

# [Commentary: heart fat infiltration in subjects with and without coronary artery d...](https://assignbuster.com/commentary-heart-fat-infiltration-in-subjects-with-and-without-coronary-artery-disease/)

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A commentary on

Heart Fat Infiltration In Subjects With and Without Coronary Artery Disease   
*by Mazzali G, Fantin F, Zoico E, Sepe A, Bambace C, Faccioli S, et al. J Clin Endocrinol Metab (2015)100 (9): 3364–71. doi: 10. 1210/jc. 2015-1787*

Mazzali et al. showed myocardial steatosis in subjects with coronary artery disease (CAD), describing a significant increase in lipid droplets (LDs) and metabolically active adipocytes interspersed among cardiomyocytes, which were positively associated with changes in BMI and circulating leptin and negatively with adiponectin ( [1](#B1) ).

The authors used perilipin (PLIN-1) and adipophilin (PLIN-2) markers to detect, respectively, adipocyte or cardiomyocytes LDs and reported that while PLIN-2 was detected in all subjects, about 39% of both CAD and non-CAD patients expressed PLIN-1, showing apparently no relationship in tissue fat distribution between patients and controls. Yet, when intra-cardiomyocyte fat deposits were evaluated, subjects with CAD expressed higher levels of both PLIN-1 and PLIN-2 and higher LD diameter than controls, besides apoptosis and hypoxia markers ( [1](#B1) ). The observed higher amount of PLIN-1 and PLIN-2, evaluated by immunohistochemistry rather than gene expression, correlated with some metabolic serum markers. While PLIN-1 seems to be associated with larger triacylglycerol LDs in mature adipocytes, PLIN-2 is mainly associated with LDs in non-steroidal adipose tissues ( [2](#B2) ). LDs are usually collectively grouped in the PAT family, which includes perilipins (P), ADRP (also called adipophilin) (A), Tip-47 (tail-interacting protein of 47 kDa) (T), hence the acronym PAT. They also include S3–12 and OXPAT (also termed MLDP or LSDP5) and recently, respectively, named PLIN1, PLIN2, PLIN3, PLIN4, and PLIN5 ( [3](#B3) ). The use of PLIN-1 and PLIN-2 is particularly useful in evaluating fat deposits in tissues, although some question still remains, as LD proteins are expressed in a highly complex way during lipidogenesis in the adipose cell ( [4](#B4) ). In this perspective, some further markers to improve adipocyte detection, such as CIDEC, might be suggested ( [5](#B5) – [7](#B7) ), in order to better differentiate adipocytes from LDs and also to reduce bias during the immunological detection of perilipin isoforms, as they share a high sequence homology and modification in their N- or C-terminus, depending on their function ( [4](#B4) ). Unlike other perilipins, PLIN-1 is widely associated with any LD moving from membranes and endoplasmic reticulum to fat droplets during lipid synthesis in any steroidogenic cells and probably may not be a specific marker of isolated white adipocytes ( [8](#B8) ). Furthermore, the expression of PLIN-2, which the authors associated with LDs in cells different from adipocytes, has also been reported in brown adipocytes ( [9](#B9) ) and adipocytes from white adipose tissue may express adipophilin (PLIN-2), in particular metabolic conditions ( [4](#B4) ). Expanding this investigation with further insights may improve the meaning of the reported evidence. For example, perilipin-5 (PLIN-5), which is an important marker in cardiac control of lipolysis ( [10](#B10) ), is particularly abundant in the heart ( [11](#B11) ), and as its overexpression could lead to myocardial steatosis, including this marker in future research on myocardial lipidology, particularly in CAD, may improve our knowledge and ability to address this issue ( [12](#B12) , [13](#B13) ).

