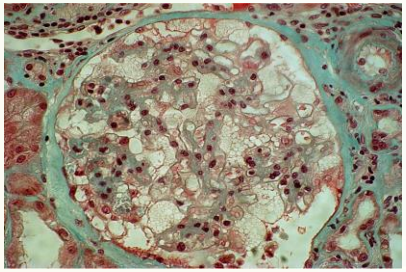
Centre de Référence Coordonnateur

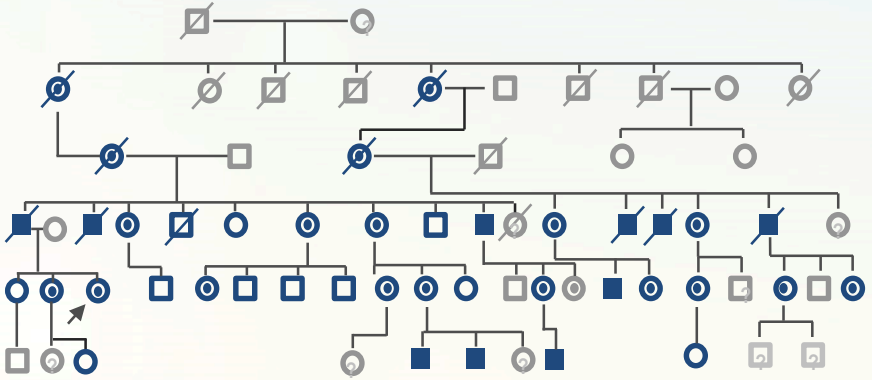
Centres de Compétences

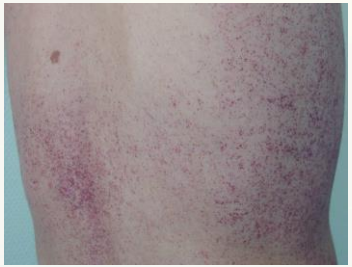
EPIDEMIOLOGIE

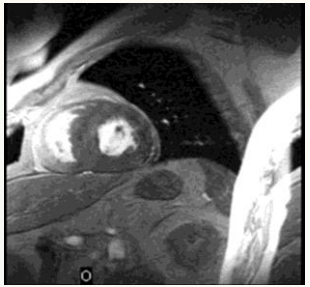
700 patients : Signes non spécifiques – Hérédité liée à l'X

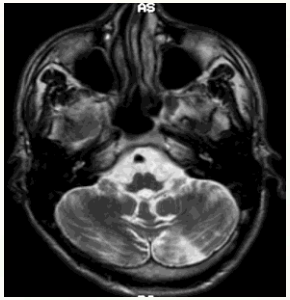


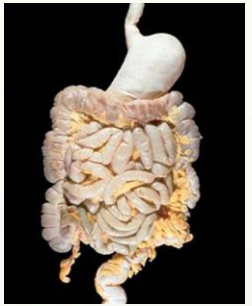












EPIDEMIOLOGIE

700 PATIENTS : VARIANT CARDIAQUE

1/8000

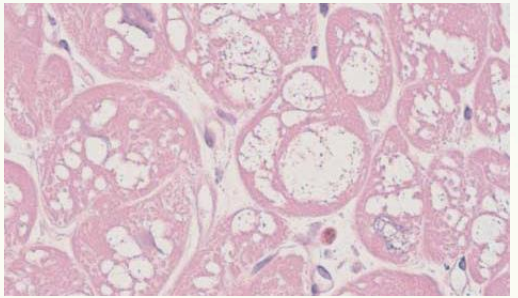
BRIEF REPORT

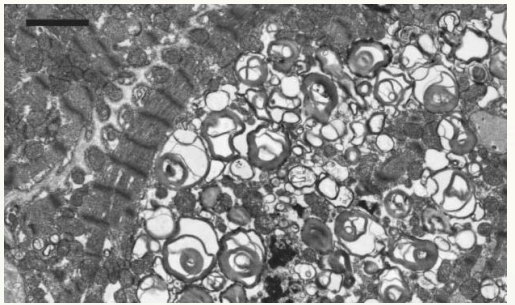
AN ATYPICAL VARIANT OF FABRY'S DISEASE WITH MANIFESTATIONS CONFINED TO THE MYOCARDIUM

WOLFGANG VON SCHEIDT, M.D.,
CHRISTINE M. ENG, M.D.,
THOMAS F. FITZMAURICE, M.S.,
ERLAND ERDMANN, M.D., GERHARD HÜBNER, M.D.,
ECKHARDT G.J. OLSEN, M.D.,
HELEN CHRISTOMANOU, M.D.,
REINHARD KANDOLF, M.D.,
DAVID F. BISHOP, PH.D.,
AND ROBERT J. DESNICK, PH.D., M.D.

manifestations result from slowly progressive myocardial infiltration. In contrast, men with atypical variants of the disorder, who have residual α-galactosidase A activity, are asymptomatic or have mild symptoms.[1,15-21] Heterozygous female carriers of the disease-causing gene usually have no symptoms or minimal disease involvement and have a normal life span.

