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Molecular Basis of Lipodystrophy: Gene Mutations, Pathophysiology, and Therapy

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Abstract

Lipodystrophy syndromes are a group of rare diseases characterized by a general or partial absence of body fat, caused by the inability to properly store and utilize adipose tissue. The lack of adipose tissue would lead to serious consequences and the development of a series of metabolic issues, including insulin resistance, leptin deficiency, and hypertriglyceridemia. Lipodystrophy syndromes are genetically and clinically heterogeneous, with different phenotypes influenced by underlying molecular defects. Both fat distribution and the molecular defect play a role in determining the type of lipodystrophy a patient has. Due to the rarity of these disorders, not many studies have been conducted on them. This results in the public's lack of awareness, increasing the difficulty of diagnosing and treating these conditions. This article examines the classification and clinical aspects of lipodystrophy syndromes, covering the onset and the differences in phenotypes of patients. It further discusses the molecular and cellular mechanisms of several types of lipodystrophies and the role they play in the development of adipose tissues. In addition, this review addresses other metabolic dysfunctions caused by lipodystrophy, such as insulin resistance, fatty liver, and hypertriglyceridemia. Lastly, we evaluate therapeutic strategies aimed at improving metabolic control and quality of life in affected patients. Future research and potential therapy may be improved with a deeper and more thorough understanding of the genetic and mechanistic basis of lipodystrophy, as it is critical for identifying key mechanisms and developing a more targeted treatment.

Keywords: lipodystrophy syndromes, adipose tissue dysfunction, adipogenesis, congenital generalized lipodystrophy (CGL), familial partial lipodystrophy (FPLD)

1. Introduction

Lipodystrophy syndromes (LD) are a heterogeneous group of rare disorders characterized by the partial or complete loss of mature adipose tissue in localized or generalized areas. This results in the inability to store body fat, ectopic lipid storage, and excess nutrients (Fourman and Grinspoon 2022). Two main classes of lipodystrophy are Congenital Generalized Lipodystrophy (CGL) and Familial Partial Lipodystrophy (FPLD).

For adipose tissues to function normally, adipogenesis is crucial for the differentiation of the precursor cells. Adipogenesis starts with mesenchymal stem cells differentiating into mature adipose tissue. During adipogenesis, lipid storage and mobilization are regulated by the triacylglycerol (TAG) fatty acid cycle. Lipid droplets undergo lipolysis (the breakdown of lipid droplets) and lipogenesis (the synthesis of new lipid droplets)(Poulos et al. 2016). However, if a gene mutation or other factors affect the components involved in the regulation of adipogenesis, this would lead to impaired adipocyte differentiation, lipid droplet formation, and adipocyte functions.

LD can be either congenital or acquired. Congenital Lipodystrophy is classified based on the location of lost adipose tissue, and further divided into subtypes according to the gene segment that is mutated (Akinci, Gular, and Oral 2024) (Table 1). Meanwhile, acquired lipodystrophy is caused by external factors or side effects of other treatments.

CGL (also called Berardinelli-Seip syndrome) is characterized by the near-complete absence of adipocytes (Oswiecimska n.d.). CGLs are inherited in an autosomal recessive manner, with symptoms typically presenting shortly after birth. It is further divided into CGL1, CGL2, CGL3, and CGL4, which link to four different gene mutations. FPLD presents as an abnormal distribution of adipose tissue, with fat loss around the limbs, torso, and hips. It can be autosomal recessive or dominant depending on the gene involved. Since the body is not able to store excess energy in those areas, other body parts, such as the face, neck, and internal organs like the liver, gain extra adipose tissue (Diagnosis and Management of Lipodystrophy Syndromes: A Multi-Society Practice Guideline | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic n.d.). This results in the abnormal distribution of adipose tissues. As with CGL, FPLD is further divided into several subtypes, including FPLD1 (Kobberling-type lipodystrophy), FPLD2 (Dunnigan Variety lipodystrophy), FPLD3, FPLD4, FPLD5, and FPLD6. The development of adipocytes is tightly regulated by various proteins and enzymes. The genes that encode these proteins or enzymes are often the genes associated with lipodystrophy.

As for Acquired Generalized Lipodystrophy (AGL, Lawrence Syndrome) and Acquired Partial Lipodystrophy (APL, Barraquer-Simons syndrome), they have similar symptoms to CGL and FPDL. However, they are caused by autoimmune diseases, side effects of antiretroviral therapy (ART) for HIV patients, or even idiopathic reasons (Misra and Garg 2003).

Table 1: Classification, clinical features, and molecular basis of lipodystrophies (Made by author with Google Sheets.)

Type	Subtype	Gene Involved	Inheritence	Clinical Phenotype	Commonly associated Features
Generalized Lipodystrophy Syndrome					
Congenital Generalized Lipodystropy (Berardinelli-Seip syndrome)	CGL1	AGPAT2	Autosomal recessive	Near total absence of adipose tissue, generalized musularity, metabolic abnormalities. Starts showing symptoms shortly after birth.	Loss of metabolic fat, retains mechanical fat tissues
	CGL2	BSCL2	Autosomal recessive		Mild mental retardation
	CGL3	CAV1	Autosomal recessive		Vitamin D resistance
	CGL4	PTRF	Autosomal recessive		Myopathy, pyloric stenosis
Acquired Generalized Lipodystrophy (Lawrence Syndrome)	NA	NA	NA	Near total absence of adipose tissue, metabolic issues. Develops during childhoold/ puberty.	Could be caused by autoimmune diseases, panniculitus, idiopathic or immunotherapy
Partial lipodystrophy syndromes					
Familial Partial Lipodystrophy	FPLD1 (Kobbering)	Unknown	Polygenic	Absence of fat around the limbs and buttock, excess adipose tissues around face, neck, and abdomen. Also shows sign of metabolic issues. Develops during purberty/ adolescense.	Palpable "ledge" between normal and lipodistrophic areas
	FPLD2 (Dunnigan)	LMNA	Autosomal dominant		High risks of cardiovascular diseases
	FPLD3	PPARG	Autosomal dominant		Less severe and distal fat loss
	FPLD4	PLIN1	Autosomal dominant		Increased fibrosis of adipose tissue, small lipid droplets in adipocytes
	FPLD5	CIDEC	Autosomal recessive		
	FPLD6	LIPE	Autosomal recessive		Increased visceral fat
Acquired Partial Lipodystrophy (Barraquer-Simons syndrome)	NA	NA	NA	Lost of subcutaneous fat around the face, neck, upper limbs and abdomen. Low limbs are not effected.	Causes could be autoimmune, MPGN- associated, immunotherapy or idiopathic

Not only will the lack of excess body fat affect the body's normal functions, but complications associated with lipodystrophy also have a significant effect on patients' lives. Some common metabolic abnormalities include leptin deficiency, insulin resistance, diabetes, hypertriglyceridemia, and fatty liver disease (Figure 1). Currently, around 200 clinical trials are underway to discover a new way to treat or cure lipodystrophy, with a particular focus on leptin deficiency (Search ClinicalTrials.Gov For, n.d.).

Metreleptin, for example, is a treatment created specifically for acquired or congenital generalized lipodystrophy patients. It is a targeted treatment for leptin deficiency, which is a common metabolic issue associated with LD (Araújo-Vilar & Santini, 2019). It is currently the only FDA- approved treatment for generalized lipodystrophy patients. However, conventional treatment, such as special diets, is still optimized before metreleptin (Meehan et al., 2016). Due to the rarity of this disease, limited research has been done, making Metreleptin the primary choice for CGL and AGL patients (Ajluni et al., 2016). As for FPLD patients, the use of Metreleptin is highly restricted. Therefore, they will need to maintain an appropriate

diet and require other medications for the metabolic complications.

