ECLip2019

4th ECLip International Meeting

7th International Symposium of Lipodystrophies

4 – 5 OCTOBER

Burgos, Spain

Book of Abstracts

ADELIP
Asociación Internacional de Familiares y Afectados de Lipodistrofias

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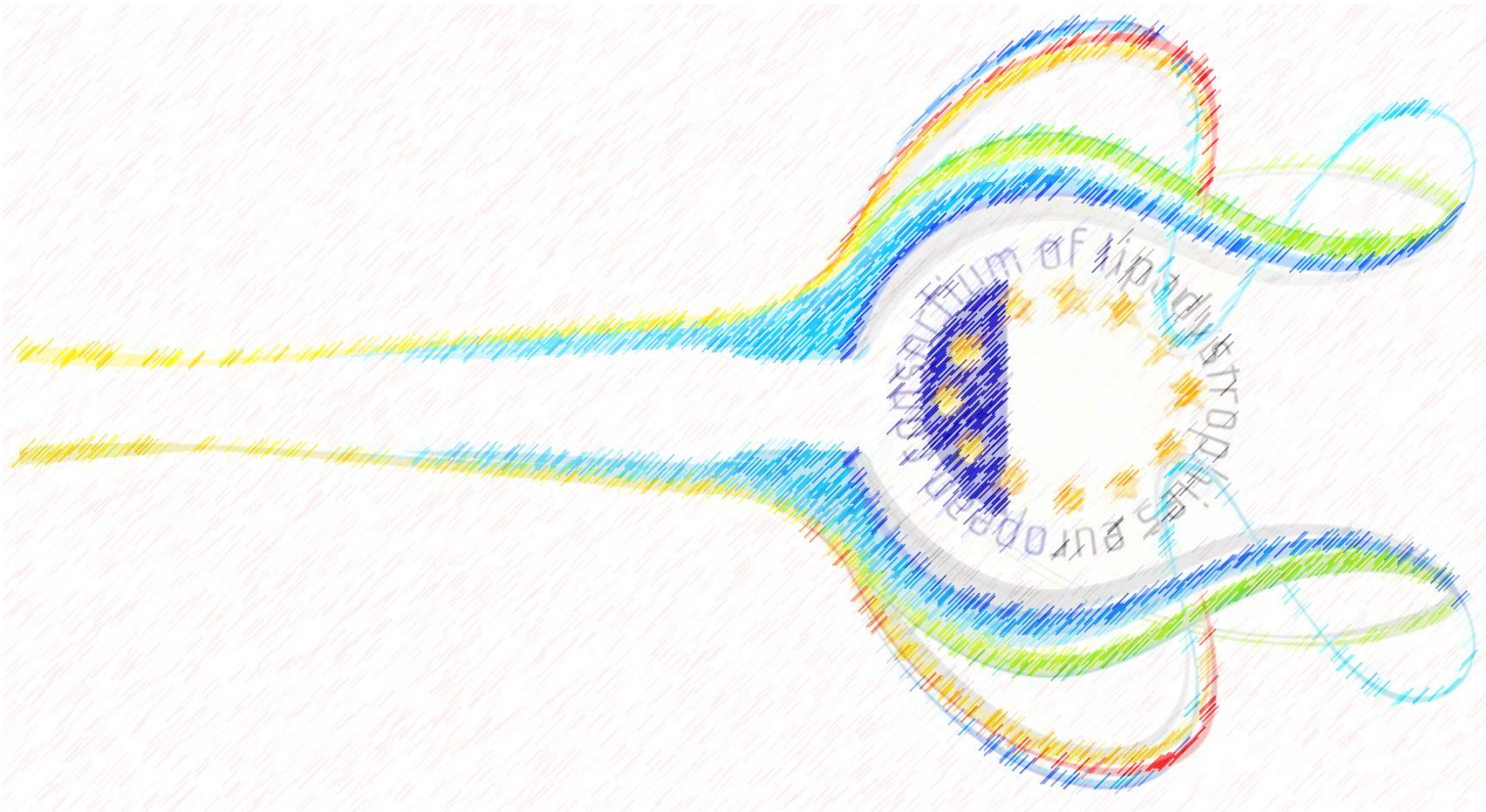

TABLE OF CONTENTS

Welcome to ECLip 2019 4
Committees 7
Support 8
ECLip 2019 Meeting Programme 9
VII Symposium of Lipodystrophies Programme 12
Plenary Speakers 13
Invited Talks 43
Authors index 78

WELCOME

Dear colleagues, patients and relatives,

Welcome to Burgos!

Once more, since ECLip was founded in Bologna in 2014, and since the foundation of AELIP in 2012, we meet to talk about lipodystrophies, share knowledge, and learn from each other. This year, for the first time, we have matched the ECLip meeting with that of AELIP in order to optimize resources, but, more importantly, to guarantee the possibility for physicians, scientists, patients and relatives to share a space and time in common. Whether the advances that have been made during this year in the research on lipodystrophies in relation to its causes, mechanisms, new treatments are of great relevance, it is probably more important to listen the patients themselves and their families about unmet needs and of the problems that they consider that scientists should try to solve.

We believe that we can be proud that year after year the number of participants in these meetings is increasing, incorporating groups, not only from other new European countries, but also from the US, Latin America, and Asia. And we are aware of the effort this entails, both for speakers and for assistants; an effort that is both economic and of agenda management. This, no doubt, is a sign of the interest that this field arouses, despite affecting only a small part of the population.

As every year we have tried to incorporate basic research talks on pathogenetic mechanisms, as well as cellular and animal models that will allow us to better understand the mechanisms that lead to the loss of adipose tissue and associated-comorbidities. We have also included talks focused on epidemiology, clinic and treatment. Especially relevant, we will present the latest results of the European Lipodystrophy Registry.

But this meeting is also the meeting of patients and their families. There is a specific program for them where different patient associations, from Europe and US, will be able to share their needs, establishing a way to optimize resources to efficiently disseminate information on lipodystrophies among the general population and policy makers. We have incorporated informative talks on genetics, immunology, dietetics, psychology, etc. in order to make understandable for the lay public crucial aspects in the field of the mechanisms that cause the disease, but also practical issues that will improve the quality of life of patients and reduce the impact of associated comorbidities.

We want to thank the CREER centre that has allowed us to hold this meeting in its excellent facilities and to our sponsors for financial support and understanding.

On behalf of Scientific and Organising Committee,

Prof. David Araújo-Vilar

WELCOME

Estimados todos,

Es una enorme satisfacción para mí, y en nombre de la asociación internacional que represento de familiares y afectados por lipodistrofias infrecuentes, "AELIP" darnos cita este año 2019, por primera vez, todos juntos, en este encuentro: y con la importancia que supone que el ECLip se desarrolle en la bella ciudad del gótico en España (Burgos), en CREER, un centro estatal para personas y entorno que participa en el abordaje de las enfermedades raras, y concretamente en nuestra cita con los afectados de las diferentes lipodistrofias

Además, con el más esperanzador de nuestros deseos y necesidades: ustedes con su labor en la investigación de estas patologías.

Creo que ya ustedes me conocen, quizás no todos, soy Naca; la mamá de Celia, diagnosticada a los 23 meses de edad, con lipodistrofia generalizada congénita Berardinelli-Seip, y que 7 años después, post-mortem recibió el diagnóstico final, "subtipo II del síndrome de Berardinelli "Encefalopatía de Celia", siendo posible este descubrimiento gracias a la participación de nuestra familia en la ejemplar dedicación a través de la INVESTIGACIÓN, en descubrir el origen de tan fatídica enfermedad, que con su cruel desarrollo, a través del sufrimiento e impotencia, sin posibilidades de esperanza, acabó con la vida de mi hija en marzo de 2012.

Les pongo en conocimiento para hacerles, una vez más, partícipes de mi vida, y de la de otras familias, que seguimos sintiéndonos agradecidos y esperanzados en conocer de primera mano su esfuerzo, dedicación y pasión por la ciencia, concretamente a través de la INVESTIGACIÓN.

Es un verdadero placer, después de varios años de intentos, e insistencia por mi parte (desde la organización del simposio anual que realiza AELIP desde 2013), que este año 2019 se cumpla mi deseo de reunirnos en un mismo centro, el evento más importante en el mundo de las lipodistrofias: el ECLip.

Sean bienvenidos a Burgos (España), desde nuestra humilde asociación (AELIP), y a lo que también se desarrollará en parte, después como encuentro de la unión de las personas afectadas con sus familiares, y las personas implicadas en el abordaje de estas patologías a través de la investigación en un futuro mejor para las familias afectadas por lipodistrofias.

Mi más sincera bienvenida y agradecimiento.

Naca Pérez de Tudela

Presidenta de AELIP

WELCOME

Dear all,

It is a huge satisfaction for me, and on behalf of the international association of relatives and affected by infrequent lipodystrophies, "AELIP", which I represent, to meet this year 2019, for the first time, all together, in this meeting. This year, the ECLip meeting is held in Burgos, one of the most beautiful gothic cities of Spain (Burgos), in CREER, the state centre for people with rare diseases, and specifically in our appointment with those people affected by the different lipodystrophies.

Moreover, with the most hopeful of our desires and needs: your work on the investigation of these pathologies.

I think you may already know me, maybe not everyone, I'm Naca; Celia's mother, diagnosed at 23 months of age, with congenital generalised lipodystrophy, and that 7 years later, received post-mortem the final diagnosis, "Celia's Encephalopathy", a subtype of type 2 CGL. This discovery was possible thanks to the participation of our family in the exemplary support of RESEARCH, enable the discovering of the origin of such a fatal disease, that with its cruel development, through suffering and impotence, without chances of hope, ended my daughter's life in March 2012.

I would like, once again, to make you participants of my life and that of other families; and that we continue to feel grateful and hopeful to know first-hand your efforts, dedication and passion for science, specifically through RESEARCH.

It is a real pleasure, after several years of attempts and insistence from my part (since the organization of the annual symposium held by AELIP since 2013), that this year 2019 fullfills my desire to meet in the same centre, the most important event in the world of lipodystrophies: ECLip.

From our humble association (AELIP), welcome to Burgos (Spain). You are also invited to attend to the meeting of the affected people with their families, as well as other people involved in addressing these pathologies, and that, through research, look for a better future for families affected by lipodystrophies.

My most sincere welcome and gratitude.