We report a variant of Fabry's disease that is apparently limited to the myocardium. The patient had unexplained angina pectoris, normal coronary arteries and hemodynamic findings, and typical lysosomal inclusions in an endomyocardial-biopsy specimen, but none of the other pathological or clinical findings of





ACTIVITE

- HOPITAL DE JOUR: 250 – 500 / an
- *CONSULTATIONS MULTI-DISCIPLINAIRES: 250 / an*
- *MEDECINE PREDICTIVE - CONSEIL GENETIQUE*
- *ESSAIS CLINIQUES +++*
- *Orphanet : Fiches Maladies Rares - Orphanet : Handicap*

- *Site Web: www.centre-geneo.com*

ACTIVITES

HOPITAUX DE JOUR

Année	Séjours HJ prévus	Séjours HC réalisés	Ecart versus cible
2017	250	442	+117%
2018	342	358	+1%
2019	367	435	+22%

ACTIVITE

ACTIVITE

- BAMARA
- ETP FILIGRANE – APMF
- *RCP CRMR – CCMR MARSEILLE 2017/ 2018 / 2019 / 2022*
- *RCP CRMR – CCMR BORDEAUX 2017/ 2018 / 2019*
- *RCP CRMR – CCMR TOULOUSE 2017/ 2018 / 2019*
- *RCP CRMR – FUTUR CCMR NICE 2020 / 2021*
- *ASSOCIATION DE PATIENTS / Association des Patients de la maladie de Fabry / AIRG*

ACTIVITES INTERNATIONALES

- METABERN (Maurizio Scarpa)
- METABERN Lysosomal Subnetwork

- *CONSORTIUMS INTERNATIONAUX*
- *ANALYSE DES DONNES DES ENZYMOTHERAPIES*

- *DISCUSSION DE DOSSIERS, MAILS et AVIS*

LYSOSOMAL STORAGE DISEASE SUBNETW
MEETING, 3 NOVEMBER 2018

PNDS

Révision du PNDS de la maladie de Fabry

CRMR Paris
CCMR Bordeaux
CCMR Marseille
Futur CCMR Montpellier
CCMR Strasbourg
CRMR Maladie lysosomales (DCSS)
CRMR Maladies métaboliques (Lyon)

Centre de Référence de la Maladie de Fabry

www.centre-geneo.com

Protocole National de Diagnostic et de Soins (PNDS)

Maladie de Fabry

Novembre 2021

Le PNDS Maladie de Fabry est disponible sur le site de la filière G2M : http://www.filiere-g2m.fr/ et le site du Centre de Référence de la maladie de Fabry : http://www.centre-geneo.com

Groupe multidisciplinaire de rédaction

- Pr Dominique Germain, centre de référence de la maladie de Fabry, CHU Raymond-Poincaré, APHP
- Dr Oana Ailioaie, néphro-génétique, CHU Raymond-Poincaré, APHP
- Madame Najya Bedreddine, présidente, Association des patients de la maladie de Fabry
- Pr Soumeya Bekri, biochimie, CHU Rouen
- Dr Gérard Besson, neurologie, CHU Grenoble
- Dr Catherine Caillaud, biochimie et génétique moléculaire, CHU Necker
- Pr Jean-Nicolas Dacher, radiologie, CHU Rouen
- Dr Alain Fouilhoux, pédiatrie, CHU Lyon
- Dr Roselyne Garnotel, biochimie, CHU de Reims
- Pr Albert Hagège, cardiologie, HEGP, APHP
- Dr Fabien Labombarda, cardiologie, CHU de Caen
- Pr Didier Lacombe, génétique médicale, CHU Bordeaux
- Dr Vanessa Leguy-Seguin, médecine interne, CHU Dijon
- Dr Hélène Maillard, médecine interne, CHU Lille
- Dr Esther Noël, médecine interne, CHU de Strasbourg
- Dr Régine Perrichot, néphrologie, CH de Vannes
- Dr Jean-Pierre Rabès, biochimie et génétique moléculaire, CHU Ambroise Paré, APHP
- Dr Fernando Vetromille, néphrologie, CHU de Montpellier

roupe de relecture

- Dr Jean-Meidi Alilli, pharmacien, Filière G2M
- Madame Najya Bedreddine, présidente, Association des patients de la maladie de Fabry
- Dr Lavinia Bernea, néphrologie, Bucarest, Roumanie
- Dr Christine Broissand, pharmacie, CHU Necker, APHP
- Pr Robert Carlier, radiologie, CHU Raymond Poincaré, APHP
- Pr Gabriel Choukroun, néphrologie, CHU Amiens
- Pr François Feillet, pédiatrie, CHU Brabois, Vandœuvre-les-Nancy
- Dr Serge Fitoussi, médecine générale, Lagny sur Marne
- Pr Dominique Germain, centre de référence de la maladie de Fabry, CHU Raymond Poincaré, Garches
- Dr Thomas Ghafari, néphrologie, Institut Arnaud Tzanck, St Laurent du Var
- Pr Gilbert Habib, cardiologie, APHM
- Dr Olivier Lidove, médecine interne, GH Diaconesses Croix Saint-Simon, Paris
- Pr Ales Linhart, cardiologie, Université Charles, Prague, République Tchèque
- Dr Hélène Maillard, médecine interne, CHU Lille
- Dr Sabrina Vergnaud, biochimie, CHU Grenoble

GUIDELINES – RECOMMENDATIONS EUROPENNES

Participation aux “European Guidelines”

Biegstraaten *et al. Orphanet Journal of Rare Diseases* (2015) 10:36
DOI 10.1186/s13023-015-0253-6

ORPHANET JOURNAL OF RARE DISEASES

RESEARCH Open Access

Recommendations for initiation and cessation of enzyme replacement therapy in patients with Fabry disease: the European Fabry Working Group consensus document