According to studies, only about 3 per million people around the world are affected by some type of lipodystrophy syndrome. While the prevalence of CGL is estimated to be 0.23 per million people, the prevalence of FPLD is around 2.84 per million people (Chiquette et al. 2017). It is also estimated to shorten a patient's lifespan by 30 or more years. The main cause of death is shown to be liver diseases and infections caused by adipose tissue dysfunction, but also varies from type to type of lipodystrophy (Lima et al. 2018).

This literature review aims to highlight the molecular mechanisms underlying lipodystrophy, with a focus on the genetic causes, differences between types of lipodystrophies, and other metabolic conditions caused by adipose tissue abnormalities, as well as the treatment developed and future directions of study, and the possibilities for fundamental treatments.

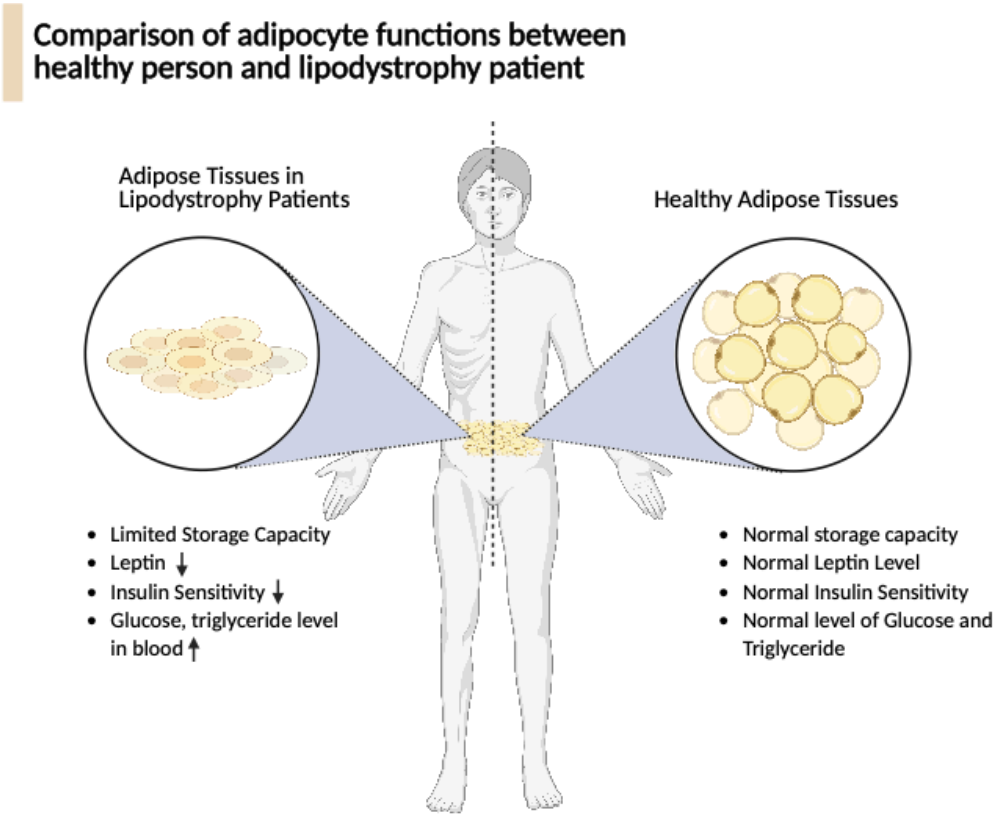


Figure 1: Comparison of adipocyte functions between a healthy person and a lipodystrophy patient. Adipocyte storage is decreased in lipodystrophy patients. Common metabolic abnormalities include leptin deficiency, insulin resistance, and elevated blood glucose levels in the bloodstream. (Made by author with BioRender.)

2. Methods

2.1. Search Strategy

A literature search was conducted using PubMed and Google Scholar databases. The search included the following keywords: “lipodystrophy genetics”, “adipocyte differentiation”, “AGPAT2”, “PTRF Cavin-1”, “LMNA mutation”, “PPARγ mutation”, “lipodystrophy metabolic abnormalities”. Titles and abstracts were first screened for relevance. Full articles were reviewed to see if they met the inclusion criteria. 97 articles were initially screened, and 55 papers were ultimately referenced in this review.

2.2. Inclusion/Exclusion Criteria

Articles published between 2000 and 2026 were included. Only English language publications were considered. Studies were included if they were peer-reviewed primary research articles or comprehensive reviews, including both narrative reviews and systematic reviews, that focused on the genetic, molecular, or metabolic mechanisms underlying lipodystrophy syndromes. Case studies were included if they provided relevant insights, such as pathological or mutation analyses or clinical findings. Non-peer-reviewed sources and articles published before 2000 are excluded. Case reports that only report descriptive quantitative data, without the discussion of mechanistic interpretation, are also excluded, as clinical data are not the focus of this review.

3. Discussion: Genetics and Pathophysiology

3.1. Type 1 Congenital Generalized Lipodystrophy (CGL1)

Type one Congenital Generalized Lipodystrophy (CGL1) is caused by a mutation in the gene AGPAT2. AGPAT2 is the gene that encodes the enzyme 1-acylglycerol-3-phosphate O-acyltransferase 2. It catalyzes the acylation of lysophosphatidic acid (1-acylglycerol-3-phosphate) to phosphatidic acid (1,2 diacylglycerol-3-phosphate) (Gale et al. 2006), as shown in Figure 2. It is an important precursor for the biosynthesis of triacylglycerol (TAG) and phospholipids from glycerol-3-phosphate. This step esterifies a second fatty acyl group at the sn-2 position of the glycerol backbone. Phosphatidic acid is further acylated by other enzymes, creating triacylglycerol and phospholipids. Impaired formation of phosphatidic acid results in the absence of triacylglycerol production, thereby disrupting the normal adipose tissue development.

The AGPAT family consists of 11 isomers. Among the isomers, AGPAT2 is expressed at higher levels in adipose tissue than the other isomers. The presence of mechanical adipose tissue can be explained by the increased expression of the other isomers (Broekema et al., 2018). However, studies have shown that the expression of AGPAT2 is required for the accumulation of triacylglycerol, especially in metabolic adipose tissues. Defects in the AGPAT2 gene also impact insulin signaling, which is a direct effect of impaired adipocyte dysfunction (Santoro et al., 2021). This also causes gluconeogenesis to be unrestricted, which leads to the development of hyperglycemia and diabetes (de Melo et al. 2025).

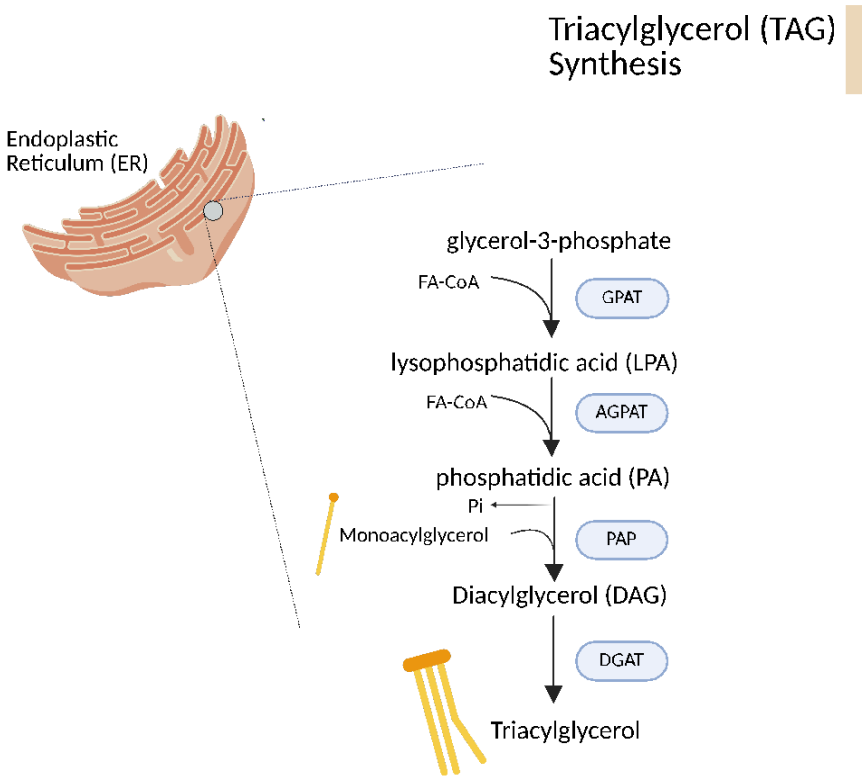


Figure 2: The process of Triacylglycerol synthesis. In the second step, where LPA is acylated to PA, AGPAT is the enzyme that catalyzes this reaction. Without it, the reactions after it will not occur properly, meaning that adipocytes cannot develop properly. (Made with BioRender).