Naca Pérez de Tudela
President of AELIP

COMMITTEES

Scientific Committee

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David Araújo-Vilar. *University of Santiago de Compostela*

Vice-Chairman:

Sofía Sánchez-Iglesias. *University of Santiago de Compostela*

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Ekaterina Sorkina. *Endocrinology Research Centre Moscow*
Giovanna Lattanzi. *CNR-Unit of Bologna*

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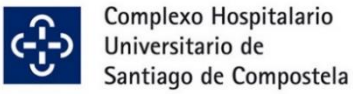
Sofía Sánchez-Iglesias. *University of Santiago de Compostela*

Organising Entities

SUPPORT & COLLABORATION



OCTOBER 4th, SCIENTIFIC SESSIONS

09:00	**Welcome**
	Prof. David Araújo Vilar, University of Santiago de Compostela, Spain Naca Pérez de Tudela, President of AELIP, Spain Juan Carrión, President of Spanish Federation of Rare Diseases Aitor Aparicio García, Director of CREER
09:20	**Epigenetic mechanisms in FPLD2**
	Prof. Philippe Collas, University of Oslo, Norway
09:40	**Human SGBS cells as in vitro model for studying cellular phenotype of defects in lipodystrophy genes**
	Prof. Martin Wabitsch, University of Ulm, Germany
10:00	**Differential expression of brown and white adipose tissue markers in FPLD2 adipocytes**
	Prof. Giovanna Lattanzi, CNR-Unit of Bologna, Italy
10:20	**Novel understandings in AGL unlock mysteries in the interaction between immune system and metabolic regulation**
	Prof. Elif A. Oral, University of Michigan, USA
10:40	**Detection and characterization of autoantibodies against perilipin 1 in patients with acquired generalized lipodystrophy**
	Dr. Fernando Corvillo, La Paz University Hospital, Madrid, Spain
11:00	**Coffee break**
11:30	**Molecular underpinnings of generalised lipodystrophies: studies of seipin and AGPAT2 function**
	Prof. Justin Rochford, University of Aberdeen, UK
11:50	**The mouse *BSCL2*$^{Celia/Celia}$: brain, liver and fat phenotype**
	Dr. Sofía Sánchez Iglesias, University of Santiago de Compostela, Spain
12:10	**Leptin restores brown adipose tissue thermogenesis in lipodystrophy potentially through improving bile acid homeostasis**
	Dr. Susan Kralisch-Jäcklein, University of Leipzig, Leipzig, Germany
12:30	**How is lipodystrophy linked to cardiometabolic disease: insights from SHORT syndrome**
	Prof. Robert Semple, University of Edinburgh, UK
12:50	**Lipodystrophy epidemiology in Spain: the experience of a nationwide reference centre**
	Dr. Antía Fernández Pombo, University of Santiago de Compostela, Spain

13:10	**The importance of European networking on lipodystrophy: the Hungarian experience**
	Dr. Éva Csajbók, University of Szeged, Hungary
13:30	**Metreleptin in Familial Partial Lipodystrophy: the Greek experience**
	Prof. Vaia Lambadiari, Athens University Medical School, Greece
14:00	**Lunch**
15:30	**Diagnostic challenge in FPLD4**
	Prof. Marie Christine Vantyghem, University of Lille, France / Dr. Isabelle Jéru, Sorbonne University, Paris, France
15:50	**Cardiovascular phenotypes in *LMNA*-linked lipodystrophy: implications for clinical practice**
	Prof. Corinne Vigouroux, Sorbonne University, Paris, France
16:10	**Generalized lipodystrophy associated with delayed neuro-somatic development and multiple dysmorphism in a neonate with a compound heterozygous missense mutation in the SYNE2 gene**
	Prof. Ferruccio Santini, University of Pisa, Italy
16:30	**Unsolved case with suspected lipohypotrophic syndrome**
	Dr. Deimante Brazdziunaite, Vilnius University, Lithuania
17:00	**Coffee break**
17:20	**Deep phenotyping reveals unusual presentations and emerging clinical phenotypes of lipodystrophy: lessons from observational registries and the LDLync study**
	Dr. Baris Akinci, Dokuz Eylul University, Izmir, Turkey / University of Michigan, USA
17:40	**Recent trials targeting hepatokines: what have we learned?**
	Prof. Elif A. Oral, University of Michigan, USA
18:00	**ECLip Lipodystrophy Registry**
	For Registry board members only
21:00	**Speakers' dinner**

OCTOBER 5th, SCIENTIFIC SESSIONS

09:00	**ECLip Lipodystrophy Registry: ongoing and future projects** *(for Registry members only)*
	Prof. Martin Wabitsch / Dr. Julia von Schnürbein, University of Ulm, Germany
09:40	**ECLip Lipodystrophy Registry: Presentation and first results**
	Prof. Martin Wabitsch / Dr. Julia von Schnürbein, University of Ulm, Germany
10:00	**LipoDDX®: a mobile application for identification of rare lipodystrophy syndromes**
	Prof. David Araújo Vilar, University of Santiago de Compostela, Spain
10:20	**Diet therapy in patients with lipodystrophy syndromes: perspectives and challenges**
	Dr. Yulia Tikhonovich, Endocrinology Research Centre, Moscow, Russia
10:40	**Leptin improves insulin sensitivity independent of food intake in patients with lipodystrophy**
	Dr. Rebecca J. Brown, National Institutes of Health, Bethesda, USA
11:00	**Coffee break**
11:20	**ECLip assembly** *(for ECLip members only)*
	Legal framework, Governing board election, ongoing and future projects
13:40	**The German and UK Lipodystrophy advocacy groups**
	Sabine Tilp, German Lipodystrophy Advocacy Group Rebecca Sanders, Lipodystrophy UK
14:00	**Final conclusions**
	Prof. David Araújo Vilar, University of Santiago de Compostela, Spain
14:30	**Lunch**

OCTOBER 4th

17:30	**Working meeting among representatives of international patient associations and delegations**

OCTOBER 5th

13:00	**Coordination Meeting for 2020 Lipodystrophy Day**
	Representatives of patient associations and delegations
14:30	**Lunch**
15:30	**Welcome to patients, relatives and entities working in the field of Lipodystrophies**
	Naca Eulalia Pérez de Tudela Cánovas, President of AELIP, Spain
15:45	**Mutual help groups, support networks to face the day to day**
	Manuel Illera Hernández, Psychologist of AELIP, Spain
16:15	**International cooperation project in Peru, International Network on Lipodystrophies**
	Juan Carrión, President of the Spanish Federation of Rare Diseases, Spain
16:45	**Immunological aspects of lipodystrophies**
	Prof. Margarita López Trascasa, Autonomous University of Madrid, IdiPAZ, Madrid, Spain
17:15	**Basic knowledges for laity people to understand genetic diseases**
	Prof. David Araújo Vilar, University of Santiago de Compostela, Spain
17:45	**Coffee break**
18:00	**Nutritional workshop: Diet and Lipodystrophies**
	Dr. María González Rodríguez, University Hospital Complex of Santiago de Compostela, Spain
18:45	**Self-care and personal image workshop**
	Maite Embid, Unidad de Maquillaje Terapéutico del Hospital Ramón y Cajal, Madrid, Spain
19:30	**Closure of the VII International Symposium of Lipodystrophies and group photo**
	Naca Eulalia Pérez de Tudela Cánovas, President of AELIP, Spain

Prof. Baris Akinci

Dokuz Eylul University School of Medicine, Izmir, Turkey
University of Michigan, USA

Dr. Baris Akinci received his M.D. degree from Ege University, Turkey. He completed his residency in Internal Medicine and his clinical fellowship in Endocrinology at Dokuz Eylul University. Dr. Akinci worked as a postdoc researcher under the supervision of Dr. Abhimanyu Garg at UT Southwestern, Dallas in 2011-2012. He traveled on a Fullbright scholarship to the University of Michigan in 2018 and worked under the supervision of Dr. Elif Oral. Dr. Akinci is the founder of the Turkish Lipodystrophy Study Group. His research focuses on the natural history of lipodystrophy, and the link to metabolic abnormalities, and end-organ complications. Dr. Akinci is a faculty member of the Division of Endocrinology at Dokuz Eylul University. He is currently working with Dr. Elif Oral at the University of Michigan.

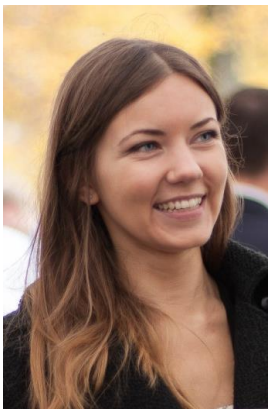
Prof. David Araújo-Vilar

CIMUS, University of Santiago de Compostela, Spain
University Hospital Complex of Santiago de Compostela, Spain

David Araújo-Vilar is an Associate Professor of Medicine at the School of Medicine in Santiago de Compostela, Spain, and a senior consultant in endocrinology and nutrition at the University Clinical Hospital of Santiago de Compostela. He earned his medical and doctorate degrees at the Universidad de Santiago de Compostela and completed postgraduate training at Oxford University in the United Kingdom and Galicia General Hospital in Spain. Dr. Araújo-Vilar's research focuses on the genetic basis of rare lipodystrophic syndromes and severe insulin resistance syndromes. He is the president of the Spanish Lipodystrophy Society and sits on the executive board of the European Consortium of Lipodystrophies.

Dr. Deimante Brazdziunaite

Vilnius University Hospital Santaros Klinikos, Lithuania



Clinical genetics resident in Vilnius University Hospital Santaros Klinikos, Centre for Medical Genetics, Vilnius, Lithuania. Graduated from Medical Faculty of Vilnius University in 2016. Areas of interest: rare, undiagnosed disorders, inborn errors of metabolism.

Prof. Rebecca J. Brown

National Institutes of Health, Bethesda, USA

Dr. Rebecca Brown graduated from Rice University and Mayo Medical School, and completed pediatric residency at Rainbow Babies and Children's Hospital. In 2005, she came to the National Institutes of Health for fellowship in pediatric endocrinology, and she has remained in the NIH intramural research program since that time. In 2015, she became the first Lasker tenure track investigator in NIDDK. Her research focuses on pathophysiology and clinical therapeutics for rare disorders of extreme insulin resistance, including lipodystrophy and dysfunction of the insulin receptor, as well as the mechanisms of action of leptin in improving metabolic disease.

Juan Carrión

Spanish Federation of Rare Diseases, Spain

Juan Carrión Tudela, Celia's father, the girl diagnosed with generalized congenital lipodystrophy, Berardinelli-Seip Syndrome - Subtype II, Celia Encephalopathy.

Social Worker of Penitentiary Institutions for 27 years.

He collaborates and participates with different health, social, cultural and sports associations.

At present, in the health field, he presides the Spanish Federation of Rare Diseases FEDER, the Foundation for research on rare diseases FEDER FOUNDATION, the Ibero-American Alliance of rare diseases ALIBER, the Association of Rare Diseases D'genes, and participates as Vice-President and director of the international association of relatives and affected by Lipodystrophy AELIP. Author of several books and publications related to rare diseases.

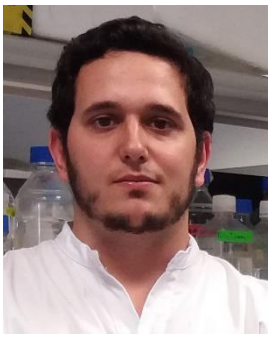
Prof. Philippe Collas

University of Oslo, Norway

Philippe Collas is Professor of medical biochemistry and Chair of the Department of Molecular Medicine at the University of Oslo. He is also member of the Norwegian Academy of Sciences and Letters. He got his undergraduate and Master's degrees from France, and his PhD from the University of Massachusetts in 1991, in the area of nuclear reprogramming. After two years in a US Biotech Company in Utah, he returned to academia as research scientist. In 1999 he established his lab at the Faculty of Medicine of the University of Oslo, where he became professor in 2003. His research focuses on chromatin-linked mechanisms driving adipose stem cell differentiation, and on how these go wrong in lipodystrophies caused by mutations in nuclear lamins. His lab has a particular interest in changes in the 3-dimensional lay out of the genome in these processes (www.collaslab.org).

Dr. Fernando Corvillo

La Paz University, Madrid, Spain



Fernando Corvillo is a postdoctoral researcher at the La Paz University Hospital Research Institute (IdiPAZ) in Madrid. Dr. Corvillo has degrees in Biology and has eventually earned his PhD in Molecular Biosciences form the Autonomous University of Madrid in 2018. His dissertation was primarily addressed to immunopathological mechanisms in acquired lipodystrophies. Dr. Corvillo has authored a recent paper where a novel autoantibody against the protein perilipin 1 has been described in patients with acquired generalized lipodystrophy. Dr. Corvillo also studies the role of the Complement System in the acquired partial lipodystrophy (Barraquer-Simons Syndrome).