Marieke Biegstraaten[1*], Reynir Arngrímsson[2], Frederic Barbey[3], Lut Boks[4], Franco Cecchi[5], Patrick B Deegan[6], Ulla Feldt-Rasmussen[7], Tarekegn Geberhiwot[8], Dominique P Germain[9], Chris Hendriksz[10], Derralynn A Hughes[11], Ilkka Kantola[12], Nesrin Karabul[13], Christine Lavery[4], Gabor E Linthorst[1], Atul Mehta[11], Erica van de Mheen[14], João P Oliveira[15], Rossella Parini[16], Uma Ramaswami[17], Michael Rudnicki[18], Andreas Serra[19], Claudia Sommer[20], Gere Sunder-Plassmann[21], Einar Svarstad[22], Annelies Sweeb[14], Wim Terryn[23], Anna Tylki-Szymanska[24], Camilla Tøndel[25], Bojan Vujkovac[26], Frank Weidemann[27], Frits A Wijburg[28], Peter Woolfson[29] and Carla EM Hollak[1]

Fabry disease revisited : Management and treatment recommendations for adult patients

Molecular Genetics and Metabolism 123 (2018) 416–427

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

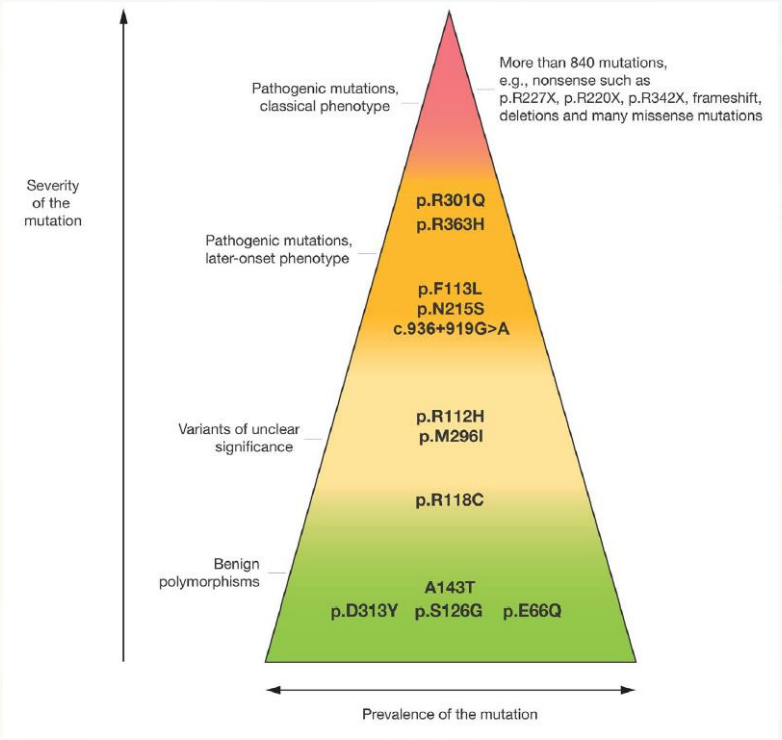
journal homepage: www.elsevier.com/locate/ymgme

Minireview

Fabry disease revisited: Management and treatment recommendations for adult patients

Alberto Ortiz[a,*], Dominique P. Germain[b], Robert J. Desnick[c], Juan Politei[d], Michael Mauer[e], Alessandro Burlina[f], Christine Eng[g], Robert J. Hopkin[h], Dawn Laney[i], Aleš Linhart[j], Stephen Waldek[k], Eric Wallace[l], Frank Weidemann[m], William R. Wilcox[i]

[a] Unidad de Dialisis, IIS-Fundacion Jimenez Diaz, School of Medicine, UAM, IRSIN and REDINREN, Madrid, Spain
[b] French Referral Center for Fabry disease, Division of Medical Genetics and INSERM U1179, University of Versailles, Paris-Saclay University, Montigny, France
[c] Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[d] Department of Neurology, Fundacion Para el Estudio de Enfermedades Neurometabolicas (FESEN), Buenos Aires, Argentina
[e] Departments of Pediatrics and Medicine, University of Minnesota, Minneapolis, MN, USA
[f] Neurological Unit, St Bassiano Hospital, Bassano del Grappa, Italy
[g] Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, USA
[h] Division of Human Genetics, Cincinnati Children's Hospital Medical Center, and Department of Pediatrics University of Cincinnati College of Medicine, Cincinnati, OH, USA
[i] Division of Medical Genetics, Department of Human Genetics, Emory University School of Medicine, Atlanta, GA, USA
[j] 2nd Department of Internal - Cardiovascular Medicine, First Medical Faculty, Charles University, Prague, Czech Republic
[k] School of Pharmacy, University of Sunderland, Sunderland, UK
[l] Department of Medicine, Division of Nephrology, University of Alabama at Birmingham, Birmingham, AL, USA
[m] Department of Internal Medicine, Katharinen-Hospital Unna, Unna, Germany



Ortiz A, Germain DP, Desnick RJ et al. Mol Genet Metab 2018

GUIDELINES - RECOMMENDATIONS

PEDIATRIE

Received: 7 January 2019 | Revised: 22 March 2019 | Accepted: 25 March 2019

DOI: 10.1111/cge.13546

ORIGINAL ARTICLE

CLINICAL GENETICS WILEY

Consensus recommendations for diagnosis, management and treatment of Fabry disease in paediatric patients