3.2. Type 2 Congenital Generalized Lipodystrophy (CGL2)

Type 2 Congenital Generalized Lipodystrophy (CGL2) is caused by pathogenic variants of the BSCL2 gene. It encodes the protein Seipin, which is found in the endoplasmic reticulum (ER) (Akinci et al., 2024), Seipin plays an important role in the regulation of lipid droplet biogenesis. It interacts with proteins involved in TAG synthesis to facilitate adipogenesis. For instance, it binds with AGPAT2 to regulate PA metabolism. Seipin deficiency could lead to abnormal accumulation of PA. This increases the surface tension of the ER and decreases its line tension, disrupting the unidirectional lipid droplet budding. It causes the accumulation of newly synthesized neutral lipids in the ER, leading to severe ER stress and potentially being toxic to the cells (Li et al., 2022).

CGL2 is the most common type of congenital lipodystrophy. But mutations in the BSCL2 also lead to the most severe symptoms. Patients are born without any fat, including mechanical and metabolic adipose tissues. They also have an earlier onset of diabetes mellitus than other types of lipodystrophies. Other than adipocytes, seipin is also expressed in the brain and testis. This leads to mild mental disability, developmental language disorders, and an impaired reproductive system.

3.3. Type four Congenital Generalized Lipodystrophy (CGL4)

Type four Congenital Generalized Lipodystrophy (CGL4) is associated with the gene mutation in the PTRF gene (Polymerase I and Transcript Release Factor)(Salle-Teyssières et al. 2016). The PTRF gene encodes cavin-1, which is one of the essential proteins that is required for the biogenesis of caveolae. Caveolae are the most abundant invaginations of the plasma membrane across a wide range of mammalian cells (Figure 3). Cavin-1 plays a critical role in the initiation of caveolae synthesis through recruiting other structural proteins, such as caveolins. Without it, cells will not be able to produce caveolae. Although it is abundant, its functions have only been understood in the past few decades. It plays a role in signal transduction, endocytosis, and mechanotransduction (Stea and D'Alessio 2025). Cavin-1 binds with the caveolins to form Caveolae.

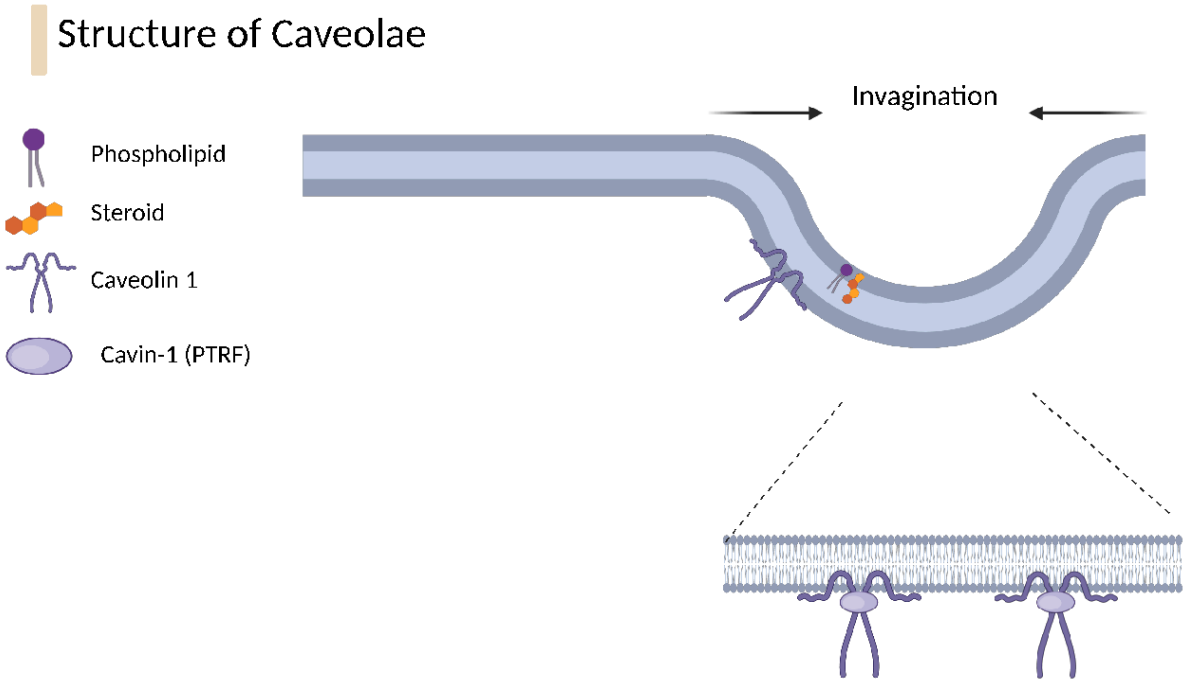


Figure 3: Structure and formation of caveolae. Caveolae are invaginations of the plasma membrane. Cavin-1 first binds with the plasma membrane, initiating caveolae synthesis. Caveolin 1 binds with cavin-1, which stabilizes its structure and forms caveolae. (Made with BioRender).

There are three members in the caveolin family: caveolin-1, caveolin-2, and caveolin-3. They are expressed in a variety of cells, like smooth muscle cells, fibroblasts, and adipocytes. Caveolin 3 is expressed exclusively in cardiac and skeletal muscle. It is shown that the lack of PTRF-CAVIN does not affect the level of caveolin expressed (Rajab et al. 2010). However, it affects caveolin's ability to localize to the cell's surface, which makes the formation of caveolae impossible. The absence of caveolae causes abnormalities and dysfunctions, including impaired signal transduction and a lack of mechanoprotection. Without the extra membranes acting as a buffer against the force of mechanical stretching, cardiac

cells are at a greater risk of rupturing (Grivas et al., 2020).

Clinical features uniquely associated with CGL4 include myopathy, which affects skeletal muscle structure, and distal metaphyseal deformation, causing bone stiffness and limited range of motion (Ardissone et al. 2013). Cardiac arrhythmias are also one of the symptoms caused by the lack of PTRF-CAVIN, and they could be life-threatening, showing the serious consequences of cavin-1 deficiency (Rajab et al. 2010). These symptoms can be explained by the location where caveolins 1, 2, and 3 are expressed.

3.4. Type Two Familial Partial Lipodystrophy (FPLD2)

The gene LMNA encodes the protein called Lamins. It is the gene that is associated with Type two Familial Partial Lipodystrophy (FPLD2). FPLD2 is the most common type of lipodystrophy syndrome (Corsa et al. 2021). In cells, Lamin A and Lamin C are expressed predominantly. The main functions of Lamin A/C are the regulation of nucleus shape, providing structural stability to the nuclear envelope and cytoskeleton, and also controlling gene regulation (Maung et al. 2026),(Bagias et al. 2020). They are important intermediate filament proteins forming the nuclear lamina. They also play a role in organizing chromatin. Mutations in Lamin A/C can lead to premature aging syndrome (Hutchinson-Gilford Progeria Syndrome). The mutated LMNA gene produces a mutant product called progerin. As progerin accumulates in the nucleus, it destabilizes DNA, triggers premature senescence, and alters the shape of the nucleus (Gonzalo et al., 2017).