Isolated adipocytes within the myocardium are not a true novelty ( [14](#B14) ), as adipose tissue was described also within myocardial ventricular walls ( [15](#B15) ) and recently confirmed in atrial dysfunction ( [16](#B16) ). Further research in this field should address the origin of these adipocytes, e. g., one could investigate the presence of fibroblast-like preadipocytes in the atrium, which may add further insights on the issue ( [17](#B17) ). The origin of these adipocytes is fundamental to comprehend their role in CAD. Epicardial adipose tissue (EAT) in specimens may cause possible bias, as adipocytes observed within the atrium may derive from epicardium or even a tissue-related mesenchymal transdifferentiation mechanism ( [1](#B1) ). Interestingly, pericytes may be sources of preadipocytes, likewise endothelial cells in the adipose tissue, and represent a possible source of the observed adipocytes ( [18](#B18) , [19](#B19) ). Once highlighted the origin of interspersed adipocytes, one could question, which is the possible role of these cells, namely if they even play a major role in some compensatory mechanism triggered by myocardial tissue to prevent serious damage due to CAD. The recently reported evidence that at least in skeletal muscle, the increase in PLIN-2 correlated with an improvement in insulin sensitivity in diabetic subjects is intriguing ( [20](#B20) ). Despite the observation of apoptotic and stress response, signals associated with hypoxia and mitochondrial impairment and dysfunction lead to LDs formation as a positive response to cellular stress ( [21](#B21) ). In this context, observed adipocytes, which would deserve further clarification about their nature, may shed a light on a possible role in the heart reaction to cardiovascular damage.

PLIN-1 is expressed also by brown adipocytes ( [8](#B8) , [22](#B22) ). Further investigation on the main brown adipocyte marker, the uncoupling protein-1 (UCP-1), should differentiate the nature of the observed adipocytes ( [23](#B23) , [24](#B24) ). This fact may be important to clarify the role of these cells in the myocardial tissue of CAD patients. Following a suggestion about the possible existence of adipocytes from adult stem cells (ASCs), brown adipose tissue (BAT) is an interesting precursor of cardiomyocytes, as subepicardial fat embryologically derives from BAT and because in aged hearts, a protective mechanism of differentiation of subepicardial stem cells into BAT was recently described ( [23](#B23) ). The use of UCP-1, to elucidate the nature of interspersed adipocytes, may support the hypothesis that adipocytes serve as an important source to compensate myocardial damage in CAD patients. Adipocytes within myocardial tissue may even have a protective, damage-repairing role, a suggestion supported by the recent evidence that adipose tissue-derived stem cells exert paracrine actions that may have therapeutic effect on myocardial dysfunction ( [25](#B25) ).

While the authors showed a greater myocardial steatosis in subjects with CAD compared with controls, further research should deepen the role of interspersed adipocytes, their origin, and cytological nature. Suggestions coming from animal models and further experimental research will add insights to the nature of this study, highlighting the mechanism of the mesenchymal source and the role of these cells in the atrium.

## Author Contributions

SC: planned, conceived, wrote, and submitted the whole manuscript.

## Conflict of Interest Statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## References

1. Mazzali G, Fantin F, Zoico E, Sepe A, Bambace C, Faccioli S, et al. Heart fat infiltration in subjects with and without coronary artery disease. *J Clin Endocrinol Metab* (2015)100 (9): 3364–71. doi: 10. 1210/jc. 2015-1787

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=26186298) | [CrossRef Full Text](http://dx.doi.org/10.1210/jc.2015-1787) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Heart+fat+infiltration+in+subjects+with+and+without+coronary+artery+disease&author=G.+Mazzali&author=F.+Fantin&author=E.+Zoico&author=A.+Sepe&author=C.+Bambace&author=S.+Faccioli&journal=J+Clin+Endocrinol+Metab&publication_year=2015&volume=100&pages=3364–71&doi=10.1210/jc.2015-1787&pmid=26186298)

2. Dalen KT, Schoonjans K, Ulven SM, Weedon-Fekjaer MS, Bentzen TG, Koutnikova H, et al. Adipose tissue expression of the lipid droplet-associating proteins S3-12 and perilipin is controlled by peroxisome proliferator-­activated receptor-gamma. *Diabetes* (2004)53 (5): 1243–52. doi: 10. 2337/diabetes. 53. 5. 1243

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=15111493) | [CrossRef Full Text](http://dx.doi.org/10.2337/diabetes.53.5.1243) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Adipose+tissue+expression+of+the+lipid+droplet-associating+proteins+S3-12+and+perilipin+is+controlled+by+peroxisome+proliferator-­activated+receptor-gamma&author=K.+T.+Dalen&author=K.+Schoonjans&author=S.+M.+Ulven&author=M.+S.+Weedon-Fekjaer&author=T.+G.+Bentzen&author=H.+Koutnikova&journal=Diabetes&publication_year=2004&volume=53&pages=1243–52&doi=10.2337/diabetes.53.5.1243&pmid=15111493)