Dominique P. Germain[1] | Alain Fouilhoux[2] | Stéphane Decramer[3] | Marine Tardieu[4] | Pascal Pillet[5] | Marc Fila[6] | Serge Rivera[7] | Georges Deschênes[8] | Didier Lacombe[9]

CRMR Paris
CCMR Bordeaux
Futur CCMR Montpellier
CCMR Toulouse
CRMR Maladies métaboliques (Lyon)
CRMR Maladies métaboliques (Tours)

Fabry disease and COVID-19

ckj OXFORD era edta

Clinical Kidney Journal, 2020, vol. 13, no. 6, 913–925

doi: 10.1093/ckj/sfaa227
Original Article

ORIGINAL ARTICLE

Fabry disease and COVID-19: international expert recommendations for management based on real-world experience

Dawn A. Laney[1,*], Dominique P. Germain[2,*], João Paulo Oliveira[3,*], Alessandro P. Burlina[4], Gustavo Horacio Cabrera[5], Geu-Ru Hong[6], Robert J. Hopkin[7], Dau-Ming Niu[8], Mark Thomas[9], Hernán Trimarchi[10], William R. Wilcox[1], Juan Manuel Politei[11] and Alberto Ortiz[12]

[1]Division of Medical Genetics, Department of Human Genetics, Emory University School of Medicine, Atlanta, GA, USA, [2]Division of Medical Genetics, University of Versailles, AP-HP Paris Saclay University, Paris, France, [3]Centro Hospitalar Universitário de São João & Faculdade de Medicina da Universidade do Porto, Porto, Portugal, [4]Neurology Unit, St Bassiano Hospital, Bassano del Grappa, Italy, [5]Santa Maria de la Salud, San Isidro, Provincia de Buenos Aires, Argentina, [6]Department of Cardiology, Yonsei University Severance Hospital, Seoul, Korea, [7]Division of Human Genetics, Cincinnati Children's Hospital Medical Center, and Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH, USA, [8]Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan, [9]Department of Nephrology, Royal Perth Hospital, Perth, Australia, [10]Nephrology service, British Hospital, Buenos Aires, Argentina, [11]Department of Neurology, Fundacion Para el Estudio de Enfermedades Neurometabolicas (FESEN), Buenos Aires, Argentina and [12]Unidad de Dialisis, IIS-Fundacion Jimenez Diaz, School of Medicine, UAM, IRSIN and REDINREN, Madrid, Spain

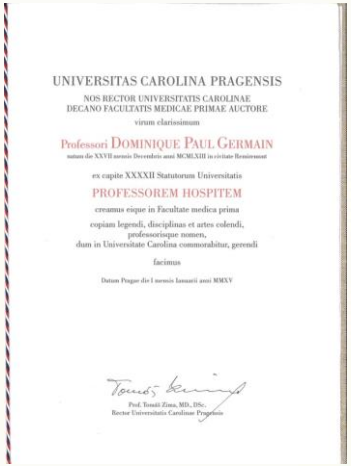
*These authors contributed equally to this work.
Correspondence to: Dawn A. Laney; E-mail: dawn.laney@emory.edu

ENSEIGNEMENTS – DIFFUSION des CONNAISSANCES

- *European Summer School on Fabry disease* (6 éditions: 2014 – 2019 – 7ème en 2022) : 100 participants
- New Horizons (2 éditions – 3ème en 2023)
- DIU Dysmorphologie (ANDDi-RARE) : maladie de Fabry
- DIU Maladies génétiques rénales rares : maladie de Fabry
- (DIU Médecine Personnalisée)
- Master CEDS : Coordonnateur d'Etudes Cliniques
- Master M2 "Conseillers en Génétique" – CCMR Marseille (Pr Karine N'GUYEN) CRMR coordonnateur

EUROPE et PAYS EN VOIE DE DEVELOPPEMENT

UNIVERSITÉ DE VERSAILLES ST-QUENTIN-EN-YVELINES


UNIVERSITAS CAROLINA PRAGENSIS

NOS RECTOR UNIVERSITATIS CAROLINAE
DECANO FACULTATIS MEDICAE PRIMAE AUCTORE
virum clarissimum

Professori DOMINIQUE PAUL GERMAIN

ex capite XXXXII Statutorum Universitatis

PROFESSOREM HOSPITEM

creamus eique in Facultate medica prima
copiam legendi, disciplinas et artes colendi,
professorisque nomen,
dum in Universitate Carolina commorabitur, gerendi
facimus

Prof. Tomáš Zima, MD., DSc.
Rector Universitatis Carolinae Pragensis


Kingdom of Cambodia
Nation Religion King

Certificate of Appointment

This is to appoint

Doctor Dominique Paul Germain

as an **Adjunct Professor** at the **University of Puthisastra**

Effective from January 15th, 2021 for a period of three years

Phnom Penh, January 15th, 2021

Professor Ian Findlay
President and Vice-Chancellor

Doctor Richard Hajbregts
Head of Health Sciences, Faculty of Health Sciences and Biotechnology