The interference with the cleavage step of post-translational regulation of Lamin A could also affect the patient. ZMPSTE24 plays an important role in this step, and it is also considered to be one of the factors that causes lipodystrophy. However, mutations in ZMPSTE24 cause another distinct form of lipodystrophy (mandibuloacral dysplasia), showing different symptoms and increased severity. Nevertheless, modification is crucial and ensures that Prelamin A (the precursor of Lamin A before post-translational regulation) functions normally. Not only will the lack of Lamin A affect cell functions, but the accumulation of Prelamin A could also be toxic to cells (Varlet, Helfer, and Badens 2020), which could affect the cell's ability to develop properly.

These cellular abnormalities contribute to broader systemic symptoms. This includes a higher risk of cardiovascular diseases. It is found that FPLD2 patients have higher Epicardial adipose tissue (EAT) volume than type two diabetes patients (Talman et al. 2014) (Godoy-Matos et al. 2015). However, it is not related to other metabolic issues that are also presented in lipodystrophy (Lamothe et al. 2025). Additional studies will need to be conducted to gain a clearer insight into this condition and its correlation.

3.5. Type three Familial Partial Lipodystrophy (FPLD3)

Type three Familial Partial Lipodystrophy (FPLD3) is caused by pathogenic variants of the PPARG gene. PPARG encodes PPARγ (Peroxisome proliferator-activated receptor γ), a member of a superfamily of nuclear receptors. PPARγ is known as the master regulator of adipocyte differentiation, maintenance, and functions(Broekema et al. 2019). It has three isoforms: PPARγ1, PPARγ2, and PPARγ3. Among them, PPARγ2 is predominantly expressed in adipocytes. PPARγ acts as a ligand-activated transcription factor. It binds to its target gene as a heterodimer with PPAR-response elements (PPREs)(Madsen et al. 2022). After binding, PPARγ regulates the transcription of downstream target genes involved in the development of adipose tissue. Including the TAG cycle, which is upregulated by PPARγ for the development of adipocytes.

Loss-of-function or dominant-negative mutations in pathogenic variants of PPARG fundamentally impair adipogenesis. Therefore, leading to increased cellular stress and dysfunctions in adipocytes(Soares et al. 2024).

Compared to FPLD2, FPLD3 patients show less severe fat loss. One way to explain this is that more large adipocytes are preserved since mutations in PPARG could lead to excess cell growth. Fat accumulation in areas such as the face and neck is also not observed (Bagias et al. 2020). However, FPLD3 patients also show more severe metabolic symptoms, specifically hypertriglyceridemia, diabetes, and insulin resistance. One possible explanation is that although patients still preserve large adipocytes, they only have a few small, insulin-sensitive adipocytes (Soares et al. 2024).

3.6. Acquired Lipodystrophy

A wide range of gene mutations that affect different cellular functions could all lead to LD. However, gene mutations are not the only cause of lipodystrophy. Other environmental factors can also trigger the onset of lipodystrophy. Acquired Generalized Lipodystrophy (AGL) and Acquired Partial Lipodystrophy (APL) are forms of lipodystrophy that are not caused by genetic mutations(Al-Jawad et al. 2025). Despite having different mechanisms, they have similar symptoms to congenital lipodystrophy.

Acquired lipodystrophy is characterized by the gradual loss of fat tissue starting from childhood or adolescence. AGL patients show a generalized loss of adipose tissue, while APL patients show loss of adipose tissue from the upper body. This includes the face, neck, upper extremities, and upper trunk. They also share similar causes, including autoimmune diseases, panniculitis-associated causes, and idiopathic causes. However, while about 25% of AGL cases are associated with panniculitis, it is rare in APL patients (Hussain & Garg, 2016).

Adverse effects of highly active antiretroviral therapy in patients with HIV are among the factors that lead to acquired lipodystrophy. The mechanism by which antiretroviral drugs play a role in the development of lipodystrophy is not fully understood (Giralt et al., 2025). One possibility is the use of thymidine analog nucleoside reverse transcriptase inhibitors in highly active antiretroviral therapies. They have been shown to disrupt adipose tissue functions (Guzman and Vijayan 2025). It decreases the expression of adiponectin, which regulates the oxidation of glucose and fatty acids. Nucleoside reverse transcriptase inhibitor also induces mitochondrial toxicity, which also plays a role in the development of acquired lipodystrophy. Lipodystrophy in HIV-infected patients is characterized by the loss of subcutaneous fat at the extremities and face.

Autoimmune diseases are also a significant cause of acquired lipodystrophy. In particular, perilipin 1 autoantibodies are found in AGL patients (Corvillo et al. 2022). Anti-perilipin is also found in patients with panniculitis-associated AGL. Perilipin is found only in adipose tissue and forms a layer that coats lipid droplets. Under normal conditions, perilipin forms a barrier between lipase and the surface of lipid droplets. However, when the autoantibodies are present, it disrupts the normal function of perilipin. It leads to an increase in lipolysis activities, which contributes to the gradual loss of adipose tissue in AGL patients (Corvillo et al. 2018).

In APL patients, the presence of C3 nephritic factor (C3NeF) is commonly associated. It acts as an autoantibody against the body's own complement system, particularly complement component C3. When C3NeF binds with C3 convertase, it stabilizes the C3 convertase and prevents its natural decay. Since the function of C3 convertase is to cleave C3 into its active fragment, prolonged activation leads to a low level of C3 (Nephritic Factor - an Overview | ScienceDirect Topics, n.d.).

In adipose tissues, the production of Factor D (adipsin) makes them more susceptible to the activation of the alternative pathway. Factor D plays an important role in the cleavage of factor B (C3bB), resulting in fragments Ba and Bb. The fragment Bb then forms the enzyme C3 convertase, also known as C3bBb. As the breakdown of C3 continues, it activates the terminal pathway. It ultimately leads to the lysis of adipocytes, which explains the fat loss. However, the factor that limits fat loss to the upper body remains unclear (Corvillo & López-Trascasa, 2018).

4. Diagnosis and Clinical Features

Since lipodystrophy is so rare, it is often misdiagnosed or left undiagnosed by clinicians. It heavily relies on clinical history and physical examinations that reveal the composition of adipose tissues. Metabolic dysfunctions are also important markers when diagnosing lipodystrophy. Although patients with CGL show symptoms such as a lack of body fat shortly after birth, it is often left undiagnosed until their childhood or adulthood, when they start showing metabolic abnormalities. As for FPLD, it is even more commonly unrecognized due to patients only losing adipose tissue partially. It could be easily misdiagnosed as other types of common metabolic diseases, like obesity or severe diabetes mellitus. Presentations of AGL and APL are generally similar to CGL and FPLD, also including the metabolic issues that come with it (Lima et al. 2025).

Lipotoxicity is a direct consequence of adipose tissue dysfunction. Since adipose tissues are not able to store as many lipid droplets as are produced, excess lipid droplets circulate in the bloodstream as free fatty acids. As the level of circulating free fatty acids elevates, it becomes toxic for non-adipose tissues, resulting in increased oxidative stress (Engin, 2017; Sies, 2020). Since the liver is the major organ that maintains the body's homeostasis, excess fatty acid accumulates at the liver, leading to fatty liver (Kikuchi & Takamura, 2017; Liu et al., 2010). This imbalance of fatty acids in the liver interferes with the insulin signaling pathways. In addition, the body stores excess fat in skeletal muscles, as it is the organ responsible for most of the energy uptake (Merz & Thurmond, 2020). Without skeletal muscles, glucose is not consumed properly, which also disrupts the insulin signaling pathways.