3. Kimmel AR, Brasaemle DL, McAndrews-Hill M, Sztalryd C, Londos C. Adoption of PERILIPIN as a unifying nomenclature for the mammalian PAT-family of intracellular lipid storage droplet proteins. *J Lipid Res* (2010)51 (3): 468–71. doi: 10. 1194/jlr. R000034

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19638644) | [CrossRef Full Text](http://dx.doi.org/10.1194/jlr.R000034) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Adoption+of+PERILIPIN+as+a+unifying+nomenclature+for+the+mammalian+PAT-family+of+intracellular+lipid+storage+droplet+proteins&author=A.+R.+Kimmel&author=D.+L.+Brasaemle&author=M.+McAndrews-Hill&author=C.+Sztalryd&author=C.+Londos&journal=J+Lipid+Res&publication_year=2010&volume=51&pages=468–71&doi=10.1194/jlr.R000034&pmid=19638644)

4. Heid H, Rickelt S, Zimbelmann R, Winter S, Schumacher H, Dörflinger Y, et al. On the formation of lipid droplets in human adipocytes: the organization of the perilipin-vimentin cortex. *PLoS One* (2014)9 (2): e90386. doi: 10. 1371/journal. pone. 0090386

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=24587346) | [CrossRef Full Text](http://dx.doi.org/10.1371/journal.pone.0090386) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=On+the+formation+of+lipid+droplets+in+human+adipocytes:+the+organization+of+the+perilipin-vimentin+cortex&author=H.+Heid&author=S.+Rickelt&author=R.+Zimbelmann&author=S.+Winter&author=H.+Schumacher&author=Y.+Dörflinger&journal=PLoS+One&publication_year=2014&volume=9&pages=e90386&doi=10.1371/journal.pone.0090386&pmid=24587346)

5. Sun Z, Gong J, Wu H, Xu W, Wu L, Xu D, et al. Perilipin1 promotes unilocular lipid droplet formation through the activation of Fsp27 in adipocytes. *Nat Commun* (2013)4 : 1594. doi: 10. 1038/ncomms2581

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=23481402) | [CrossRef Full Text](http://dx.doi.org/10.1038/ncomms2581) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Perilipin1+promotes+unilocular+lipid+droplet+formation+through+the+activation+of+Fsp27+in+adipocytes&author=Z.+Sun&author=J.+Gong&author=H.+Wu&author=W.+Xu&author=L.+Wu&author=D.+Xu&journal=Nat+Commun&publication_year=2013&volume=4&pages=1594&doi=10.1038/ncomms2581&pmid=23481402)

6. Moreno-Navarrete JM, Ortega F, Serrano M, Rodriguez-Hermosa JI, Ricart W, Mingrone G, et al. CIDEC/FSP27 and PLIN1 gene expression run in parallel to mitochondrial genes in human adipose tissue, both increasing after weight loss. *Int J Obes (Lond)* (2014)38 (6): 865–72. doi: 10. 1038/ijo. 2013. 171

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=24126816) | [CrossRef Full Text](http://dx.doi.org/10.1038/ijo.2013.171) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=CIDEC/FSP27+and+PLIN1+gene+expression+run+in+parallel+to+mitochondrial+genes+in+human+adipose+tissue,+both+increasing+after+weight+loss&author=J.+M.+Moreno-Navarrete&author=F.+Ortega&author=M.+Serrano&author=J.+I.+Rodriguez-Hermosa&author=W.+Ricart&author=G.+Mingrone&journal=Int+J+Obes+(Lond)&publication_year=2014&volume=38&pages=865–72&doi=10.1038/ijo.2013.171&pmid=24126816)

7. Grahn TH, Zhang Y, Lee MJ, Sommer AG, Mostoslavsky G, Fried SK, et al. FSP27 and PLIN1 interaction promotes the formation of large lipid droplets in human adipocytes. *Biochem Biophys Res Commun* (2013)432 (2): 296–301. doi: 10. 1016/j. bbrc. 2013. 01. 113

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=23399566) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.bbrc.2013.01.113) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=FSP27+and+PLIN1+interaction+promotes+the+formation+of+large+lipid+droplets+in+human+adipocytes&author=T.+H.+Grahn&author=Y.+Zhang&author=M.+J.+Lee&author=A.+G.+Sommer&author=G.+Mostoslavsky&author=S.+K.+Fried&journal=Biochem+Biophys+Res+Commun&publication_year=2013&volume=432&pages=296–301&doi=10.1016/j.bbrc.2013.01.113&pmid=23399566)