Kingdom of Cambodia
Nation Religion King

Certificate of Appointment

This is to appoint

Doctor Dominique Paul Germain

as an **Adjunct Professor** at the **University of Puthisastra**

Effective from February 24th, 2020 for a period of three years

Phnom Penh, February 24th, 2020

Professor Ian Findlay
President and Vice-Chancellor

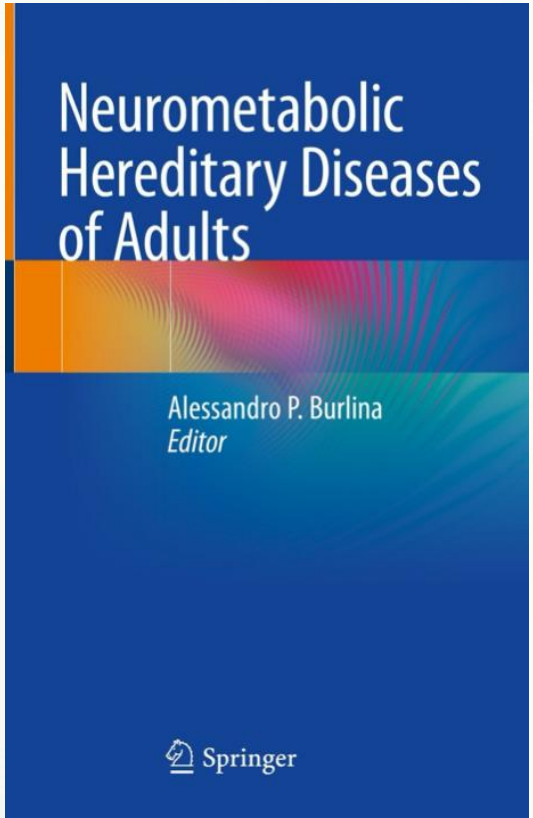
Doctor Sandro Vento
Dean, Faculty of Medicine

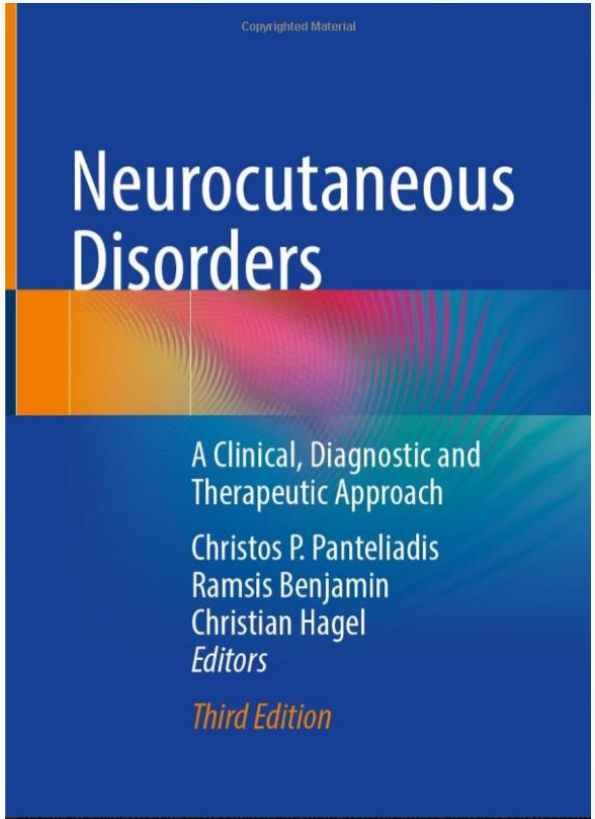
CRMR
Futur CCMR Montpellier

Cambodge, Vietnam, Taiwan

CHAPITRES DE LIVRES

Génétique de la Maladie de Fabry / Maladie de Fabry

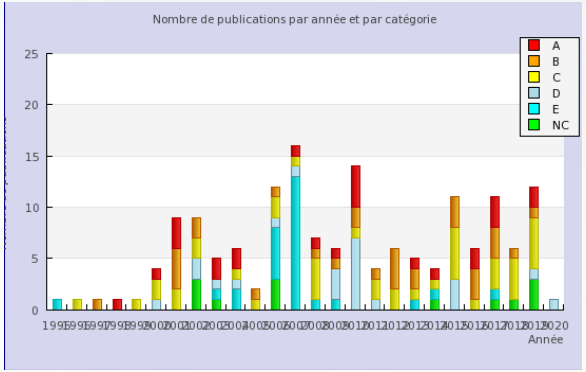


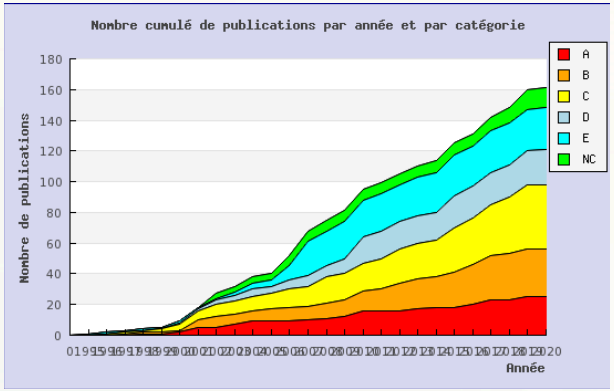


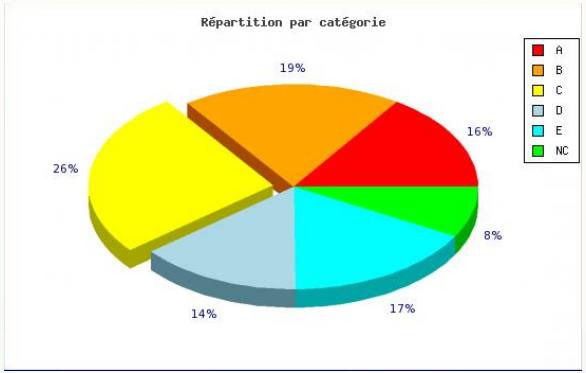
RECHERCHE CLINIQUE et FONDAMENTALE

SIGAPS : 605

2015	11	0	3	5	3	0	0	121
2016	6	2	3	1	0	0	0	80
2017	11	3	3	3	0	1	1	101
2018	6	0	1	4	0	0	1	47
2019	12	2	1	5	1	0	3	158