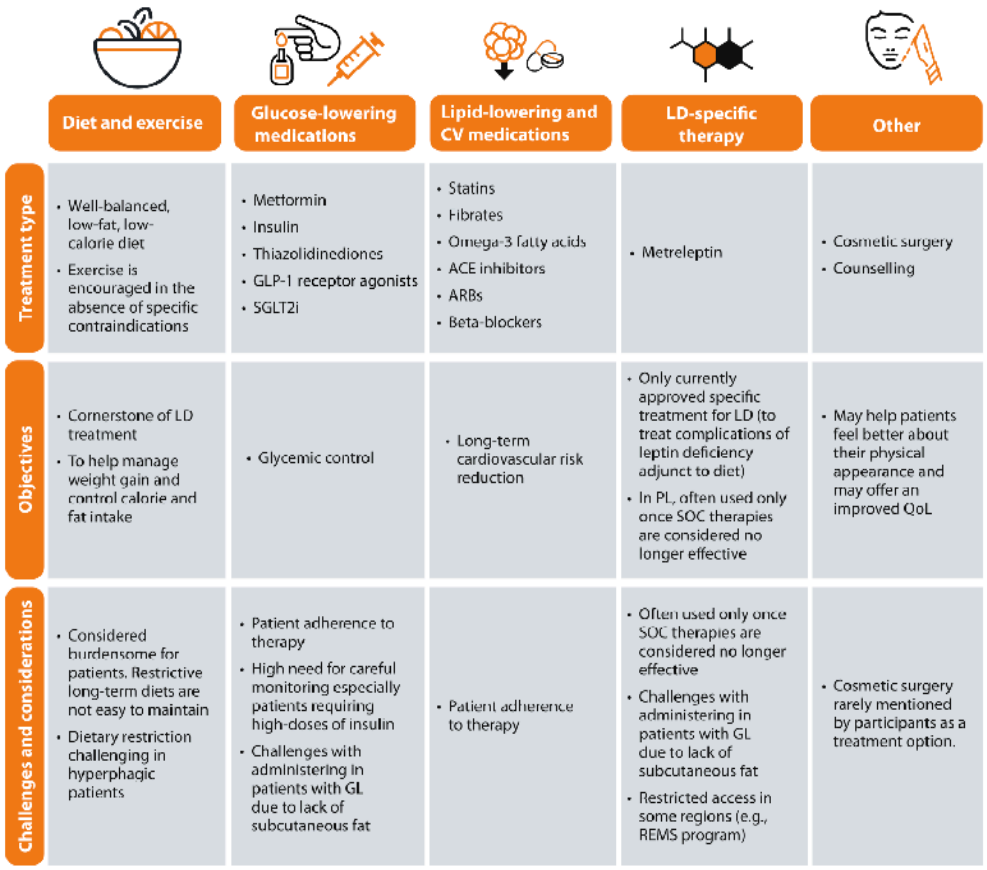
Some phenotypes associated with lipodystrophy include a muscular appearance, prominent veins, and a lack of body fat. Two main types of fat tissue serve different functions in the body: metabolic and mechanical adipose tissue. Metabolic adipose tissue is responsible for energy storage and hormone secretion, while mechanical tissue, also known as subcutaneous fat, is found under the skin and internal organs to provide protection and support. For CGL patients, the loss of metabolic adipose tissues is more severe than the loss of mechanical tissues. Yet patients still, to some degree, lack functional mechanical fat tissues. Only CGL2 patients are born without mechanical and metabolic adipose tissues (Garg 2011).

In contrast, FPLD is characterized by the abnormal distribution with a slight loss of adipose tissue, meaning that patients still acquire most of their functional fat tissues. In addition, as mentioned before, the onset of CGL is often shortly after birth, but for FPLDs, its onset is usually around puberty or adolescence. In general, CGL patients lack the ability to build up mature adipose tissue, while FPLD patients cannot store or regulate adipose tissue properly. The following section will address potential treatments and their underlying mechanisms.

5. Treatments

5.1. Metreleptin

Table 2: Possible medications to control metabolic issues that arise with lipodystrophy, including the objectives, possible challenges, and other considerations. Reproduced from Patni et al. (2024) under the terms of the CC BY license.



	Diet and exercise	Glucose-lowering medications	Lipid-lowering and CV medications	LD-specific therapy	Other
Treatment type	• Well-balanced, low-fat, low-calorie diet • Exercise is encouraged in the absence of specific contraindications	• Metformin • Insulin • Thiazolidinediones • GLP-1 receptor agonists • SGLT2i	• Statins • Fibrates • Omega-3 fatty acids • ACE inhibitors • ARBs • Beta-blockers	• Metreleptin	• Cosmetic surgery • Counselling
Objectives	• Cornerstone of LD treatment • To help manage weight gain and control calorie and fat intake	• Glycemic control	• Long-term cardiovascular risk reduction	• Only currently approved specific treatment for LD (to treat complications of leptin deficiency adjunct to diet) • In PL, often used only once SOC therapies are considered no longer effective	• May help patients feel better about their physical appearance and may offer an improved QoL
Challenges and considerations	• Considered burdensome for patients. Restrictive long-term diets are not easy to maintain • Dietary restriction challenging in hyperphagic patients	• Patient adherence to therapy • High need for careful monitoring especially patients requiring high-doses of insulin • Challenges with administering in patients with GL due to lack of subcutaneous fat	• Patient adherence to therapy	• Often used only once SOC therapies are considered no longer effective • Challenges with administering in patients with GL due to lack of subcutaneous fat • Restricted access in some regions (e.g., REMS program)	• Cosmetic surgery rarely mentioned by participants as a treatment option.

Currently, there is not a definitive cure for lipodystrophy, but some treatments targeting specific metabolic abnormalities have been developed (Araújo-Vilar and Santini 2019). For example, Metreleptin (Recombinant methionyl human leptin) is a drug invented specifically for lipodystrophy. It targets leptin deficiency in patients. Leptin is secreted by adipose tissue, and it regulates a person's appetite and food intake (Tsoukas, Farr, and Mantzoros 2015). Since lipodystrophy patients lack functional adipose tissue, leptin secretion also decreases. This causes patients to show extreme hyperphagia, which means the excessive intake of food. This worsens insulin resistance and creates excess fat that must be stored in internal organs or muscles. Metreleptin's main purpose is to mimic the naturally occurring leptin hormone, and it must be administered at least once daily (Rodriguez, Mastronardi, and Paz-Filho 2015). It helps reduce patients' appetite and decreases the intake of

calories, which contributes to the accumulation of lipid droplets. The use of metreleptin in FPLD patients is not approved by the FDA since it does not work as efficiently in FPLD patients as in CGL patients(Gilio, Foss-Freitas, and Oral 2025). Individual cases of FPLD could be evaluated for whether the requirements for the metreleptin treatment are met. However, the risk of using Metreleptin for special groups of people with generalized lipodystrophy, such as pregnant women, is not certain. Other common drugs, such as insulin or metformin, can also help patients control their symptoms; however, they are not a cure for LD. Cosmetic surgery is also an option for patients to minimize the psychological discomfort and to have a better quality of life (Table 2).

5.2. Lifestyle Modification

Although Metreleptin can generally help with metabolic dysfunctions, lifestyle modification also plays a significant role in managing lipodystrophy. A low-fat diet is recommended for patients. Carbohydrate intake is also restricted to control diabetes. Since the body cannot store excess energy properly, it would be beneficial for patients to reduce the intake of food that will be metabolized into excess fat or energy. Physical exercises are also encouraged. However, patients with cardiovascular issues should avoid excessive exercise to prevent further complications (Akinci et al. 2024).

