Niemann-Pick disease

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in collaboration with
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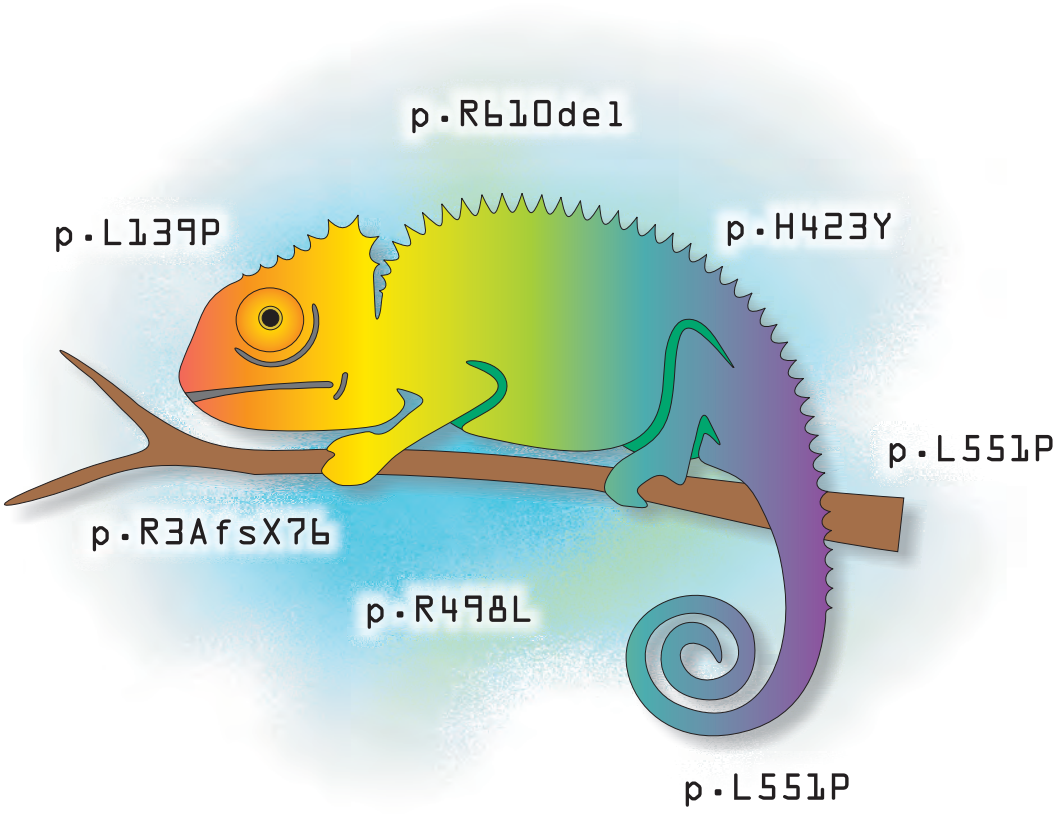

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Preface

It's been a few years since I visited Seville and especially the magnificent Casa de Pilatos from the 15th century in the old city center. The building represents a wonderful synthesis of Moorish and Spanish cultures. A Janus head can be found in the inner courtyard. The two faces look curiously, but also a little fearfully, in opposite directions. Niemann-Pick disease spontaneously came to my mind. The sculpture seems to be of one person, but the two faces represent two different identities. This is the exact association I have with Niemann-Pick disease. We have to distinguish the sphingomyelinase deficiency, Niemann-Pick disease type A & B, from the intracellular lipid transport defect, Niemann-Pick disease type C. This book presents these two entities as genetically and molecular-biologically distinct diseases, and for that reason, they will be discussed seperately in the following. The fact that the Janus faces look in opposite directions is a meaningful symbol that the different biology of the diseases also requires different therapeutic approaches. While the sphingomyelinase deficiency suggests the therapeutic principle of enzyme replacement, therapeutic substrate reduction must be considered in Niemann-Pick type C.

Families and patients, as well as their physicians, often ask me for an English-language edition of our book on Niemann-Pick disease. New findings in the field of basic research, a better understanding of clinical features, improved diagnostic options – especially to differentiate more easily between Niemann-Pick type C and sphingomyelinase deficiency (Niemann-Pick type A & B) –, and specific new therapeutic approaches are further arguments for creating such an edition. Prof. Michael Beck and I had already revised and updated the previous chapters for the second German-language edition that has just been published. At the suggestion of colleagues, we have added an additional chapter on "Diagnosis". This chapter in particular can be used as a quick reference work. The chapter shows which clinical symptoms corroborate a suspected diagnosis and how the diagnosis is confirmed in the laboratory.

This edition is especially dedicated to all patients with a Niemann-Pick disease and the active Niemann-Pick advocacy group.

This edition could be realized with the support of the company Gen-Orph. Thank you very much!

Hochheim, December 2021 *Eugen Mengel*

In addition, I dedicate this book to my chief, teacher, advisor, colleague, role model, comrade-in-arms, and friend Professor Michael Beck, who passed away too soon in September 2022.

Foreword

Eugen Mengel did his studies of medicine at Phillipps-University, Marburg, and Goethe-University in Frankfurt from October 1986 to September 1992. Since 1994, the medical practice has been conducted in the pediatric setting with infants, toddlers, school-age children, and adolescents and adults in some trials.

In 1994 Eugen Mengel joined the lysosomal storage disorders group named Villa metabolica of Michael Beck UMC Mainz. He was the responsible consultant for Gaucher and Niemann-Pick outpatient clinic since 1999 and later on Pompe. From 2001 to 2019 he assisted as consultant in pediatric inborn errors of metabolism in the Children´s Hospital, University of Mainz (Germany).

As sub investigator and deputy of Michael Beck he has worked on international multicenter trials for ERT in Fabry disease, Mannosidosis, Pompe disease, MPS II, MPS VI and MPS I and assisted the outpatient clinic for general metabolic, MPS, Gaucher, Niemann-Pick and Fabry patients. As principal investigator he has acted in international trials concerning NPC, ASMD, Pompe disease, Gaucher disease, LALD, Mannosidosis and Morquio disease. He has worked on biochemical diagnostic LSD laboratory from the beginning with extensive knowledge in the clinical and biochemical diagnostics of LSDs. In 2001 he received the certification for Investigator in clinical trials: KKSin Johannes-Gutenberg-Mainz. Since 2002 continuous activity as Principle Investigator in more than 25 studies according to AMG in the field of lysosomal diseases.

He has participated on student's education in pediatric hematological, oncological and metabolic diseases and given lectures about sphingolipidosis and MPS for students of medicine in biochemistry. He has been a colossal teacher, with a passionate love for medicine, metabolic diseases, and great affection for his students. One of its great virtues is his ability to synthesize and structure the most complicated ideas, concepts, and mechanisms. He makes what is difficult easy. He is a great communicator and a great teacher.

He is an active member of the SSIEM, ESGLD and EWGGD and also Board Member of several company Registries in Pompe disease (Sanofi Genzyme), Gaucher disease (Sanofi Genzyme) and Niemann-Pick type C (Actelion). As for the human side, he is an excellent person, of good character, kind and always willing to collaborate. His renowned reputation as a physician dedicated to metabolic diseases is adorned by his human qualities.

Since 2019 he is the Principle investigator, founder and CEO of the SphinCS GmbH & SphinCS Lyso nonprofit UG, independed institute of clinical science in LSDs.

Barcelona, June 2022 *Mercedes Pineda*

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