Currently, Dr. Corvillo is the leader of a research project with the main objective to expand the knowledge of the pathogenic role of perilipin 1 autoantibodies in a largest cohort of patients with acquired generalized lipodystrophy. He received a research award from the Asociación Internacional de Familiares y Afectados de Lipodistrofias (AELIP) in 2017. He acted as the keynote speaker at the 41 National Congress of Spanish Society for Immunology in 2019.

Dr. Éva Csajbók

University of Szeged, Hungary

Dr. Éva Csajbók was born in Szeged, Hungary in 1970. After finishing a high school specialized for french language she was admitted to the Albert Szent-Györgyi Medical University, Szeged, Hungary where she received her undergraduate degree as a medical doctor (MD, summa cum laude, 1994). She joined the 1st Department of Internal Medicine of the same University. Two years later she completed her MA studies as medical economist at the József Attila University, Szeged, Hungary (cum laude,1996). After 5 years of training, she became a specialist in Internal Medicine (summa cum laude, 1999) and 3 years later a specialist in Endocrinology (summa cum laude, 2003) and Diabetologist of the Hungarian Diabetes Society (2006). She has special licenses in diabetology, hypertonology and obesitology (2014). She is a medical advisor for the Research Group for Cortical Microcircuits of the Hungarian Academy of Sciences. She recently defended her PhD thesis entitled: “Expression of insulin and GLP-1 receptors in interneurons of the cerebral cortex” (summa cum laude, 2019).

María Teresa Embid Pardo

Ramón y Cajal University Hospital, Madrid, Spain

Teresa Embid, Mayte for peers and colleagues, is a nurse who has been exercising her vocation in the Hospital Ramon y Cajal for over 40 years, always having the welfare of the patient as the engine of her actions.

First, since 1977, she developed her activity in the Service of Endocrinology and then in the Metabolic Unit of that same service.

Later, since 2007, she continued in the Day Hospital of the Dermatology service, where one year then she was entrusted with the implementation of the Therapeutic Make-up Workshop.

Today she maintains these two activities in the Day Hospital and the Makeup Workshop and makes them compatible with the occasional task of teaching courses in therapeutic make-up masters for dermatologists.

Dr. Antía Fernández-Pombo

CIMUS, University of Santiago de Compostela, Spain
University Hospital Complex of Santiago de Compostela, Spain

Graduate in Medicine and Surgery from the University of Santiago de Compostela (USC), Spain, 2015.

Master's degree in the field of Internal Medicine (2016): "Medical practice and professionalism" from the University of Alcalá (Madrid).

Specialist registrar in Endocrinology, Nutrition and Metabolism in the University Hospital of Santiago, Spain.

Fellowship in the Department of Endocrinology, in the University Hospital of Cambridge (Addenbrooke's Hospital, UK) in 2019.

Pre-doctoral researcher in the Unidade de Enfermidades Tiroideas e Metabólicas of the Centro de Investigación en Medicina Molecular y Enfermedades Crónicas (CiMUS), USC.

Dr. María González Rodríguez

University Hospital Complex of Santiago de Compostela, Spain

Degree in Human Nutrition and Dietetics from the University of the Basque Country. Bachelor's Degree in Food Science and Technology from the University of Vigo. Master in Nutrition from the University of Vigo. PhD in health sciences from the University of Santiago de Compostela in 2018.

Since 2007, I work as a dietitian-nutritionist in the Endocrinology and Nutrition Service of the University Hospital Complex of Santiago de Compostela, where I carry out, among other activities, the dietary advice of patients with obesity, as well as the education of patients with diabetes and nutritional assessment and follow-up of patients with head and neck cancer.

I have recently joined the research group of Dr. David Araújo Vilar and I have begun to collaborate with AELIP through the Dietary Counseling Service.

Manuel Illera Hernández

AELIP, Spain

Manuel Illera Hernández, is a psychologist and social educator who has been working for 33 years in treatment programs in prisons, in addition to combining his work with volunteering in different NGOs, helps social inclusion, anti-violence committee of the Football Federation of the Region of Murcia. In the last 10 years he has been a member of the AELIP family and of DGENES, as a psychology professional in their psychological support service in the Celia Carrión centre in Totana and in the Pilar Bernal centre in Murcia.

On the other hand, he also participates as a psychologist in the online care of various patients affected by lipodystrophy, providing a psychological support service both personal and systemic family, facilitating integration, therapeutic intervention and biopsychological and social improvement of users of the service.

His greatest contribution to AELIP has been and will continue to be his constant enthusiasm and passion for an objective: to improve the quality of psychosocial life of users.

Prof. Isabelle Jéru

Sorbonne University, Paris, France

Isabelle Jéru is an Associate Professor in Human Genetics in Sorbonne University in Paris (France). She has worked more than ten years on autoinflammatory diseases and is now involved in the study of lipodystrophic syndromes. She works in Saint-Antoine Hospital in a department performing routine genetic diagnosis of lipodystrophies. She teaches Genetics at the Medical School. She is also part of a research laboratory, in the subgroup headed by Corinne Vigouroux, which investigates the molecular and cellular bases of lipodystrophic syndromes.

Dr. Susan Kralisch-Jäcklein

University of Leipzig, Germany

Susan Kralisch-Jäcklein is a Postdoctoral research fellow in the research group of Professor Dr. M. Stumvoll, University of Leipzig, Medical Department, Division of Endocrinology and Diabetes, Germany. She earned her diploma and PhD degrees at Biochemistry, Faculty of Life Sciences, University of Leipzig. Dr. Kralisch is a basic scientific researcher and the focus of her research is the endocrinology of adipose tissue in obesity and lipodystrophy in particular the impact of adipokines on insulin sensitivity, lipid and glucose metabolism as well as vascular function. She is an active member of the Lipodystrophy Centre Leipzig.

Prof. Vaia Lambadiari

Athens University Medical School, Greece

Dr. Vaia Lambadiari is an Endocrinologist, Associate Professor of Internal Medicine and Clinical Diabetology in the 2nd Dpt. Of Medicine, Research Unit and Diabetes Centre, Attikon University Hospital, Athens University Medical School. Apart from Diabetes, she specializes in metabolism and obesity, and she has been trained in lipid disorders and lipodystrophies at the Oxford Centre of Diabetes, Endocrinology and Metabolism, Nuffield Dpt. of Medicine, Oxford, UK. In Attikon University Hospital her clinical assignment involves following patients from the whole spectrum of endocrinology, diabetes and metabolism, and she runs the Lipodystrophy outpatient clinic.

Prof. Giovanna Lattanzi

CNR-Unit of Bologna, Italy

I'm a Senior Researcher at the National Research Council of Italy (CNR). Since 2013, I'm the head of the CNR Institute of Molecular Genetics Unit of Bologna. My research activity is focused on cell biology of lamins and nuclear envelope proteins and pathogenetic mechanisms of lamin-related diseases (laminopathies), including type 2 Familial Partial Lipodystrophy, Emery-Dreifuss Muscular Dystrophy and Hutchinson-Gilford Progeria Syndrome. I published 80 peer reviewed papers in the field, participated in two European Projects on Laminopathies (FP6 Euro-Laminopathies and FP5 Myo-Cluster) and in two COST Actions (COST Action NanoNET 2012-2016 and COST Action EuroCellNet 2016-2020). My main research achievements are the involvement of prelamin A in pathological and physiological pathways and the identification of drugs able to rescue some pathogenetic mechanisms of laminopathies. I'm a partner of the European Consortium for Lipodystrophies (ECLip) and member of its executive board. In 2009 I founded the Italian Network for Laminopathies, which in 2019 counts 50 Italian clinical and research centers and currently I'm the Network coordinator. I organized several national and international meetings on Laminopathies. I published more than 110 scientific papers. My H index (Scopus) is 32.

Prof. Margarita López-Trascasa

Autonomous University of Madrid, Spain

I am an Immunologist with a large expertise in several fields like, the complement system and Immunopathology. I was starter and responsible of the Immunochemistry Section in Hospital La Paz in Madrid. In this hospital, I have developed clinical, research and teaching activities for longer than 30 years. Because of these activities, I have a large experience in the diagnosis and research in rare diseases as hereditary angioedema, complement deficiencies, acquired lipodystrophies and different renal pathologies as C3glomerulonephritis and atypical Hemolytic Uremic Syndrome. This experience was recognizing with the incorporation of my research group in CIBERER in 2008 (U754). I have published articles in scientific journals and I have more than 100 indexed articles in PubMED. I have academicals responsibilities at the Universidad Autónoma de Madrid, where I teach Immunology courses for undergraduate students in Medicine, Biology and Biochemistry. Moreover, along these years, 11 graduated students obtained their PhD under my supervision.

Prof. Elif A. Oral

University of Michigan, USA

Dr. Elif Arioglu Oral, M.D., is a Professor in the Division of Metabolism, Endocrinology and Diabetes (MEND) at the University of Michigan and a member of the American Society for Clinical Investigation (ASCI). She completed her medical education in her home country of Turkey at the University of Istanbul. In 1996, she completed her residency in Internal Medicine at Sinai Hospital of Detroit (Michigan). She then completed a Fellowship in Endocrinology, Metabolism and Diabetes at the National Institutes of Health, where she also chose to stay as a Senior Fellow under the mentorship of Drs. Simeon Taylor and Phillip Gorden in the Diabetes Branch of NIDDK. Since joining The University of Michigan in 2002 as an Assistant Professor of Medicine, along with her regular faculty responsibilities, Dr. Oral also completed a Masters of Science Degree in Clinical Research Design and Biostatistics at the School of Public Health. She got her tenure at Michigan in 2011. Dr. Oral's research focuses on the importance of adipocytes in human metabolism and adipocyte hormones such as leptin. She is best known for her work showing the efficacy of leptin in rare Lipodystrophy syndromes which is now an approved drug for treatment of lipodystrophy both in the US and in Europe. She is currently working on developing additional therapies and best treatment algorithms for various lipodystrophy syndromes and on improving the precision of clinical diagnosis. In addition to her roles as physician, educator, and researcher, Dr. Oral is also the director of three unique clinical programs in Michigan Medicine: Atypical Diabetes Program, Post Bariatric Surgery, Program and Obesity and Metabolic Disorders Program.

Naca Pérez de Tudela

AELIP, Spain

Mother of Celia, the girl born in 2004 and diagnosed with PELD (Celia's encephalopathy), an ultrarare and congenital autosomal recessive disease.

Founder and President of the D'genes Rare Disease Association from 2008 to 2014. Founder and president since 2012 of AELIP (International Association of Relatives and Affected of Lipodystrophies). Co-founder of ALIBER (Ibero-American Alliance of Rare or Rare Diseases) since 2013. She has participated in many social and health events on Rare Diseases. She has participated as a speaker in several congresses, symposiums and meetings of patients from different countries.

She mainly describes herself as willing to share experiences, information and knowledge about the field of rare diseases, in the positioning of those affected, of which she feels included for living together during the scarce 8 years of life of her daughter Celia.

She is especially a defender of the rights of patients and relatives, equity in the health services needed to live with this type of low incidence diseases and difficulty in diagnosis, which usually have no treatment.