5.3. Limitations and Possibility of Gene Editing

Although Metreleptin is an effective way for LD patients to manage metabolic complications, it is not able to cure them. In the future, gene editing could be applied to treating this disease. Preclinical trials have been conducted on mouse models with CGL2, which has a gene mutation at the BSCL2 gene. Seipin knockout (SKO) mice, which generally show similar metabolic symptoms to CGL2 patients, were generated and injected with adeno-associated virus (AAV) vectors (Sommer et al. 2022). AAV can be engineered to transduce adipocytes, enabling targeted gene therapy for lipodystrophy. The results of the trials show that gene therapy effectively restores adipose tissue development and function (Tiwari et al. 2024). However, even though AAV is commonly used in clinical trials, it has not been used to directly target adipose tissue. Novel AAV serotypes that target adipose tissue or an alternative promoter are critical for the development of an improved gene therapy strategy for LD patients. Therefore, there is not enough evidence currently to suggest that the results from mouse models can be translated to humans. Continued research on LD and advances in gene therapy are necessary to develop a more effective therapeutic strategy for this rare disorder.

6. Conclusion and Future Directions

Genes involved in lipodystrophy syndromes affect various cellular processes, such as lipid synthesis, signal transduction, and nuclear structure. They all lead to a common outcome: impaired adipocyte development and function. The examples discussed in this review, including CGL1, CGL4, FPLD2, and FPLD3, demonstrate how different stages of adipogenesis and gene mutations that are involved in adipogenesis all lead to similar consequences (Figure 4). In addition to genetic causes, acquired factors can also contribute to adipocyte dysfunctions, as seen in AGL.

LD highlights the essential role of adipose tissue as an endocrine and metabolic organ. It not only stores energy but also maintains metabolic homeostasis and regulates hormones. The absence of adipocytes, as shown in this review, could cause life-threatening disorders. Understanding this condition not only helps people recognize the role of adipose tissue in metabolism but also helps raise awareness of rare diseases. For conditions like lipodystrophy, many patients remain

undiagnosed throughout their lives. Not only is conducting research with so few samples challenging, but scientists may be less willing to dedicate time to studying rare diseases compared to diseases that affect a larger population. Increased awareness and improved diagnostic tools not only help identify individuals affected by this disease earlier but also give them a chance to manage their condition in a more effective way.

Since the discovery of lipodystrophy syndromes in the mid-20th century, significant progress has been made in understanding lipodystrophy. From phenotypes and metabolic abnormalities to underlying genetic causes, research has been conducted to find ways to reduce patients' pain and suffering. Having a deep understanding of lipodystrophy, such as the mechanisms of various genes and their relationship with adipogenesis, will be crucial to the development of a more effective and targeted therapeutic strategy.

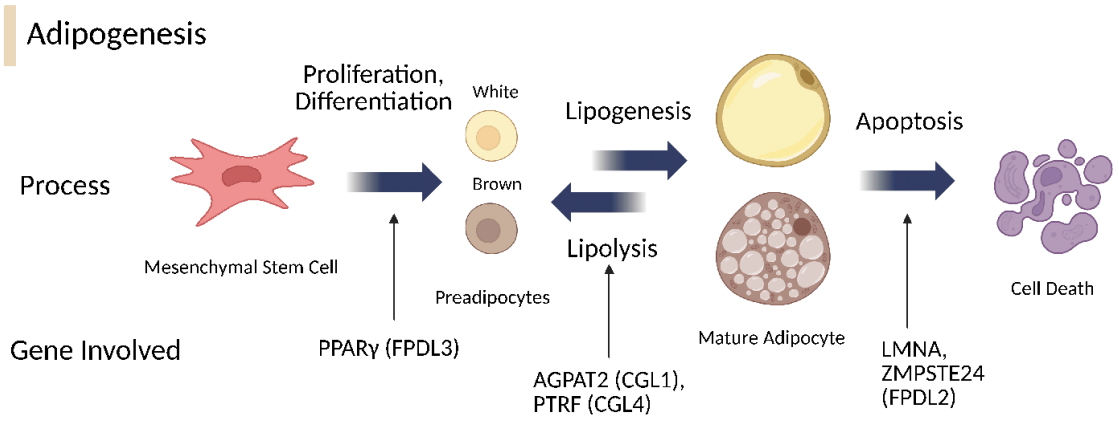


Figure 4: Steps of adipogenesis. Starting from mesenchymal stem cells, after proliferation and differentiation, it develops into preadipocytes. Then, through lipogenesis, preadipocytes grow into mature adipocytes. When a person is fasting, adipocytes go through lipolysis to produce energy by breaking down triglycerides into glycerol and free fatty acids. The last step is apoptosis, which ultimately leads to cell death. (Made with BioRender).

7. References

Ajluni, N., Dar, M., Xu, J., Neidert, A. H., & Oral, E. A. (2016). Efficacy and safety of metreleptin in patients with partial lipodystrophy: Lessons from an expanded access program. *Journal of Diabetes & Metabolism*, 7(3), 659. https://doi.org/10.4172/2155-6156.1000659

Akinci, B., Gular, M. C., & Oral, E. A. (2024). Lipodystrophy syndromes: Presentation and treatment. In *Endotext [Internet]*. MDText.com, Inc. https://www.ncbi.nlm.nih.gov/sites/books/NBK513130/

Al-Jawad, M., Mawaldi, L., Mawaldi, N., Krimsty, M., & Ishkanian, S. (2025). Acquired partial lipodystrophy (Barraquer-Simons syndrome) with both-side axillary breasts: A case report. *International Journal of Surgery Case Reports*, 129, 111202. https://doi.org/10.1016/j.ijscr.2025.111202

Araújo-Vilar, D., & Santini, F. (2019). Diagnosis and treatment of lipodystrophy: A step-by-step approach. *Journal of Endocrinological Investigation*, 42(1), 61–73. https://doi.org/10.1007/s40618-018-0887-z

Ardissone, A., Bragato, C., Caffi, L., Blasevich, F., Maestrini, S., Bianchi, M. L., Morandi, L., Moroni, I., & Mora, M. (2013). Novel PTRF mutation in a child with mild myopathy and very mild congenital lipodystrophy. *BMC Medical Genetics*, 14(1), 89. https://doi.org/10.1186/1471-2350-14-89

Bagias, C., Xiarchou, A., Bargiota, A., & Tigas, S. (2020). Familial partial lipodystrophy (FPLD): Recent insights. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, 13, 1531–1544. https://doi.org/10.2147/DMSO.S206053

Broekema, M. F., Massink, M. P. G., De Ligt, J., Stigter, E. C. A., Monajemi, H., De Ridder, J., Burgering, B. M. T., van Haaften, G. W., & Kalkhoven, E. (2018). A single complex Agpat2 allele in a patient with partial lipodystrophy. *Frontiers in Physiology*, 9. https://doi.org/10.3389/fphys.2018.01363

Broekema, M. F., Massink, M. P. G., Donato, C., De Ligt, J., Schaarschmidt, J., Borgman, A., Schooneman, M. G., Melchers, D., Gerding, M. N., Houtman, R., Bonvin, A. M. J. J., Majithia, A. R., Monajemi, H., Van Haaften, G. W., Soeters, M. R., & Kalkhoven, E. (2019). Natural helix 9 mutants of PPARγ differently affect its transcriptional activity. *Molecular Metabolism*, 20, 115–127. https://doi.org/10.1016/j.molmet.2018.12.005

Chiquette, E., Oral, E. A., Garg, A., Araújo-Vilar, D., & Dhankhar, P. (2017). Estimating the prevalence of generalized and partial lipodystrophy: Findings and challenges. *Diabetes, Metabolic Syndrome and Obesity*, 10, 375–383. https://doi.org/10.2147/DMSO.S130810

Corsa, C. A. S., Walsh, C. M., Bagchi, D. P., Foss Freitas, M. C., Li, Z., Hardij, J., Granger, K., Mori, H., Schill, R. L., Lewis, K. T., Maung, J. N., Azaria, R. D., Rothberg, A. E., Oral, E. A., & MacDougald, O. A. (2021). Adipocyte-specific deletion of lamin A/C largely models human familial partial lipodystrophy type 2. *Diabetes*, 70(9), 1970–1984. https://doi.org/10.2337/db20-1001