8. Skinner JR, Harris LA, Shew TM, Abumrad NA, Wolins NE. Perilipin 1 moves between the fat droplet and the endoplasmic reticulum. *Adipocyte* (2013)2 (2): 80–6. doi: 10. 4161/adip. 22864

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=23805403) | [CrossRef Full Text](http://dx.doi.org/10.4161/adip.22864) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Perilipin+1+moves+between+the+fat+droplet+and+the+endoplasmic+reticulum&author=J.+R.+Skinner&author=L.+A.+Harris&author=T.+M.+Shew&author=N.+A.+Abumrad&author=N.+E.+Wolins&journal=Adipocyte&publication_year=2013&volume=2&pages=80–6&doi=10.4161/adip.22864&pmid=23805403)

9. Yu J, Zhang S, Cui L, Wang W, Na H, Zhu X, et al. Lipid droplet remodeling and interaction with mitochondria in mouse brown adipose tissue during cold treatment. *Biochim Biophys Acta* (2015)1853 (5): 918–28. doi: 10. 1016/j. bbamcr. 2015. 01. 020

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=25655664) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.bbamcr.2015.01.020) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Lipid+droplet+remodeling+and+interaction+with+mitochondria+in+mouse+brown+adipose+tissue+during+cold+treatment&author=J.+Yu&author=S.+Zhang&author=L.+Cui&author=W.+Wang&author=H.+Na&author=X.+Zhu&journal=Biochim+Biophys+Acta&publication_year=2015&volume=1853&pages=918–28&doi=10.1016/j.bbamcr.2015.01.020&pmid=25655664)

10. Pollak NM, Jaeger D, Kolleritsch S, Zimmermann R, Zechner R, Lass A, et al. The interplay of protein kinase A and perilipin 5 regulates cardiac lipolysis. *J Biol Chem* (2015)290 (3): 1295–306. doi: 10. 1074/jbc. M114. 604744

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=25418045) | [CrossRef Full Text](http://dx.doi.org/10.1074/jbc.M114.604744) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=The+interplay+of+protein+kinase+A+and+perilipin+5+regulates+cardiac+lipolysis&author=N.+M.+Pollak&author=D.+Jaeger&author=S.+Kolleritsch&author=R.+Zimmermann&author=R.+Zechner&author=A.+Lass&journal=J+Biol+Chem&publication_year=2015&volume=290&pages=1295–306&doi=10.1074/jbc.M114.604744&pmid=25418045)

11. Kuramoto K, Okamura T, Yamaguchi T, Nakamura TY, Wakabayashi S, Morinaga H, et al. Perilipin 5, a lipid droplet-binding protein, protects heart from oxidative burden by sequestering fatty acid from excessive oxidation. *J Biol Chem* (2012)287 (28): 23852–63. doi: 10. 1074/jbc. M111. 328708

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=22532565) | [CrossRef Full Text](http://dx.doi.org/10.1074/jbc.M111.328708) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Perilipin+5,+a+lipid+droplet-binding+protein,+protects+heart+from+oxidative+burden+by+sequestering+fatty+acid+from+excessive+oxidation&author=K.+Kuramoto&author=T.+Okamura&author=T.+Yamaguchi&author=T.+Y.+Nakamura&author=S.+Wakabayashi&author=H.+Morinaga&journal=J+Biol+Chem&publication_year=2012&volume=287&pages=23852–63&doi=10.1074/jbc.M111.328708&pmid=22532565)

12. Wang H, Sreenivasan U, Gong DW, O’Connell KA, Dabkowski ER, Hecker PA, et al. Cardiomyocyte-specific perilipin 5 overexpression leads to myocardial steatosis and modest cardiac dysfunction. *J Lipid Res* (2013)54 (4): 953–65. doi: 10. 1194/jlr. M032466

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=23345411) | [CrossRef Full Text](http://dx.doi.org/10.1194/jlr.M032466) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Cardiomyocyte-specific+perilipin+5+overexpression+leads+to+myocardial+steatosis+and+modest+cardiac+dysfunction&author=H.+Wang&author=U.+Sreenivasan&author=D.+W.+Gong&author=K.+A.+O’Connell&author=E.+R.+Dabkowski&author=P.+A.+Hecker&journal=J+Lipid+Res&publication_year=2013&volume=54&pages=953–65&doi=10.1194/jlr.M032466&pmid=23345411)