She is a constant advocate of research, specifically rare diseases, as well as promoting the participation of health research in civil society.

In 2014 she received the medal of the order of civil merit from the King and Queen of Spain, for the always altruistic work of the aforementioned, and for continuing even more dedicatedly after Celia's death.

As a current profession Naca is a commercial agent of vorwerk España Thermomix since 2005.

Prof. Justin Rochford

University of Aberdeen, United Kingdom

Justin Rochford is a Reader in Metabolic Health at the Rowett Institute, and the Aberdeen Cardiovascular and Diabetes Centre, University of Aberdeen UK. He trained at Newcastle University, UK and INSERM U145 in Nice, France and previously led a research group at the Metabolic Research Laboratories at the University of Cambridge, UK.

Dr. Sofía Sánchez-Iglesias

CIMUS, University of Santiago de Compostela, Spain

Sofía Sánchez-Iglesias was born in Geneva (Switzerland) where she earned her Bachelor's degree in Biochemistry. She received her Ph.D. at the University of Santiago de Compostela (Spain). The incorporation in 2011 within the group of Prof. David Araújo-Vilar allowed her to get involved in new lines of research such as the molecular basis and clinical characterisation of familial lipodystrophies, and the PELD encephalopathy, a neurodegenerative disease associated with the *BSCL2* c.985C>T variant. Fruits of her research were 25 publications. She received also various grants and a research prize awarded by AELIP, and participated in several research projects. She is at present the lab and community manager of the UETeM.

Prof. Ferruccio Santini

University of Pisa, Italy

Dr. Ferruccio Santini leads the Obesity and Lipodistrophy Center at the University Hospital of Pisa. He graduated in medicine from Pisa University in 1985, where he continued his training to achieve his specialisation in Endocrinology in 1988. From 1990 to 1993 he was a researcher at the at the Division of Endocrinology, University of California Los Angeles, performing laboratory-based research on thyroid hormone metabolism. In 1996 he obtained his PhD in Endocrinological and Metabolic Sciences.

He is a clinical academic at the University of Pisa, as a Professor of Endocrinology, and leads specialist services for severe obesity at the University Hospital of Pisa – designated a Centre for Obesity Management by the European Association for the Study of Obesity. The research objectives focus on the pathophysiology of obesity and related comorbidities, and on the effects of pharmacological and surgical therapies.

Dr. Santini has published over one hundred and thirty articles in peer reviewed journals, related to his clinical and laboratory research interests in thyroid diseases, obesity and lipodystrophies. He is an Associate Editor of The Journal of Endocrinological Investigation, President of the Italian Society of Obesity, past Council Member of the Italian Society of Obesity Surgery and member of several scientific societies.

Prof. Hartmut H-J. Schmidt

University of Münster, Germany

Professor Dr. med. Hartmut H.-J. Schmidt is the director of the Department of Gastroenterology, Endocrinology, Infectious Diseases at the University Hospital in Münster. He graduated in medicine at the Medical University in Hannover 1982-1988 including two years of scientific research at the National Institutes of Healths in Bethesda, USA. He is specialized in Internal Medicine (1996), Gastroenterology (1997), Transplant Medicine (2011) and Infectious Diseases (2016). Doctorate in 1989, Habilitation in 1998. He received training as postdoc at the Medical University in Hannover 1988-1999 and at the Charité in Berlin 1999-2005 (C2-professor). C3-professor of Experimental Transplant Hepatology at the University Hospital Münster 2005-2010; 2010-2017 Director of the Clinic of Transplantation with the main focus on visceral organ transplantation, cell transplantation, hepatology, and amyloidosis research. Since 2017 director of the above mentioned department. In recognition of his work he received the Prevention Award of German Society of Internist Medicine in 1996 and 2001 and the Ludolph Brauer price of Northwest German Society of Gastroenterology in 1988.

Prof. Robert Semple

University of Edinburgh, United Kingdom

Prof. Semple is a clinician scientist based at the Centre for Cardiovascular Science at the University of Edinburgh. He is a Wellcome Trust Senior Research Fellow in Clinical Science, and Dean of Postgraduate Research at the University of Edinburgh. He trained first in Biochemistry and then in Medicine in Cambridge, where he undertook doctoral research in the laboratory of Prof. Sir Stephen O'Rahilly. Over the past 15 years his clinical and research interests have centred on the genetic basis of monogenic human disorders of growth and insulin action, focusing on the use of such rare human conditions to improve understanding of the nature of pandemic "insulin resistance", and of the mechanisms linking it to major disease, and on translating findings from the research laboratory into clinical benefits for patients. A major focus at present is on using human genetics to gain insights into the determinants of resilience of the adipose energy buffer across the lifespan.

Andra Stratton

Lipodystrophy United, USA

Andra Stratton is an advocate for the lipodystrophy community. She has led the efforts to increase awareness and support among patients for all types of lipodystrophy around the world since co-founding Lipodystrophy United in 2012. Andra works closely with lipodystrophy stakeholders and has been a key opinion leader and the patient voice in meetings and conferences with lipodystrophy experts in the United States and Europe. In addition to her work in Lipodystrophy, Andra is a recognized leader in the rare disease community and is frequently consulted on best practices in patient focused drug development initiatives. In addition to advocacy, Andra host for Rare In Common, a podcast featuring rare stories.

Dr. Yulia Tikhonovich

Endocrinology Research Centre, Moscow, Russia

I, Yulia Tikhonovich, have been involved in the medical sphere since university. I currently hold a PhD in Pediatric Endocrinology and constantly upgrade my existing knowledge and skills and develop new ones in my field. The fields of my scientific interest, in particular, are monogenic forms of diabetes mellitus, lipodystrophy in children and endocrine causes of neonatal hypoglycaemia.

My university degree and experience gained throughout the years have served as a strong basis for my current work. I hold a degree from the Far East Medical University in Khabarovsk where I graduated from in 2001. They were followed by clinical residencies in the pediatric department in the university and later on, in the National Endocrinology Research Centre. This has led me to my current position as a research assistant in the Department and Laboratory of Inherited Endocrine Disorders in the National Endocrinology Research Centre in Moscow.

Prof. Marie Christine Vantyghem

University of Lille, France

Prof. Marie-Christine Vantyghem, MD, PhD, received his specialty trainings in Endocrinology, Diabetology and Metabolism at the University of Lille, France. She has been involved in the diagnosis of lipodystrophic syndromes at Lille University Hospital, North of France, since 1990 on the clinical side, and on both clinical and genetic sides since 2000 with Prof Vigouroux, Paris France. MC Vantyghem is head of the Endocrinology Department of Lille University Hospital, which cares for a population of more than 4 million people in whom the prevalence of lipodystrophic syndromes seems especially high. In 2009, she obtained an interface contract with the INSERM Unit U1190, devoted to «Translational Research in Diabetes".

Her main research areas are islet transplantation and lipodystrophic syndromes with a large cohort of more than two hundred investigated patients. A biobank (plasmatheque, DNAtheque and adipose tissue bank) has been organised under the name project PHRC IL7 lipodystrophies supported by the French Ministry of Health (PHRC 2009; Clinical Trial Registration Number: Clin.gov2009-AO-1169-48).

Lille belongs to the ECLIP executive board and to the FIRENDO Reference centre of rare diseases of insulin secretion and insulin resistance (PRISIS), as a competence centre.

MC Vantyghem is a former member of the executive board of the French Endocrine Society, a current member of the European Society of Endocrinology, of the Endocrine Society, of the Société Francophone du Diabete, the French and European Societies of Transplantation and has been involved in two FP7 programs and in the CITR registry. She works as an Associate editor for the Annals of Endocrinology.

Prof. Corinne Vigouroux

Sorbonne University, Paris, France

Prof. Corinne Vigouroux is an endocrinologist and a molecular and cellular biologist working at Saint-Antoine University Hospital, Assistance-Publique Hôpitaux de Paris, France. She has been involved for many years in translational research on molecular biology, pathophysiology, diagnosis and patient care in the field of lipodystrophies and insulin resistance syndromes. She is the coordinator of the French National Reference network for “Rare Diseases of Insulin Sensitivity and Insulin Secretion” and the leader of the research group “Genetic Lipodystrophy” at Saint-Antoine Research Centre, Sorbonne Medical University, Paris.

Dr. Julia von Schnürbein

University of Ulm, Germany

Present position
Senior Consultant (Funktionsoberärztin) at the Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, University of Ulm

Scientific Scholarships
2015-2016/2018: Research-scholarship of the Hertha-Nathorff-Program
2006-2008: Scholarship of the Arbeitsgemeinschaft Pädiatrische Endokrinologie und Diabetologie (APE)

Scientific Positions
2017-present: Speaker of the working group obesity of the German Society for Pediatric Endocrinology and Diabetes together with Prof. Susanna Wiegand
2018-present: Board Member of the European Consortium of Lipodystrophies (ECLip) Registry

Prof. Martin Wabitsch

University of Ulm, Germany

Martin Wabitsch MD, PhD is Professor of Pediatrics, Head of the Division of Paediatric Endocrinology and Diabetes at Ulm's University Children's Hospital (www.uniklinik-ulm.de/pedu) and chair of the University's Centre for Rare Endocrine Diseases. His experimental research focus is the biology of the human adipocyte. His research group has established in vitro models for studying the biology of the human white and brown adipocyte including the human SGBS cell strain. Martin's clinical research focus comprises childhood obesity, the physiology of body weight regulation, leptin deficiency and rare lipodystrophy syndromes. He is a member of the ECLip registry board (www.eclip-web.org).

Deep phenotyping reveals unusual presentations and emerging clinical phenotypes of lipodystrophy: lessons from observational registries and the LD Lync study

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In my talk, I would like to present several lipodystrophy patients with unusual features and highlight the importance of patient registries under development. When the disease states are so heterogeneous, it is very important to collect as much information as possible from as many patients as possible. There are two multinational studies currently registering patients with lipodystrophy. The ECLip registry is recruiting patients mostly in Europe which will be discussed in details in this meeting. I would like to also summarize another effort to create a worldwide registry on lipodystrophy syndromes which is called LD Lync. This prospective international multicenter study targets to enroll a total of 500 patients with lipodystrophy at various clinical centers and collect longitudinal information. Besides, I will share some data from our national study group in Turkey.

LipoDDX®: a mobile application for identification of rare lipodystrophy syndromes

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Lipodystrophy syndromes are a group of disorders characterized by a loss of adipose tissue once other situations of nutritional deprivation or exacerbated catabolism have been ruled out. With the exception of the HIV-associated lipodystrophy, they have a very low prevalence, which together with their big phenotypic heterogeneity makes their identification difficult, even among specialists such as endocrinologists and pediatricians. This leads to significant delays in the diagnosis or misdiagnosis.

Based on our own experience as a reference center for lipodystrophies in Spain, the significant number of patients evaluated over more than 15 years, and a thorough study of the scientific literature, our group has developed an algorithm that identifies the more than 30 rare lipodystrophy subtypes described to date. This algorithm has been implemented in a free mobile application, LipoDDx®, developed in three programming languages, Typescript that compiles to Javascript, HTML5 and SCSS that compiles to CSS, and which is presented in versions for IOS and Android operating systems. The aim of our work was to establish the effectiveness of LipoDDx®.