Corvillo, F., & López-Trascasa, M. (2018). Acquired partial lipodystrophy and C3 glomerulopathy: Dysregulation of the complement system as a common mechanism. *Nefrología (English Edition)*, 38(3), 258–266. https://doi.org/10.1016/j.nefroe.2018.04.002

Corvillo, F., Aparicio, V., López-Lera, A., Garrido, S., Araújo-Vilar, D., de Miguel, M. P., & López-Trascasa, M. (2018). Autoantibodies against perilipin 1 as a cause of acquired generalized lipodystrophy. *Frontiers in Immunology*, 9. https://doi.org/10.3389/fimmu.2018.02142

Corvillo, F., Abel, B. S., López-Lera, A., Ceccarini, G., Magno, S., Santini, F., Araújo-Vilar, D., Brown, R. J., Nozal, P., & López-Trascasa, M. (2022). Characterization and clinical association of autoantibodies against perilipin 1 in patients with acquired generalized lipodystrophy. *Diabetes*, 72(1), 71–84. https://doi.org/10.2337/db21-1086

de Melo, M. E. C., da Silva, L. M. G., Cavalcante, A. C. C., Lima, J. G., & Campos, J. T. A. de M. (2025). The role of the AGPAT2 gene in adipose tissue biology and congenital generalized lipodystrophy pathophysiology. *International Journal of Molecular Sciences*, 26(11), 5416. https://doi.org/10.3390/ijms26115416

Diagnosis and management of lipodystrophy syndromes: A multi-society practice guideline | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic. (n.d.). Retrieved January 19, 2026, from https://academic.oup.com/jcem/article/101/12/4500/2764979

Engin, A. B. (2017). What is lipotoxicity? In A. B. Engin & A. Engin (Eds.), *Obesity and lipotoxicity* (pp. 197–220). Springer International Publishing. https://doi.org/10.1007/978-3-319-48382-5_8

Fourman, L. T., & Grinspoon, S. K. (2022). Approach to the patient with lipodystrophy. *The Journal of Clinical Endocrinology & Metabolism*, 107(6), 1714–1726. https://doi.org/10.1210/clinem/dgac079

Gale, S. E., Frolov, A., Han, X., Bickel, P. E., Cao, L., Bowcock, A., Schaffer, J. E., & Ory, D. S. (2006). A regulatory role for 1-acylglycerol-3-phosphate-O-acyltransferase 2 in adipocyte differentiation. *Journal of Biological Chemistry*, 281(16), 11082–11089. https://doi.org/10.1074/jbc.M509612200

Garg, A. (2011). Lipodystrophies: Genetic and acquired body fat disorders. *The Journal of Clinical Endocrinology & Metabolism*, 96(11), 3313–3325. https://doi.org/10.1210/jc.2011-1159

Gilio, D., Foss-Freitas, M., & Oral, E. A. (2025). Clinical guidance for lipodystrophy syndromes: From diagnosis and work-up to treatment. *Current Diabetes Reports*, 25(1), 47. https://doi.org/10.1007/s11892-025-01603-4

Giralt, M., Domingo, P., Quesada-López, T., Cereijo, R., & Villarroya, F. (2025). Lipodystrophy in HIV: Evolving challenges and unresolved questions. *International Journal of Molecular Sciences*, 26(14), 6546. https://doi.org/10.3390/ijms26146546

Godoy-Matos, A. F., Valério, C. M., Bragança, J. B. e., Oliveira, R. de A., Zagury, R. L., Lustosa, R. de P., Camargo, G. C., Nascimento, C. A. da S., & Moreira, R. O. (2015). Evaluation of epicardial adipose tissue in familial partial lipodystrophy. *Diabetology & Metabolic Syndrome*, 7(1), 29. https://doi.org/10.1186/s13098-015-0024-5

Gonzalo, S., Kreienkamp, R., & Askjaer, P. (2017). Hutchinson-Gilford progeria syndrome: A premature aging disease caused by LMNA gene mutations. *Ageing Research Reviews*, 33, 18–29. https://doi.org/10.1016/j.arr.2016.06.007

Grivas, D., González-Rajal, Á., Guerrero Rodríguez, C., Garcia, R., & de la Pompa, J. L. (2020). Loss of caveolin-1 and caveolae leads to increased cardiac cell stiffness and functional decline of the adult zebrafish heart. *Scientific Reports*, 10(1), 12816. https://doi.org/10.1038/s41598-020-68802-9

Guzman, N., & Vijayan, V. (2025). HIV-associated lipodystrophy. In *StatPearls*. StatPearls Publishing.

Hussain, I., & Garg, A. (2016). Lipodystrophy syndromes. *Endocrinology and Metabolism Clinics of North America*, 45(4), 783–797. https://doi.org/10.1016/j.ecl.2016.06.012

Kikuchi, A., & Takamura, T. (2017). Where does liver fat go? A possible molecular link between fatty liver and diabetes. *Journal of Diabetes Investigation*, 8(2), 152–154. https://doi.org/10.1111/jdi.12573

Lamothe, S., Ancel, P., Belalem, I., Lecaque, L., Fournel, J., Jacquier, A., Houhou, Z., Julla, J.-B., Gautier, J.-F., Vigouroux, C., Gaborit, B., & Vatier, C. (2025). Increased epicardial adipose tissue is part of the phenotype of LMNA-associated partial lipodystrophy and could contribute to increased cardiovascular risk. *Diabetes & Metabolism*, 51(6), 101710. https://doi.org/10.1016/j.diabet.2025.101710

Li, Y., Yang, X., Peng, L., Xia, Q., Zhang, Y., Huang, W., Liu, T., & Jia, D. (2022). Role of seipin in human diseases and experimental animal models. *Biomolecules*, 12(6), 840. https://doi.org/10.3390/biom12060840

Lima, J. G., Nobrega, L. H. C., Lima, N. N., dos Santos, M. C. F., Silva, P. H. D., Baracho, M. de F. P., Lima, D. N., Campos, J. T. A. de M., Ferreira, L. C., Freire Neto, F. P., Mendes-Aguiar, C. de O., & Jeronimo, S. M. B. (2018). Causes of death in patients with Berardinelli-Seip congenital generalized lipodystrophy. *PLOS ONE*, 13(6), e0199052. https://doi.org/10.1371/journal.pone.0199052

Lima, J. G., Lima, L. N., Araujo, V. Y. B., Nobrega, L. H. C., & Campos, J. T. A. de M. (2025). Diagnosis of congenital and acquired generalized lipodystrophies—Similarities and differences. *Endocrines*, 6(4), 55. https://doi.org/10.3390/endocrines6040055

Liu, Q., Bengmark, S., & Qu, S. (2010). The role of hepatic fat accumulation in pathogenesis of non-alcoholic fatty liver disease (NAFLD). *Lipids in Health and Disease*, 9, 42. https://doi.org/10.1186/1476-511X-9-42

Madsen, M. S., Broekema, M. F., Madsen, M. R., Koppen, A., Borgman, A., Gräwe, C., Thomsen, E. G. K., Westland, D., Kranendonk, M. E. G., Koerkamp, M. G., Hamers, N., Bonvin, A. M. J. J., Pittol, J. M. R., Natarajan, K. N., Kersten, S., Holstege, F. C. P., Monajemi, H., van Mil, S. W. C., Vermeulen, M., … Kalkhoven, E. (2022). PPARγ lipodystrophy mutants reveal intermolecular interactions required for enhancer activation. *Nature Communications*, 13(1), 7090. https://doi.org/10.1038/s41467-022-34766-9