13. Pollak NM, Schweiger M, Jaeger D, Kolb D, Kumari M, Schreiber R, et al. Cardiac-specific overexpression of perilipin 5 provokes severe cardiac steatosis via the formation of a lipolytic barrier. *J Lipid Res* (2013)54 (4): 1092–102. doi: 10. 1194/jlr. M034710

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=23345410) | [CrossRef Full Text](http://dx.doi.org/10.1194/jlr.M034710) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Cardiac-specific+overexpression+of+perilipin+5+provokes+severe+cardiac+steatosis+via+the+formation+of+a+lipolytic+barrier&author=N.+M.+Pollak&author=M.+Schweiger&author=D.+Jaeger&author=D.+Kolb&author=M.+Kumari&author=R.+Schreiber&journal=J+Lipid+Res&publication_year=2013&volume=54&pages=1092–102&doi=10.1194/jlr.M034710&pmid=23345410)

14. Su L, Siegel JE, Fishbein MC. Adipose tissue in myocardial infarction. *Cardiovasc Pathol* (2004)13 (2): 98–102. doi: 10. 1016/S1054-8807(03)00134-0

[CrossRef Full Text](http://dx.doi.org/10.1016/S1054-8807(03)00134-0) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Adipose+tissue+in+myocardial+infarction&author=L.+Su&author=J.+E.+Siegel&author=M.+C.+Fishbein&journal=Cardiovasc+Pathol&publication_year=2004&volume=13&pages=98–102&doi=10.1016/S1054-8807(03)00134-0)

15. Ichikawa Y, Kitagawa K, Chino S, Ishida M, Matsuoka K, Tanigawa T, et al. Adipose tissue detected by multislice computed tomography in patients after myocardial infarction. *JACC Cardiovasc Imaging* (2009)2 (5): 548–55. doi: 10. 1016/j. jcmg. 2009. 01. 010

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=19442939) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.jcmg.2009.01.010) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Adipose+tissue+detected+by+multislice+computed+tomography+in+patients+after+myocardial+infarction&author=Y.+Ichikawa&author=K.+Kitagawa&author=S.+Chino&author=M.+Ishida&author=K.+Matsuoka&author=T.+Tanigawa&journal=JACC+Cardiovasc+Imaging&publication_year=2009&volume=2&pages=548–55&doi=10.1016/j.jcmg.2009.01.010&pmid=19442939)

16. Chilukoti RK, Giese A, Malenke W, Homuth G, Bukowska A, Goette A, et al. Atrial fibrillation and rapid acute pacing regulate adipocyte/adipositas-related gene expression in the atria. *Int J Cardiol* (2015)187 : 604–13. doi: 10. 1016/j. ijcard. 2015. 03. 072

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=25863735) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.ijcard.2015.03.072) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Atrial+fibrillation+and+rapid+acute+pacing+regulate+adipocyte/adipositas-related+gene+expression+in+the+atria&author=R.+K.+Chilukoti&author=A.+Giese&author=W.+Malenke&author=G.+Homuth&author=A.+Bukowska&author=A.+Goette&journal=Int+J+Cardiol&publication_year=2015&volume=187&pages=604–13&doi=10.1016/j.ijcard.2015.03.072&pmid=25863735)

17. Cawthorn WP, Scheller EL, MacDougald OA. Adipose tissue stem cells meet preadipocyte commitment: going back to the future. *J Lipid Res* (2012)53 (2): 227–46. doi: 10. 1194/jlr. R021089

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=22140268) | [CrossRef Full Text](http://dx.doi.org/10.1194/jlr.R021089) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Adipose+tissue+stem+cells+meet+preadipocyte+commitment:+going+back+to+the+future&author=W.+P.+Cawthorn&author=E.+L.+Scheller&author=O.+A.+MacDougald&journal=J+Lipid+Res&publication_year=2012&volume=53&pages=227–46&doi=10.1194/jlr.R021089&pmid=22140268)

18. Tran KV, Gealekman O, Frontini A, Zingaretti MC, Morroni M, Giordano A, et al. The vascular endothelium of the adipose tissue gives rise to both white and brown fat cells. *Cell Metab* (2012)15 (2): 222–9. doi: 10. 1016/j. cmet. 2012. 01. 008