Subjects and Methods: 40 clinical records of patients with a diagnosis of certainty of most lipodystrophy subtypes were analyzed, including subjects without lipodystrophy. The medical records, blinded for diagnosis, were evaluated by 15 doctors specialized in Endocrinology, Internal Medicine or Pediatrics, with no knowledge in the field of lipodystrophies. After reading the medical records, each physician had to give his/her results based on his/her own criteria, and afterwords he/she had to use LipoDDx®. The results were analyzed based on a score table according to the complexity of the case and its prevalence.

Results: Without using LipoDDx® the success rate was 17 ± 20% [range: 0-58%], while with LipoDDx® the success rate was 79 ± 20% ($p < 0.01$) [range: 60-100%].

LipoDDx® provides a user-friendly environment, based on usually dichotomous questions or choice of clinical signs from drop-down menus. The final result provided by this app for a particular case can be a low/high probability to suffer a particular lipodystrophy subtype, with links to OMIM and/or Orphanet, plus an updated bibliography. In addition, LipoDDx® presents a left side menu where information on European clinical reference centers in lipodystrophy and ECLip Lipodystrophy Registry is provided, as well as links to the websites of patients' advocacy groups.

Conclusions: LipoDDx® is a free app that allows to identify subtypes of rare lipodystrophies with around 80% effectiveness, which will undoubtedly be of help to doctors who are not experts in this field. The use of this app independently by other experts in lipodystrophies will certainly help to improve the algorithm in the future. LipoDDx® is available for free on Apple Store and Google Play.
(*Project financed with an intramural grant from the Xunta de Galicia, ED341b 2017/19, and with the support of the University of Santiago de Compostela, the Servicio Galego de Saude (SERGAS) and AELIP*).

Unsolved case with suspected lipohypotrophic syndrome

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Patient, 34-years-old male, referred to clinical geneticist complaining of increased sweating, palpitation, general weakness, headaches and mild dysphagia. In childhood he underwent cryptorchidism surgery and had 4 teeth removed due to irregular growth. Since the age of 21 years he is followed up by cardiologist due to Barlow disease, mitral valve and tricuspid valve prolapse, atrial septal aneurysm and bradycardia. On examination, patient was asthenic, body mass index – 15,4. He had progeria-like facial phenotype, bifid uvula, high-arched palate, transverse palmar crease on the left hand as well as large gap between I and II toes, and hypernasal voice. Brain MRI revealed craniocervical deformation with radiological signs of platybasia, narrow *foramen magnum* canal without compression and on cervical spine MRI degeneration signs were observed. Laboratory tests (glucose, electrolytes, TTH, troponin I, creatinine, creatine kinase) were normal as well as SNP-CGH result. Mandibuloacral dysplasia with type B lipodystrophy was suspected, based on phenotypic features, however, *ZMPESTE24* gene sequencing did not detect pathogenic variants and patient remains without confirmed diagnosis.

Leptin improves insulin sensitivity independent of food intake in patients with lipodystrophy

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Recombinant leptin ameliorates hyperphagia and metabolic abnormalities in leptin-deficient humans with lipodystrophy syndromes. Paired-feeding studies in rodents suggest that leptin improves glycemia independent of its effects on food intake. We aimed to determine whether leptin improves glucose and lipid metabolism in humans when food intake is held constant.

Patients with lipodystrophy syndromes were hospitalized for 19 days with food intake held constant by controlled diet in an inpatient metabolic ward. In a non-randomized cross-over design, previously leptin-treated patients (N=8) were continued on leptin for five days, and off leptin for the next 14 days (withdrawal cohort). This order was reversed in leptin-naïve patients (N=14; initiation cohort).

With food intake held constant, peripheral insulin sensitivity measured by hyperinsulinemic clamp was higher in the leptin-treated condition in both cohorts (41% in withdrawal cohort; 32% in initiation cohort). In the initiation cohort only, leptin decreased fasting glucose by 11%, triglycerides by 41%, increased hepatic insulin sensitivity, and decreased hepatic triglyceride from 21.8% to 18.7%. There was no change in intramyocellular triglyceride in either cohort. Improved insulin sensitivity correlated with lower hepatic triglyceride content.

Using lipodystrophy as a human model of leptin deficiency and replacement, we showed that leptin improves insulin sensitivity, and decreases hepatic and circulating triglycerides, independent of its effects on food intake. Improved insulin sensitivity with leptin may be mediated by reduced ectopic fat in the liver. Whether food intake independent effects of leptin are relevant in obese patients with leptin sufficiency remains to be determined.

International cooperation project in Peru, International Network on Lipodystrophies

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The President of Spanish Federation of Rare Diseases will present the experience of the International Association of Relatives and Affected by Lipodystrophy (AELIP) in relation to the International Cooperation Project in Peru carried out in 2018 and consisting of two main actions:

A study of social and health needs of people and families affected by Berardinelli-Seip syndrome in Piura (endemic area) and training sessions for health professionals in Peru.

The establishment of an International Lipodystrophy Network to enable an exchange of good practices between associations and organizations working in the field of lipodystrophy internationally with a clear objective: to work together to improve the quality of life of people and families living with lipodystrophy in the world.

Epigenetic mechanisms in FPLD2

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Mutations in the LMNA gene encoding A-type lamins cause partial lipodystrophies. We have investigated the effects of the lamin A p.R482W mutation causing FPLD2 on the epigenetics and 3-dimensional (3D) topology of the genome in patient cells and in FPLD2 model systems. The R482W mutation inhibits adipogenic differentiation of human preadipocytes by promoting overexpression of the anti-adipogenic microRNA gene MIR335 [1]. The mutation deregulates lamin A binding to the MIR335 locus, the epigenetic makeup of MIR335 enhancers, and MIR335 enhancer-promoter 3D interactions. Genome editing of the mutated LMNA gene in FPLD2 patient-derived pluripotent stem cells shows that the R482W mutation exacerbates endothelial gene expression by Polycomb deregulation of a key gene controlling mesodermal differentiation [2]. Finally, computational models of 3D genome structure predict aberrant associations of lamin A with chromatin in FPLD2 patient cells [3], and deregulation in the position of specific genes in the 3D nucleus space which can be related to gene expression defects [2]. We propose that the lamin A R482W mutation disrupts the fate of multiple developmental lineages through epigenetic and topological deregulations, resulting in multi-organ phenotypes. It will be interesting to determine the impact of the lamin A R482W mutation on changes in 4D genome conformation during adipogenesis [4].

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Detection and characterization of autoantibodies against perilipin 1 in patients with acquired generalized lipodystrophy

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Acquired generalized lipodystrophy (AGL) is a rare condition characterized by an altered distribution of adipose tissue and predisposition to develop hepatic steatosis and fibrosis, diabetes, and hypertriglyceridemia. Diagnosis of AGL is based on the observation of generalized fat loss, autoimmunity and lack of family history of lipodystrophy. The pathogenic mechanism of fat destruction remains unknown but evidences suggest an autoimmune origin. Anti-adipocyte antibodies have been previously reported in patients with AGL, although their involvement in the pathogenesis has been poorly studied and the autoantibody target/s remain/s to be identified.

Using a combination of immunochemical and cellular studies, we investigated the presence of anti-adipocyte autoantibodies in 10 patients with AGL, acquired partial lipodystrophy, localized lipoatrophy due to intradermic insulin injections or systemic lupus erythematosus. Moreover, the impact of anti-adipocyte autoantibodies from AGL patients was assessed in cultured mouse preadipocytes. Additionally, epitope mapping was performed using an ELISA assay.

We identified anti-perilipin 1 (PLIN1) IgG autoantibodies in the serum of 4 patients with autoimmune variety-AGL, but in no other lipodystrophies tested. These autoantibodies altered the ability of PLIN1 to regulate lipolysis in cultured preadipocytes causing abnormal, significantly elevated basal lipolysis. Our data provide strong support for the conclusion that PLIN1 autoantibodies are a cause of generalized lipodystrophy in these patients.

The studies of epitope mapping showed that anti-PLIN1 autoantibodies recognized a span length between the central region of the carboxi-terminal domain and the amino-terminal domain of the protein. More functional studies are required to characterize the exact mechanism triggering the adipose tissue abnormalities by the anti-PLIN1 autoantibodies.

The importance of European networking on lipodystrophy: the Hungarian experience

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A 42 years old female patient observed changes in her body composition and spontaneous hypoglycaemias since many years. Her medical history revealed temporarily elevated prolactin levels (800-900 mIU/L) treated with bromergocriptine, gestational diabetes mellitus (GDM) requiring high doses of insulin (i.e. total dose: >100 IU/day). She was first consulted by a neurologist due to suspicion of muscular dystrophy. In 2017, her total body fat was 8.8% (android: 17%, gynoid: 20%) with high muscle mass (32.5 kg) and a BMI of 20.5 kg/m^2. Her endocrine status revealed no alterations in the function of the pituitary nor in adrenals and thyroid. No alterations were found in hepatic nor in kidney functions, serum lipids and uric acid. Her fasting glucose was 5.4 mmol/l, HbA1c: 5.4% with normal C-peptide (3.2 ng/ml) and negative anti-GAD and anti-IA2. The long oral glucose tolerance test (OGTT, 75 g, 0, 30, 60, 120, 180 min) revealed hypoglycaemia 3 hours postload (serum glucose: 5.2,10.6, 12, 9.5, 7.5, 2.6 mmol/l, serum insulin: 22, 162, 189, 228, 21,3 mIU/l). The patient's physical appearance raised the question of acromegaly, however her hGH rythm was normal (8, 10, 13, 15, 17, 20 h: <0.05, 23 h: 0.12 ng/ ml) as well as her IGF1-levels (IGF-1: 126 ng/ml). Abdominal, chest and pituitary MRI, pancreas endosonography and somatostatine scintigraphy (mTc99, 900 MBq) were performed with negative results.

Her physical appearance suggested Dunningam syndrome. In Hungary the genetic testing for lipodystrophies is not available. The LMNA sequencing has been done in Santiago de Compostela having found the classical variant c.1444C>T (p.Arg482Trp) in heterozygosity.

Hereby I refer the first Hungarian patient with confirmed Dunningam syndrome. Since lipodystrophies are very rare conditions, the patient's case was instrumental in joining the European Consortium of Lipodystrophies (ECLip).

Self-care and personal image workshop

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Dermatological and oncological patients have a great variety of skin alterations that affect their daily life, among them lipodystrophies, changes in skin color, vitiligo, rosacea, melasma, discoid lupus, nebus, angiomas, burns or post-surgical scars. Two other types of patients are also treated in this workshop: people with gender identity disorders and eating disorders. It is known that 25% of dermatological patients suffer psychological alterations.

For these reasons, the Therapeutic Make-up Corrector Unit was set up, in which the following steps were taken correct and disguise these alterations. The makeup helps in the aesthetic plane favoring the interpersonal relationships and makes them assume the problem that affects them, even de-dramatizing it.

The patient is taught to do it by himself and, in a transversal way, he is given the following tools to increase their self-esteem and well-being, this being an important factor that helps to solve the problem.

The aim of this communication is to describe the care nurses of the make-up workshop and comment on the results obtained along its trajectory.

Lipodystrophy epidemiology in Spain: the experience of a nationwide reference centre

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Lipodystrophies comprise a group of heterogeneous disorders presenting with lack of body fat and, as a result, insulin resistance and metabolic disturbances. They can be acquired or genetic and, depending on the pattern of fat loss, partial or generalized. They are also considered to be very rare diseases. In fact, although the true prevalence of these disorders is unknown, it has recently been estimated to be 1.3–4.7 cases/million. Our research group (UETeM Lab; https://www.uetem.com) is a nationwide Reference Centre for the study and treatment of lipodystrophies in Spain, and receives patients from the whole country and abroad. The aim of this scientific session is to describe the main epidemiological features of the patients evaluated in our Unit in the last decade, without considering lipomatosis, HIV-related lipodystrophies and Köbberling syndrome (the genetic origin of which is unknown) according to the current classification of lipodystrophies in the 2016 Multi-Society Practice Guideline.