Maung, J. N., Schill, R. L., Nishii, A., Foss de Freitas, M., Obua, B. N., Nygård, M., Mendez-Casillas, M. D., Hermsmeyer, I. D. K., Gilio, D., Besci, O., Chen, Y., Desrosiers, B., Adler, R. E., Gomes, A. D., Guler, M. C., Mori, H., Uranga, R. M., Li, Z., Hariri, H., … MacDougald, O. A. (2026). Altered lipid metabolism and inflammatory programs associate with adipocyte loss in familial partial lipodystrophy 2. *The Journal of Clinical Investigation*, 136(1). https://doi.org/10.1172/JCI198387

Meehan, C. A., Cochran, E., Kassai, A., Brown, R. J., & Gorden, P. (2016). Metreleptin for injection to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy. *Expert Review of Clinical Pharmacology*, 9(1), 59–68. https://doi.org/10.1586/17512433.2016.1096772

Merz, K. E., & Thurmond, D. C. (2020). Role of skeletal muscle in insulin resistance and glucose uptake. *Comprehensive Physiology*, 10(3), 785–809. https://doi.org/10.1002/cphy.c190029

Misra, A., & Garg, A. (2003). Clinical features and metabolic derangements in acquired generalized lipodystrophy: Case reports and review of the literature. *Medicine*, 82(2), 129–146. https://doi.org/10.1097/00005792-200303000-00007

Nephritic factor—An overview | ScienceDirect Topics. (n.d.). Retrieved May 3, 2026, from https://www.sciencedirect.com/topics/medicine-and-dentistry/nephritic-factor

Oswiecimska, J. (n.d.). *A patient with Berardinelli-Seip syndrome, novel AGPAT2 splicesite mutation and concomitant development of non-diabetic polyneuropathy - Journal of Clinical Research in Pediatric Endocrinology*. Retrieved January 19, 2026, from https://jcrpe.org/articles/doi/jcrpe.galenos.2018.2018.0227

Patni, N., Chard, C., Araújo-Vilar, D., Phillips, H., Magee, D. A., & Akinci, B. (2024). Diagnosis, treatment and management of lipodystrophy: The physician perspective on the patient journey. *Orphanet Journal of Rare Diseases*, 19(1), 263. https://doi.org/10.1186/s13023-024-03245-3

Poulos, S. P., Dodson, M. V., Culver, M. F., & Hausman, G. J. (2016). The increasingly complex regulation of adipocyte differentiation. *Experimental Biology and Medicine*, 241(5), 449–456. https://doi.org/10.1177/1535370215619041

Rajab, A., Straub, V., McCann, L. J., Seelow, D., Varon, R., Barresi, R., Schulze, A., Lucke, B., Lützkendorf, S., Karbasiyan, M., Bachmann, S., Spuler, S., & Schuelke, M. (2010). Fatal cardiac arrhythmia and long-QT syndrome in a new form of congenital generalized lipodystrophy with muscle rippling (CGL4) due to PTRF-CAVIN mutations. *PLOS Genetics*, 6(3), e1000874. https://doi.org/10.1371/journal.pgen.1000874

Rodriguez, A. J., Mastronardi, C. A., & Paz-Filho, G. J. (2015). New advances in the treatment of generalized lipodystrophy: Role of metreleptin. *Therapeutics and Clinical Risk Management*, 11, 1391–1400. https://doi.org/10.2147/TCRM.S66521

Salle-Teyssières, L., Auclair, M., Terro, F., Nemani, M., Elsayed, S. M., Elsobky, E., Lathrop, M., Délépine, M., Lascols, O., Capeau, J., Magré, J., & Vigouroux, C. (2016). Maladaptative autophagy impairs adipose function in congenital generalized lipodystrophy due to cavin-1 deficiency. *The Journal of Clinical Endocrinology & Metabolism*, 101(7), 2892–2904. https://doi.org/10.1210/jc.2016-1086

Santoro, A., McGraw, T. E., & Kahn, B. B. (2021). Insulin action in adipocytes, adipose remodeling, and systemic effects. *Cell Metabolism*, 33(4), 748–757. https://doi.org/10.1016/j.cmet.2021.03.019

Search ClinicalTrials.gov for: Lipodystrophy | list results | ClinicalTrials.gov. (n.d.). Retrieved April 15, 2026, from https://clinicaltrials.gov/search

Sies, H. (2020). Oxidative stress: Concept and some practical aspects. *Antioxidants*, 9(9), 852. https://doi.org/10.3390/antiox9090852

Soares, R. M. V., Silva, M. A. da, Campos, J. T. A. de M., & Lima, J. G. (2024). Familial partial lipodystrophy resulting from loss-of-function PPARγ pathogenic variants: Phenotypic, clinical, and genetic features. *Frontiers in Endocrinology*, 15. https://doi.org/10.3389/fendo.2024.1394102

Sommer, N., Roumane, A., Han, W., Delibegović, M., Rochford, J. J., & Mcilroy, G. D. (2022). Gene therapy restores adipose tissue and metabolic health in a pre-clinical mouse model of lipodystrophy. *Molecular Therapy Methods & Clinical Development*, 27, 206–216. https://doi.org/10.1016/j.omtm.2022.09.014

Stea, D. M., & D'Alessio, A. (2025). Caveolae: Metabolic platforms at the crossroads of health and disease. *International Journal*

of Molecular Sciences, *26*(7), 2918. https://doi.org/10.3390/ijms26072918

Talman, A. H., Psaltis, P. J., Cameron, J. D., Meredith, I. T., Seneviratne, S. K., & Wong, D. T. L. (2014). Epicardial adipose tissue: Far more than a fat depot. *Cardiovascular Diagnosis and Therapy*, *4*(6), 416–429. https://doi.org/10.3978/j.issn.2223-3652.2014.11.05

Tiwari, M., Roumane, A., Sommer, N., Han, W., Delibegović, M., Rochford, J. J., & Mcilroy, G. D. (2024). Preclinical evaluation of tissue-selective gene therapies for congenital generalised lipodystrophy. *Gene Therapy*, *31*(9), 445–454. https://doi.org/10.1038/s41434-024-00471-z

Tsoukas, M. A., Farr, O. M., & Mantzoros, C. S. (2015). Leptin in congenital and HIV-associated lipodystrophy. *Metabolism*, *64*(1), 47–59. https://doi.org/10.1016/j.metabol.2014.07.017

Varlet, A.-A., Helfer, E., & Badens, C. (2020). Molecular and mechanobiological pathways related to the physiopathology of FPLD2. *Cells*, *9*(9), 1947. https://doi.org/10.3390/cells9091947

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Chiao Yun Cheng is a high school junior at Great Hearts Anthem Prep in Anthem, Arizona. She is a young researcher with a deep interest in biochemistry, genetics, and chemical engineering. She plans to pursue a degree in biochemistry or a related field, such as chemical engineering, in college. Through this research project, Chiao Yun developed a deeper passion for lab research and gained a deeper understanding of people with rare diseases. In the future, she hopes to develop more treatments for individuals with rare diseases and aims to solve existing problems in medical and scientific areas.

Beyond her studies and research, Chiao Yun is passionate about playing piano and drawing. She uses them as a way to relax and generate ideas. She also enjoys traveling and learning about different cultures, which helps broaden her perspective on the world.

Mentor Contribution Statement

Dr. Hamidreza Shaye provided guidance throughout the research and writing process by offering conceptual advice, academic direction, and methodological choices. In addition, he offered guidance on choosing research questions and identifying relevant and appropriate sources for citation. He advised on using academic tools to produce images and

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analyze information. He helped refine the paper's tone and scope by giving advisory feedback.

Dr. Lauren Tetz served as an advisor to the research project. She gave suggestions on how to structure the paper and strengthen the academic rigor. She also provided resources that helped structure the paper's content.

Dr. Shaye and Dr. Tetz did not participate in the writing process of the manuscript or the production of the images. The student determined the aim of this research and conducted the literature review independently.