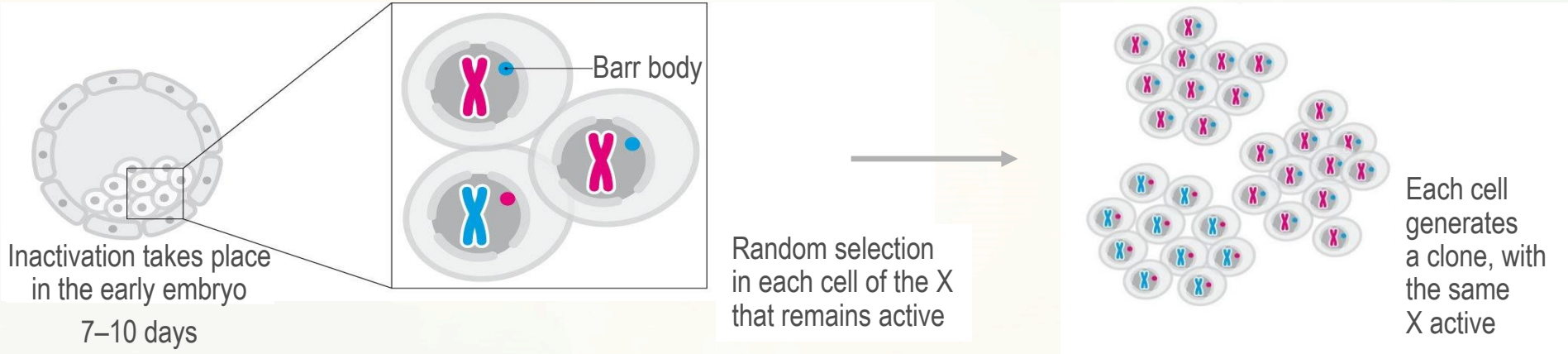




RECHERCHE FONDAMENTALE

Inactivation du chromosome X

Gene dosage compensation between eutherian mammalian females (XX) and males (XY)



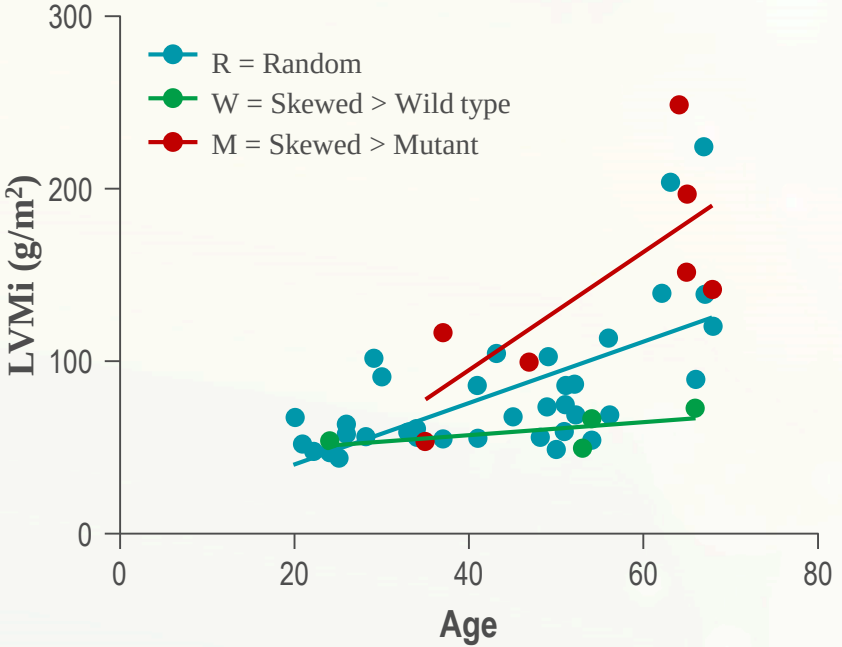
- Process leading to the **global transcriptional silencing** of the genes of an entire X chromosome
- Occurs randomly in each cell during early female embryogenesis
- Clonally inherited thereafter

Lyon, MF. Nature. 1961;190:372-3 .