Thus, we handle 141 cases (25.5% male; 74.5% female) from 4 to 76 years old (average 39.41±19.61). Ninety-two (65.2%) patients present congenital lipodystrophy, 40 (28.4%) acquired and 9 (6.4%) systemic. Ninety-three percent of the patients are Spanish, coming from 12 different autonomous regions (36.9% Galicia, 14.2% Andalucía, 9.2% Asturias, 4.3% Canary Islands, 4.3% Castilla y León, 4.3% Madrid, 3.5% Catalonia, 3.5% Murcia, 2.1% Comunidad Valenciana, 1.4% Extremadura, 0.7% Melilla, 0.7% Balearic Islands). Seven percent of the remaining patients come from Saudi Arabia, Venezuela, Portugal, Colombia, Brazil, Morocco, Hungary, Romania, USA and Pakistan. The most frequent disease is Dunnigan disease (53.9%), followed by Barraquer-Simons syndrome (10.6%), and then by congenital type 2 generalized lipodystrophy (7.8%). The most frequently mutated gene is *LMNA* (56.7%) followed by *BSCL2* (7.8%). Moreover, there is more than one affected relative in 18 of the families studied.

Lipodystrophies are, unrecognized syndromes and are, therefore, underdiagnosed, probably because of a deficiency of information among clinicians. As it is important to have a greater knowledge of the main epidemiological features and natural history of these patients to increase awareness and funding, future research is needed to help to further refine the estimates.

Nutritional workshop: Diet and Lipodystrophies

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A diet is considered balanced when it allows to maintain an adequate state of health, while enabling the exercise required by each type of work. Moreover, it must meet the nutrients and energy requirements to ensure the proper organism function and development. Among the existing dietary patterns, it is worth mentioning the Mediterranean Diet that is associated with a lower cardiovascular risk, prevention of certain chronic diseases and some types of cancer. The features of this diet are the following: high consumption of vegetables, whole grains and cereals, legumes, fruit, nuts and fish, use of olive oil, moderate consumption of milk and dairy products and low intake of meat and processed meat products.

In order to know the energy and nutrient intake of an individual and to know if it complies with a healthy and balanced dietary pattern, it is necessary to previously know the food intake.

There are several methods to assess individual dietary intake. The most used are the following: dietary record (weighing food or weight estimation, 3-7 days), 24-hour food recall and food frequency questionnaire.

More specifically, the degree of adherence to the Mediterranean Diet pattern can be assessed by means of the Mediterranean Diet Test.

Mutual help groups, support networks to face the day to day

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When we talk about mutual help groups (*grupos de ayuda mutua, GAM*) we always find it difficult to specify that it is a help group, that it is a mutual support group, a therapeutic group, etc.

The definition of GAM is none other than a space in which several people who share the same problem or difficulty come together to try to overcome or improve their situation. It is born from this exchange of personal experiences, of giving and receiving.

In our case, we are people with the experience of rare disease, we are people with experiences in lipodystrophies.

The most important characteristics of a GAM are that people share experience and/or need, that there are values focused on people such as listening, respect, emotional support, tolerance. Understanding, etc. that form the basic nucleus for its functioning.

On the other hand, participation is voluntary and those who are part of a mutual aid group attend the meetings on their own initiative, the meetings are held periodically, the number of people involved is small and there are no differences in role or status between members.

Leptin restores brown adipose tissue thermogenesis in lipodystrophy potentially through improving bile acid homeostasis

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Aim: Lipodystrophy (LD) is a leptin-deficient state characterised by insulin resistance and dyslipidaemia. The aim of the present study was to assess brown adipose tissue (BAT) and liver physiology, as well as hepatic bile acids synthesis, in LD after chronic leptin treatment.

Methods: At 8 weeks of age, lipodystrophic aP2-nSREBP1c-Tg mice housed under room temperature (21 °C) were treated with murine recombinant leptin at physiological concentrations (3 mg/kg body weight/day) or vehicle for 6 weeks and metabolically characterised. Histological examination and gene expression analysis of browning markers in BAT and rate-limiting enzymes in the synthesis of bile acids in liver were then performed. Age-matched C57Bl6 mice served as non-LD controls.

Results: Core body temperature was significantly lower in 12 week old LD mice compared to non-LD controls ($p<0.01$) which was reversed by recombinant leptin treatment ($p<0.05$ compared to vehicle). Mean BAT and liver weight were significantly increased in the saline-treated LD group compared to non-LD controls ($p<0.0001$) and significantly decreased upon leptin treatment ($p<0.001$ compared to vehicle). Expression of the BAT markers *Ucp-1* and *Pgc1α* was significantly downregulated in BAT of LD mice compared to non-LD controls. More hypertrophic and fat-laden cells resembling immature white adipocytes were detected in BAT of LD animals as compared to non-LD controls and leptin treatment reversed this effect. Expression of the bile acid synthesis markers *Cyp7a1* and *Cyp7b1* was downregulated in liver of LD mice compared to non-LD controls and reversed in LD under leptin treatment. The cholesterol and triglyceride content of the liver was increased in LD mice compared to non-LD animals and restored in leptin treated LD mice.

Conclusion: Elevated hepatic synthesis of bile acids under leptin treatment in LD might influence the crosstalk between liver and BAT thereby correcting impaired thermoregulation.

Metreleptin in Familial Partial Lipodystrophy: the Greek experience

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During the last 5 years we have developed an outpatients' Lipodystrophy clinic within the Diabetes Center of Attikon University Hospital in Athens. We have been following a cohort of lipodystrophic patients with metabolic derangement of various degrees and some of them with known or new mutations. In one particular patient with extreme metabolic phenotype and misdiagnosed as type 1 diabetes, ie. uncontrolled diabetes and hypertension since early childhood, with high insulin requirements, hypertriglyceridaemia, NASH, and gradual total fat loss, generalized atherosclerosis, hypertrophic cardiomyopathy and nephropathy. We identified a PPARγ mutation in this particular patient and practically zero serum leptin levels. Metreleptin was then administered at an appropriate dose sc. Within 2 months the metabolic improvement was impressive, and liver and cardiac function is to be reassessed within a 4 months period. Apart from a slight appetite loss, metreleptin was very well tolerated.

Immunological aspects of lipodystrophies

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Lipodystrophies are heterogeneous disorders characterized by selective loss of body fat. Although many patients develop lipodystrophy due to genetic defects, where there are many involved genes, others develop it due to various acquired conditions.

In the acquired lipodystrophies, there are demonstrated implications of immunological mechanisms. The immune system, as a defense mechanism, is prepared to alert the body of aggressions and launch its own tools. There is an innate immunity very committed to the defense in the initial moments, when an individual is exposed to an agent that could harm him. This occurs in an infection by a bacterium, a virus, or a transformed own cell such as tumors. This response involves proteins such as those that integrate the complement system and certain cells such as e.g. the granulocytes.

Besides, the individual, throughout life will be able to store the information and has mechanisms to defend against pathogens with which he previously had contact. This memory mechanism is exerted either, through adaptive or acquired immunity, with cells such as lymphocytes or, molecules such as antibodies, which are called autoantibodies, when directed against own tissues or components.

In some of the lipodystrophies studied in our group, such as the case of acquired partial lipodystrophy (Barraquer-Simons syndrome), we have been able to observe that parameters of innate immunity, such as some components of the complement system (C3, Factor B), are altered. Moreover, we have verified the existence of autoantibodies against components of this system. All this indicates that both, innate and acquired immunity, are involved in this disease, although we do not know both the molecular processes that cause the disease, and the mechanisms by which adipose tissue is destroyed.

Regarding the generalized lipodystrophy acquired (Lawrence syndrome) we have also detected autoantibodies against a protein of the lipid gout and identified the antigen involved. These facts also lead us to deepen the origins and meaning of these autoantibodies.

Novel understandings in AGL unlock mysteries in the interaction between immune system and metabolic regulation

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Acquired generalized lipodystrophy (AGL) syndromes are a heterogeneous group of diseases characterized by selective dysfunction and loss of adipose tissue after birth. This causes ectopic lipid deposition and deficiency of the adipokine leptin, which promotes metabolic dysfunction through impaired glucose handling resulting in insulin-resistant diabetes mellitus, dyslipidemia and steatohepatitis. Many AGL cases are suspected to have an autoimmune etiology. Effector and regulatory T cells, dendritic cells and macrophages reside in normal adipose tissue. T cells within adipose tissue highly express PD-1 and regulatory T cells express CTLA4, which limits immune activation in the adipose tissue under normal circumstances. Thus, inhibition of these immune checkpoints may hypothetically cause immune activation, leading to adipocyte dysfunction and autoimmune destruction.

We initially encountered two cases that raise clinical concern for this process. Patient 1 was a 16-year-old female who diagnosed with both Type 1 diabetes and AGL. Along with other autoimmune diseases autoimmune enteropathy, autoimmune hepatitis, hemolytic anemia. thrombotic microangiopathy, nephrotic syndrome and progressive kidney insufficiency. Evaluation for her multi-faceted autoimmune presentation identified a familial heterozygous pathogenic variant in the *CTLA4* gene (c.4_5insGTTGG,p.Ala2GlyfsTer14). Family members had other autoimmune diseases, but not AGL. Despite aggressive immune therapies, including CTLA4-Ig (abatacept), her kidney disease and enteropathy have progressed. Patient 2 is a 55-year-old male diagnosed with metastatic melanoma who was treated with anti-PD-1 therapy with the humanized antibody drug pembrolizumab in April 2017 but discontinued the drug in February 2018 in the setting of toxicities including hypothyroidism. Subsequently, he developed up to 7.5% weight loss with progressive loss of subcutaneous fat first in his face, then generalized to the rest of his body. In the ensuing months, imaging with PET-CT demonstrated loss of subcutaneous fat concurrent with elevations in ALT and triglyceride levels plus a low leptin level consistent with AGL.

These cases made us evaluate our known AGL patients for genetic variants in known immunoregulatory genes and also our patients seen in the immunohematology clinic for metabolic and body composition aberrations. Both of these efforts have yielded numerous interesting insights that suggest that there are substantial metabolic and body composition changes noted in patients with

immune dysregulatory syndromes and the AGL cases potentially represent only a subset of more generalized preponderance to immune dysregulation. As a result of these observations, we suggest that disorders of immune dysregulation should be considered in the etiology of AGL. Patients and family of AGL probands should be closely studied for more generalized presence of autoimmune diseases. Similarly, patients with either genetic or pharmacologic inhibition of immune modulation should be monitored for the development of AGL which can be seen only in a small subset, but more generally for development of metabolic perturbations in glucose and lipid metabolism and body composition changes.

Recent trials targeting hepatokines: What have we learned?

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Partial lipodystrophy syndromes represent a heterogeneous cluster of diseases characterized by partial loss of subcutaneous fat with potential hypertrophy of residual depots. These diseases typically present with more severe metabolic derangements than typical truncal obesity associated Type 2 diabetes with far more insulin resistance, hepatic steatohepatitis and metabolic dyslipidemia. While many of these patients are not leptin deficient owing to the increased fat in residual depots, they still display severe hypertriglyceridemia with levels >500 mg/d, putting them at risk for recurrent pancreatitis. The overall conclusions of the partial lipodystrophy treatment experience in the US suggests that while there may be patients who benefit from leptin therapy among partial lipodystrophy patients, this therapy is likely not very effective in those patients with higher leptin levels. In addition, leptin therapy is not approved for treatment of partial lipodystrophy in the US while it may be an option for patients whose leptin levels are less than 12 ng/ml in Europe.

Given the lack of options and the underwhelming evidence of efficacy of leptin therapy in the majority of partial lipodystrophy patients in the US, we have recently sought additional therapies that may be of benefit in partial lipodystrophy. We first conducted a global placebo controlled double-blinded trial using an anti-sense ApoC3 inhibitor (Volenosorsen) for a period of 1 year. The top-line results announced in July 2019 suggest substantial efficacy of this drug over placebo in lowering triglycerides and hepatic steatosis. At the same time, we also completed two proof-of-concept open label studies using two additional drugs still targeting hepatic mediators of lipid metabolism. We will present the topline results of these two trials for the first time in this meeting.

These trials suggest that targeting hepatokine-mediated peripheral and lipid metabolism interaction points may provide value for treatment of metabolic pathology in partial lipodystrophy diseases. Understanding how these pathways are regulated in specific subtypes of partial lipodystrophy may allow a more personalized approach for metabolic therapy.

Generalized lipodystrophy associated with delayed neuro-somatic development and multiple dysmorphism in a neonate with a compound heterozygous missense mutation in the SYNE2 gene

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Generalized lipodystrophies are extremely rare diseases. Despite remarkable progress in identifying genes responsible for the most common forms of genetic lipodystrophies, the molecular basis of disease in some patients with distinctive phenotypes remains unclear.

We herein describe the case of a male patient born from non-consanguineous parents and affected by a syndrome characterized by generalized lipodystrophy, psycho-somatic growth retardation, cleft palate, macroglossia, right cryptorchidism, fingers with extended base and short femurs. In the third month of life, an abnormally increased appetite, the lack of weight growth and the dystrophic appearance became very evident. Moreover, the ultrasound analysis revealed hepatic steatosis and blood test showed high triglyceride values (up to 1577 mg/dl), low serum leptin levels (0.1 ng/ml). Based on patient's clinical features, instrumental and laboratory results, Berardinelli-Seip syndrome was initially hypothesized. The entire coding region of candidate genes involved in congenital generalized lipodystrophy (BSCL1, AGPAT2, CAV1, PTRF) and other forms of lipodystrophy (LMNA) were sequenced by Sanger method but no mutations were found. To have a better insight on the possible genetic alterations causing the disease, we performed exome sequencing using Illumina NextSeq500. After data filtering and segregation analysis, we identified compound heterozygous missense variants in the spectrin repeat containing nuclear envelope protein 2 gene (SYNE2): c.18632C> T (p.T89M) and c.20410G> A (p.D326N). The first genetic variant is shared with the father, the second one with the mother. The mutation p.T89M is classified as pathogenetic for Emery-Dreyfuss muscular dystrophy (EDMD) in ClinVar Database, and it was previously reported in two families with EDMD.

In conclusion we describe a likely novel syndrome characterized by generalized lipodystrophy, severe delayed psycho somatic development and multiple dysmorphism, possibly related to a compound heterozygous missense mutation in the SYNE2 gene.

Molecular underpinnings of 63isorganize lipodystrophies: Studies of seipin and AGPAT2 function

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The study of genes causing syndromes of lipodystrophy can reveal potential novel therapeutic avenues for the treatment of these rare diseases as well as fundamental insights regarding adipose tissue development and function. Disruption of the gene *BSCL2*, encoding the protein seipin, causes severe 63isorganize lipodystrophy. We have investigated the molecular functions of seipin in order to understand more fully how the loss of this protein causes a near complete absence of adipose tissue in affected individuals. This has included investigating an interaction between seipin and AGPAT2, whose disruption also causes 63isorganize lipodystrophy. We have also studied *in vivo* models of seipin disruption, which have revealed new insights regarding the physiological effects of seipin loss as well as uncovering new information about the development of different adipose depots and their influence on metabolic health.

The mouse BSCL2$^{Celia/Celia}$: brain, liver and fat phenotype

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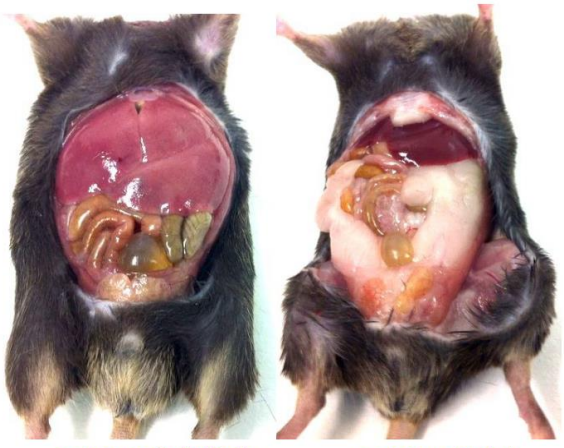
In our attempt to deepen the molecular basis of Celia's encephalopathy and its possible treatments, we have generated a knock-in murine model of Celia's encephalopathy (C57BL/6 BSCL2$^{Celia/Celia}$, called post-cre). The targeting strategy used enabled us, in a previous step, to also generate a knock-out (KO, called pre-cre) mouse for seipin (C57BL/6 Bscl2$^{-/-}$).

Both pre-cre and post-cre homozygous mice had a generalized lipoatrophy from the first weeks of life, that affected both white fat and brown fat, and hepatomegaly as a consequence of a non-alcoholic steatohepatitis (Fig. 1). This disorder starts early and gets worse over time. The size of the liver comes to be, in some cases, 25% of the weight of the mouse. These mice have increased NASH score in comparison with wt and heterozygous animals. A remarkable fact is that the post-cre homozygous mice that presented neurological involvement showed a lower steatohepatitis and the size of their liver was similar to that of the wt mice.

Figure 1: Large hepatomegaly in homozygous post-cre mouse (BSCL2$^{Celia/Celia}$)

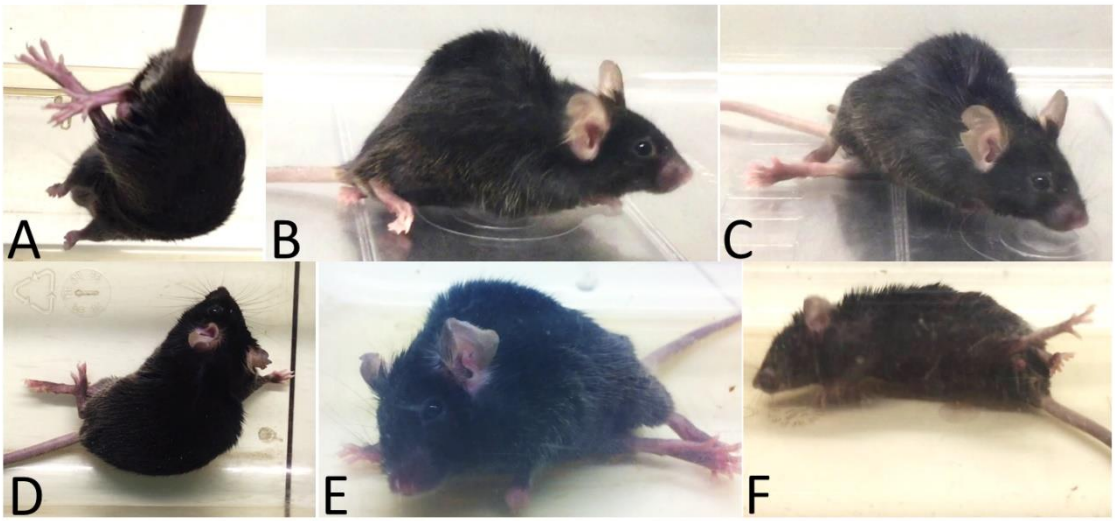


Homozygous post-cre mice showed an open field activity significantly lower than the other mice. The rate of gnawing of post-cre homozygous mice was less than that the wt, but there were no differences with pre-cre mice. We observed that post-cre homozygous mice show a nesting clearly more disorganized.

We noticed neurological signs, as ponderal stagnation, abnormal crossing of the hind limbs (Fig. 2A), kyphosis (Fig. 2B), tremor/myoclonus, tail spasticity, parapararesia/paraplegia (Fig. 2C-E), and tetraparesis (Fig. 2F) associated with death due to deterioration of the general condition in 21% of homozygous post-cre mice and 7.3% of heterozygous post-cre mice. We did not detect this clinic until the third generation and the precocity in the appearance of the signs was increasing throughout the following generations (4^{th} and 5^{th}).

We quantified the relative expression of the Celia-seipin transgene in different samples of brains through qPCR. As expected, it was significantly higher in post-cre heterozygous and more elevated in post-cre homozygous mice. Moreover, it was higher in the neurologically affected post-cre homozygous mice than in the unaffected ones. The expression of the Fgf21 gene, related to the pathogenesis of insulin resistance, was significantly elevated in the liver of homozygous mice, both pre- and post-cre.

Figure 2: Neurological signs in affected post-cre mice



Cerebral areas (cerebellum, mesencephalon, hippocampus, cortex, hypothalamus, striatum) of different mice were stained with H-E and for immunohistochemistry (anti-seipin, anti-GFAP, anti-CD68 and reticulin). No differences could be observed in the analyzed samples of the different mouse genotypes in relation to neuronal loss, astrogliosis or microgliosis.

Immunohistochemistry studies for 6xHis-Tag Celia seipin revealed intranuclear aggregates in the hypothalamus of a homozygous post-cre mouse that do not appear to correspond to nucleoli by size and number. Preliminary studies of transmission electron microscopy showed that striatum of an affected homozygous post-cre mouse presented a clear nuclear involvement, with loss of heterochromatin, and expansion of the neuronal body with rarefaction of the rough endoplasmic reticulum, which seemed to be also observed in neuropil prolongations.

The main objective of this project was to generate a transgenic mouse model that recapitulates Celia's Encephalopathy. The results of the clinical and histological evaluations are conclusive with regard to the adipose and hepatic phenotype. Homozygous mice, both KO and KI, show generalized lipodystrophy and non-alcoholic steatohepatitis. Regarding the neurological phenotype, we make the following points: 1. We have achieved a severe neurodegenerative phenotype, which is present in 21% of the mice, leading to a shortening of life expectancy. 2. This phenotype differs from that observed in the classical form of PELD in that it appears chronologically later. 3. The expression of Celia-BSCL2 transgene was higher in the encephalon of affected mice. 4. Ultrastructural studies showed loss of heterochromatin in the striatum of an affected post-cre homozygous mouse.

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Differential expression of brown and white adipose tissue markers in FPLD2 adipocytes

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Adipose tissue is severely affected in type 2 Familial Partial Lipodystrophy (FPLD2), a rare disease caused by heterozygous mutations in *LMNA* gene. In FPLD2, white adipose tissue is lost in most body districts, while adipose tissue of brown origin is accumulated in the neck area. Moreover, visceral adipose tissue can be accumulated in patients. Despite this precise clinical characterization of affected tissue, little is known on FPLD2-specific gene expression in white and brown adipocytes. We took advantage of well characterized tissue biopsies from different body districts of FPLD2 patients and obtained brown and white adipocyte precursors. The expression of white and brown adipose tissue genes was examined by quantitative RT-PCR in FPLD2 pre-adipocytes and adipocytes differentiated in vitro and the most interesting gene products were evaluated by biochemical analysis. Our results show an altered expression profile of genes related to adipogenesis in FPLD2, consistent with an aberrant differentiation program of brown and white adipose tissue precursors.