RECHERCHE FONDAMENTALE

Inactivation du X chromosome

LVMi assessment with cardiac MRI



Clin Genet 2015
Printed in Singapore. All rights reserved

CLINICAL GENETICS
doi: 10.1111/cge.12613

Original Article

X-chromosome inactivation in female patients with Fabry disease

Echevarria L., Benistan K., Toussaint A., Dubourg O., Hagege A.A., Eladari D., Jabbour F., Beldjord C., De Mazancourt P., Germain D.P. X-chromosome inactivation in female patients with Fabry disease. Clin Genet 2015. © John Wiley & Sons A/S. Published by John Wiley & Sons Ltd, 2015

Fabry disease (FD) is an X-linked genetic disorder caused by the deficient activity of lysosomal α-galactosidase (α-gal). While males are usually severely affected, clinical presentation in female patients may be more variable ranging from asymptomatic to, occasionally, as severely affected as male patients. The aim of this study was to evaluate the existence of skewed X-chromosome inactivation (XCI) in females with FD, its concordance between tissues, and its contribution to the phenotype. Fifty-six females with FD were enrolled. Clinical and biological work-up included two global scores [Mainz Severity Score Index (MSSI) and DS3], cardiac magnetic resonance imaging, measured glomerular filtration rate, and measurement of α-gal activity. XCI was analyzed in four tissues using DNA methylation studies. Skewed XCI was found in 29% of the study population. A correlation was found in XCI patterns between blood and the other analyzed tissues although some punctual variability was detected. Significant differences in residual α-gal levels, severity scores, progression of cardiomyopathy and deterioration of kidney function, depending on the direction and degree of skewing of XCI were evidenced. XCI significantly impacts the phenotype and natural history of FD in females.

Conflict of interest

Nothing to declare.

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Key words: enzyme replacement therapy – Fabry disease – heterozygotes – phenotype – X-chromosome inactivation

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RECHERCHE FONDAMENTALE

GENETIQUE de *GLA*

Mutation Types	Number	% of Total
Missense (Classic, Later Onset, Benign)	556	61.4
Nonsense (Classic)	80	8.8
Splicing (Classic, Later Onset)		
Splice Site Consensus(Classic)	38	4.2
Cryptic (Classic, Later Onset)	5	0.6
Frameshift (Classic)	216	25
Small deletions	124	13.7
Large deletions	37	4.1
Small insertions	40	4.4
Small Indels	13	1.4
Large insertions/ Duplications	6	0.7
Complex rearrangements	7	0.8
Total Mutations	906	100

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REVIEW

CLINICAL GENETICS WILEY

Challenging the traditional approach for interpreting genetic variants: Lessons from Fabry disease

Dominique P. Germain[1,2] | Thierry Levade[3,4] | Eric Hachulla[5] | Bertrand Knebelmann[6] | Didier Lacombe[7,8] | Vanessa Leguy Seguin[9] | Karine Nguyen[10] | Esther Noël[11] | Jean-Pierre Rabès[2,12]

CRMR coordonnateur
CCMR Bordeaux
CCMR Marseille
CCMR Strasbourg
CCMR Toulouse
CRMR Maladies Métaboliques (Lille)

RECHERCHE CLINIQUE ACADEMIQUE

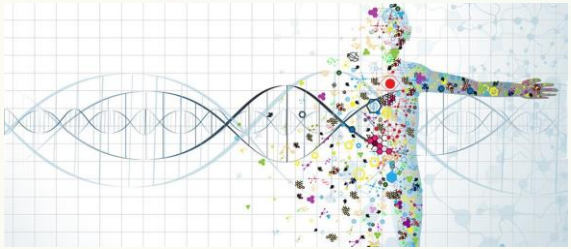
q734. Le cas échéant, veuillez indiquer leurs numéros d'inscription sur le registre ClinicalTrials.gov
NCT02450604 (DOUFABIS, CHU de Bordeaux) NCT 02843334 (FABRYDIAL, Hospices Civils de Lyon) NCT 02719249 (SNOUFY, CHU de Rennes)
Lister les numéros en les séparant par des ";"

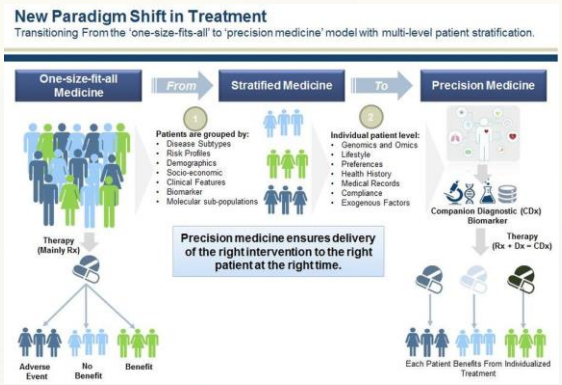
q735. Parmi l'ensemble de ces projets de recherche non-industriels (inscrits ou non dans le registre ClinicalTrials.gov), veuillez indiquer le nombre de projets pour lesquels le responsable ou un médecin du CRMR est investigateur principal	0

q2512. Lister les projets non-industriels (1 ligne par projet)
NCT02450604 (DOUFABIS, CHU de Bordeaux): prevalence of Fabry's Disease in a population of patients with chronic pain NCT02843334 (FABRYDIAL, Hospices Civils de Lyon): Study of the Prevalence of Fabry Disease in French Dialysis Patients NCT02719249 (SNOUFY, CHU de Rennes): : Fabry Disease Screening in ESRD Patients in West of France

PI : ESSAIS THERAPEUTIQUES

MEDECINE DE PRECISION





The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Treatment of Fabry's Disease with the Pharmacologic Chaperone Migalastat

D.P. Germain, D.A. Hughes, K. Nicholls, D.G. Bichet, R. Giugliani, W.R. Wilcox, C. Feliciani, S.P. Shankar, F. Ezgu, H. Amartino, D. Bratkovic, U. Feldt-Rasmussen, K. Nedd, U. Sharaf El Din, C.M. Lourenco, M. Banikazemi, J. Charrow, M. Dasouki, D. Finegold, P. Giraldo, O. Goker-Alpan, N. Longo, C.R. Scott, R. Torra, A. Tuffaha, A. Jovanovic, S. Waldek, S. Packman, E. Ludington, C. Viereck, J. Kirk, J. Yu, E. Benjamin, F. Johnson, D.J. Lockhart, N. Skuban, J. Castelli, J. Barth, C. Barlow, and R. Schiffmann