Variable phenotype of *LMNA*-associated lipodystrophy

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Type 2 familial partial lipodystrophy (FPLD2, OMIM #151660) is an autosomal-dominant disease (Dunnigan-type familial partial lipodystrophy), caused by mutations in the LMNA gene encoding the splice variants lamin A and C. Patients lose subcutaneous fat from extremities, trunk, and gluteal regions. Excess fat is deposited in the face, neck, back, abdominal cavity, and ectopically in the liver. FPLD2 patients develop and insulin resistance that often progresses to type 2 diabetes mellitus. FPLD2 patients also show early fatigue, skeletal muscle hypertrophy in the legs, and intrinsic muscular metabolic abnormalities with excessive. Here we present a family carrying the R482Q variant within LMNA illustrating the range of phenotype.

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How is lipodystrophy linked to cardiometabolic disease: insights from SHORT syndrome

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Insulin signaling via phosphoinositide 3-kinase (PI3K) depends on *PIK3R1*-encoded regulatory subunits. C-terminal *PIK3R1* mutations cause lipodystrophy and insulin resistance (IR), surprisingly without fatty liver or metabolic dyslipidemia. We hypothesized that this is due to attenuation of insulin-driven lipogenesis in the hyperinsulinaemic state. The human pathogenic *Pik3r1* Y657X mutation was knocked into mice. *Pik3r1*$^{Y657X/WT}$ mice were small with severe IR, but had low plasma lipid concentrations on chow or high fat diet. Insulin-stimulated hepatic lipogenesis was not increased despite hyperinsulinemia, and lipogenic gene expression was reduced only on overnight fasting. Liver transcriptomics suggested reduced endoplasmic reticulum stress in the fed state and diminished Rictor-dependent transcription on fasting. Adipose expansion on high fat diet was reduced without adipocyte hypertrophy or adipose inflammation, but with increased energy expenditure and compensatory increased food intake. *Pik3r1*$^{Y657X/WT}$ mice were not markedly hyperglycemic, and no evidence of intestinal malabsorption was found. *Pik3r1* dysfunction thus produces IR and metabolic inflexibility with reduced diet-induced adipose expansion, but without fatty liver and dyslipidemia, modelling the discordant severe IR and normolipidemia of human SHORT syndrome. This is accounted for by increased energy expenditure. We conclude that reduced adiposity in SHORT syndrome does not represent *bona fide* lipodystrophy.

How patient organizations can partner with lipodystrophy stakeholders in all phases of research and development

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Patient Focused Drug Development (PFDD) has continued to gain momentum in rare disease research. The FDA strongly supports PFDD initiatives and with their enhanced policies and recommended guidelines for working with patient foundations. Regulators in other countries have similar guidelines in place or are beginning to adopt new patient-centered practices. Many rare diseases, like lipodystrophy, lack strong natural history studies leaving the true burden of disease for a disease community not well understood. Engaging with the patient community at the beginning of a research process and continuing this engagement has been found to lead to stronger study protocols and outcomes. Further, patient-centered research outcomes with collaboration between patients and clinicians are increasingly encouraged and open new funding opportunities. Patient engagement should be early and often and can occur on a continuum from stakeholder input to shared leadership. Ms Stratton will review the current state of US PFDD and will share experiences and suggested opportunities for the lipodystrophy community to continue patient-centered research, education, and awareness activities.

Video link: https://youtu.be/qF0t1avZm3o

Diet therapy in patients with lipodystrophy syndromes: perspectives and challenges

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Background: Generalized lipodystrophy (GLD) syndromes form a heterogeneous group of orphan disorders characterized by total deficiency of adipose tissue in the absence of nutritional deprivation or catabolic state. Major causes of mortality in GLD include heart disease, liver disease, acute pancreatitis, sepsis and kidney failure.

According to the Practice Guideline metreleptin with the diet is a first-line treatment for metabolic complications in patients with GLD. In consideration of unavailability of metreleptin therapy in Russia the well-balanced diet remains the main way to correct metabolic abnormalities, however no specific clinical recommendations on a diet in lipodystrophy syndromes have been worked out yet.

Aim: We present our clinical experience in 4 Russian adolescents with congenital generalized LD (CGL)during 4 ear follow-up to show perspectives and challenges of such therapy.

Results: All patients with CGL were prescribed with normal calorie low-fat diet with restriction of simple sugar and moderate physical activity. All of them showed a remarkable metabolic response (glucose and triglycerides reduction) while staying in the endocrinology department for 10-14 days and worsening after the discharge. The main difficulties in achieving metabolic control at home were associated with hyperphagia, high cost of healthy food, difficulties in complying with the diet at school, psychological problems (being bullied by other kids at school), low compliance in children and adolescents due to the lack of fear of possible complications.

Conclusion: Our experience supports the results of previous investigations and highlights the necessity of the multi-society practice guideline on a diet in lipodystrophy syndromes.

Diagnostic challenge in *PLIN1*-associated Familial Partial Lipodystrophy

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Heterozygous frameshift variants in *PLIN1* encoding perilipin-1, a key protein for lipid droplet formation and triglyceride metabolism, have been implicated in familial partial lipodystrophy type 4 (FPLD4), a rare entity with only 6 families reported worldwide. The pathogenicity of other *PLIN1* null variants identified in patients with diabetes and/or hyperinsulinemia was recently questioned based on the absence of lipodystrophy in these individuals and on the elevated frequency of PLIN1 null variants in the general population.

Objectives: To reevaluate the pathogenicity of *PLIN1* null variants in light of new data obtained in the largest series of patients with FPLD4.

Methods: We performed clinical, histological, and molecular studies in patients referred for lipodystrophy and/or insulin resistance and carrying *PLIN1* null variants.

Results: We identified three heterozygous *PLIN1* null variants segregating with the phenotype in 12 patients from 5 unrelated families: two frameshifts and one deletion abrogating a splice site. The FPLD4 stereotypical signs include postpubertal onset of partial lipoatrophy of various severity, muscular hypertrophy, acromegaloid features, PCOS and/or hirsutism, metabolic complications (hypertriglyceridemia, insulin resistance, diabetes), and 72isorganized subcutaneous fat lobules with fibrosis, and macrophage infiltration.

Conclusions: A set of arguments support that some FPLD4-associated *PLIN1* variants are deleterious. The pros and cons regarding the pathogenicity of each variant has to be weighed carefully for genetic counseling, considering the importance of early diagnosis for proper disease management. In this regard, we recommend detailed familial investigation, adipose tissue-focused examination, and follow-up of metabolic evolution.

Cardiovascular phenotypes in LMNA-associated lipodystrophy: implications for clinical practice

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Pathogenic variants in LMNA encoding type A lamins, are responsible for different lipodystrophic syndromes ranging from typical Familial Partial Lipodystrophy Type 2 to complex multisystemic diseases. Patients with LMNA-associated lipodystrophies can present with different cardiovascular comorbidities, including accelerated atherosclerosis with precocious and severe coronary artery disease, and dilated cardiomyopathy with rhythm and/or conduction disturbances. Each cardiovascular complication can lead to life-threatening risks, and each requires specific detection and management procedures, which render the clinical decision trees particularly complex.

By sharing clinical cases, we will illustrate the complex and sometimes unexpected cardiovascular complications that can affect patients with lipodystrophic laminopathies.

We will also discuss our recent results obtained using the OPALE observatory data (French Observatory of Patients with Laminopathies and Emerinopathies, coordinated by Gisèle Bonne, Paris, France), that attempt to describe the specific determinants of the different cardiovascular risks in patients referred for lipodystrophic syndromes due to LMNA pathogenic variants.

Early diagnosis of cardiovascular complications is crucial for global management of laminopathies. In addition to initial standardized procedures aiming to systematically detect any cardiovascular laminopathic involvement, both genotype and clinical presentation should help to manage the specific cardiovascular risks, which is a key issue in LMNA-associated lipodystrophy.

European Lipodystrophy Registry: background, structure and first results

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Background: Lipodystrophy syndromes comprise a group of extremely rare and heterogeneous diseases characterized by a selective loss of adipose tissue in the absence of nutritional deprivation or catabolic state. Because of the rarity of each lipodystrophy subform, research in this area is difficult and international co-operation mandatory. Therefore, in 2016, the European Consortium of Lipodystrophies (ECLip) decided to create a registry for patients with lipodystrophy.

Methods: The aim of the ECLip registry is to build a basis for sound research in the area of lipodystrophy to enable an improved estimate of the prevalence of lipodystrophy in Europe, provide a study base for patient-centred Europe-wide lipodystrophy research and a platform for nested investigations on specific topics. All patients with any form of lipodystrophy (with the exception of HIV-associated lipodystrophy) presenting at a participating centre are asked to participate in the ECLip registry. The information technology of the registry is based on the Open Source Registry System for Rare Diseases in the EU (OSSE). The registry complies with the General Data Protection Regulation (EU) 2016/679 ("GDPR") by ensuring patient pseudonymization, informational separation of powers, secure data storage and security of communication, user authentication, person specific access to data, and recording of access granted to any data.

Results: From the 16th Dec 2016 to the 15th April 2019, 212 patients (20% men) were recruited.

Conclusion: A European registry for all patients with lipodystrophy will provide a platform for improved research in the area of lipodystrophy. All physicians from Europe and neighbouring countries caring for patients with lipodystrophy are invited to participate in the ECLip registry.

Study Registration: ClinicalTrials.gov (ClinicalTrials.gov ID: NCT03553420).

Human SGBS cells as in vitro model for studying cellular phenotypes of lipodystrophies

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Objectives: Studies on human adipocytes have been challenging due to technical difficulties, limited supply of cells and to some extent the variability in quality of human adipose tissue specimens. We have established a human preadipocytes cell strain (SGBS) which provides a unique and useful tool for studies of human adipocyte biology.

Methods: Cells were initially derived from the stromal cells fraction of subcutaneous adipose tissue of a diseased infant with Simpson-Golabi-Behmel syndrome (SGBS) and characterized intensively.

Results: SGBS cells are neither transformed nor immortalised and have been tested in a panel of different assays. The cells are efficiently differentiated in the presence of PPARγ agonists and in the absence of serum and albumin (1,2).

Figure: Adipogenic differentiation of human SGBS cells 14d in a chemically-defined, serum-free, adipogenic medium (1,2)

During the differentiation process SGBS cells develop a gene expression pattern similar to that found in differentiating human preadipocytes. In mature SGBS adipocytes insulin stimulation induces glucose uptake (5-10 fold; EC_{50}~100pM) and a strong antilipolytic effect (IC_{50}~15pM). Mature SGBS adipocytes secrete leptin, adiponectin, IGF-1, and all other adipokines.

Studies using adipogenic differentiation, glucose uptake, de novo lipogenesis, lipolysis, apoptosis, transient and stable transfections have been performed. The biology of adipocyte expressed lipodystrophy genes can be studied by gene silencing, gene know out by CRISPR/Cas-9 or overexpression studies as well as by various functional studies (3-6).

Conclusion: The human SGBS preadipocyte cell strain offers an excellent tool for studies of human adipocyte biology. SGBS cells provide a suitable model system to study the biological function of lipodystrophy genes.

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