16 | ACTUALITÉS
C'EST POUR DEMAIN

INNOVATION PHARMACOLOGIQUE

Des chaperons pour une thérapie en 3D

Le Monde
PAYS :France
PAGE(S) :2
SURFACE :32 %
PÉRIODICITÉ :Quotidien
RUBRIQUE :Actualité
DIFFUSION :273111
JOURNALISTE :Florence Rosier
24 août 2016 - Science et Medecine

ACTUALITÉ

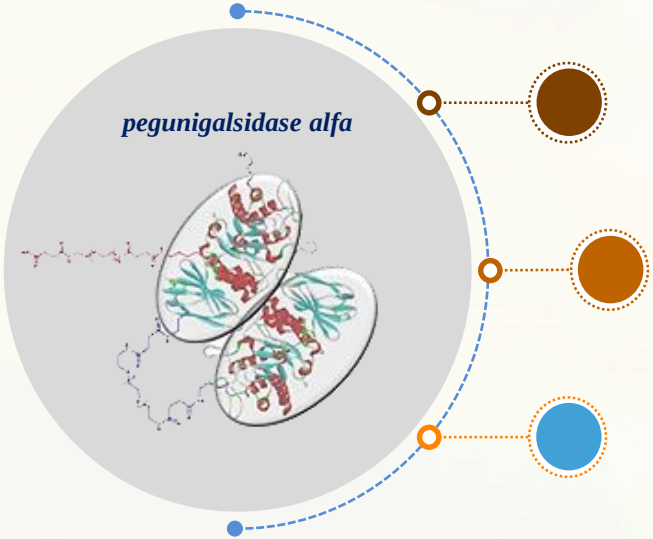
Un premier traitement « chaperon » autorisé en Europe

BALANCE clinical trial : PRX-102 (pegunigalsidase alfa)

PHASE 3	Design	Number of patients
balance	1 mg/kg 2-weeks *24 mos.* Head-to-Head vs. agalsidase beta in switch renal impaired patients switch renal impaired patients	78 100% Enrolled
bridge	1 mg/kg 2-weeks *12 mos.* Switch –over from agalsidase alfa in renal impaired & clinically stable patients stable patients	22 100% Enrolled
bright	2 mg/kg 4-weeks *12 mos.* Switch –over from agalsidase beta & agalsidase alfa in renal impaired & clinically stable patients patients	30 100% Enrolled

PRX-102 (pegunigalsidase alfa)

PEGylated covalently-linked homodimer composed of two subunits produced in plant cells



Mammalian Cell Production

- Slow product roll-out
- Risk of viral contamination
- Expensive stainless steel reactors / long timeline for capacity expansion
- Strict controlled environment
- High Initial investment (>$250m)

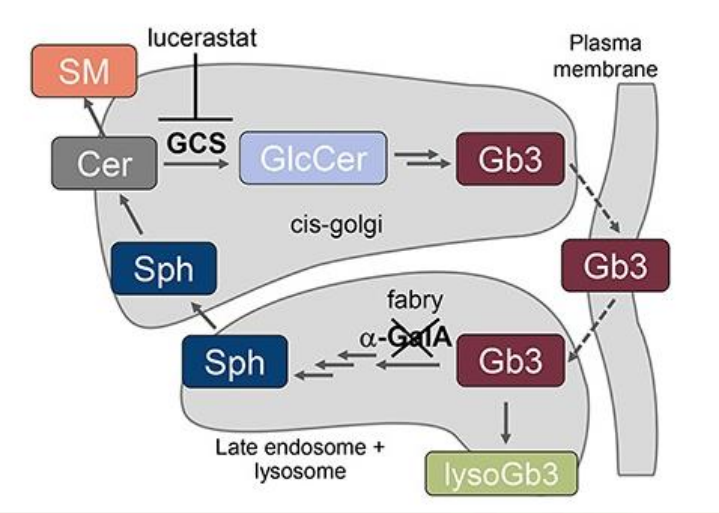
Plant Cell Production

- Rapid product roll-out and development
- No risk of viral contamination
- Flexible horizontal scale up in accordance with changing production needs
- Flexible infrastructure design allows for keeping equivalent volume in each added bioreactor during horizontal scale up
- Low Initial investment (>$20m)

Enzyme maintains its catalytic activity and translocation to the lysosome of target cells

Lucerastat

Key steps in the synthesis and degradation of Gb_3



α-GalA, α-galactosidaseA; Cer, ceramide; Gb3, globotriaosylceramide; GCS, glucosylceramide synthase; GlcCer, glucosylceramide; SM, sphingomyelin; Sph, sphingosine.

An oral iminosugar inhibitor of glucosylceramide synthase that reduce substrate

MODIFY – Phase 3, prospective, multicenter, double-blind, randomized, placebo-controlled, to determine the effect of lucerastat monotherapy on neuropathic pain in subjects with Fabry disease through daily collection of PRO with an electronic diary.

N=108, male or female FD patients with pain

Status: *Completed*

CARTOGRAPHIE

CARTOGRAPHIE DU CRMR « Maladie de Fabry »

Centre de Référence Coordonnateur

Centres de Compétences