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=22326223) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.cmet.2012.01.008) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=The+vascular+endothelium+of+the+adipose+tissue+gives+rise+to+both+white+and+brown+fat+cells&author=K.+V.+Tran&author=O.+Gealekman&author=A.+Frontini&author=M.+C.+Zingaretti&author=M.+Morroni&author=A.+Giordano&journal=Cell+Metab&publication_year=2012&volume=15&pages=222–9&doi=10.1016/j.cmet.2012.01.008&pmid=22326223)

19. Caplan AI. All MSCs are pericytes? *Cell Stem Cell* (2008)3 (3): 229–30. doi: 10. 1016/j. stem. 2008. 08. 008

[CrossRef Full Text](http://dx.doi.org/10.1016/j.stem.2008.08.008) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=All+MSCs+are+pericytes?&author=A.+I.+Caplan&journal=Cell+Stem+Cell&publication_year=2008&volume=3&pages=229–30&doi=10.1016/j.stem.2008.08.008)

20. Bosma M, Hesselink MK, Sparks LM, Timmers S, Ferraz MJ, Mattijssen F, et al. Perilipin 2 improves insulin sensitivity in skeletal muscle despite elevated intramuscular lipid levels. *Diabetes* (2012)61 : 2679–90. doi: 10. 2337/db11-1402

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=22807032) | [CrossRef Full Text](http://dx.doi.org/10.2337/db11-1402) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Perilipin+2+improves+insulin+sensitivity+in+skeletal+muscle+despite+elevated+intramuscular+lipid+levels&author=M.+Bosma&author=M.+K.+Hesselink&author=L.+M.+Sparks&author=S.+Timmers&author=M.+J.+Ferraz&author=F.+Mattijssen&journal=Diabetes&publication_year=2012&volume=61&pages=2679–90&doi=10.2337/db11-1402&pmid=22807032)

21. Lee SJ, Zhang J, Choi AM, Kim HP. Mitochondrial dysfunction induces formation of lipid droplets as a generalized response to stress. *Oxid Med Cell Longev* (2013)2013 : 327167. doi: 10. 1155/2013/327167

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=24175011) | [CrossRef Full Text](http://dx.doi.org/10.1155/2013/327167) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Mitochondrial+dysfunction+induces+formation+of+lipid+droplets+as+a+generalized+response+to+stress&author=S.+J.+Lee&author=J.+Zhang&author=A.+M.+Choi&author=H.+P.+Kim&journal=Oxid+Med+Cell+Longev&publication_year=2013&volume=2013&pages=327167&doi=10.1155/2013/327167&pmid=24175011)

22. Souza SC, Christoffolete MA, Ribeiro MO, Miyoshi H, Strissel KJ, Stancheva ZS, et al. Perilipin regulates the thermogenic actions of norepinephrine in brown adipose tissue. *J Lipid Res* (2007)48 (6): 1273–9. doi: 10. 1194/jlr. M700047-JLR200

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17401109) | [CrossRef Full Text](http://dx.doi.org/10.1194/jlr.M700047-JLR200) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Perilipin+regulates+the+thermogenic+actions+of+norepinephrine+in+brown+adipose+tissue&author=S.+C.+Souza&author=M.+A.+Christoffolete&author=M.+O.+Ribeiro&author=H.+Miyoshi&author=K.+J.+Strissel&author=Z.+S.+Stancheva&journal=J+Lipid+Res&publication_year=2007&volume=48&pages=1273–9&doi=10.1194/jlr.M700047-JLR200&pmid=17401109)

23. Rusu MC, Vrapciu AD, Hostiuc S, Hariga CS. Brown adipocytes, cardiac protection and a common adipo- and myogenic stem precursor in aged human hearts. *Med Hypotheses* (2015)85 (2): 212–4. doi: 10. 1016/j. mehy. 2015. 04. 027

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=25956736) | [CrossRef Full Text](http://dx.doi.org/10.1016/j.mehy.2015.04.027) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Brown+adipocytes,+cardiac+protection+and+a+common+adipo-+and+myogenic+stem+precursor+in+aged+human+hearts&author=M.+C.+Rusu&author=A.+D.+Vrapciu&author=S.+Hostiuc&author=C.+S.+Hariga&journal=Med+Hypotheses&publication_year=2015&volume=85&pages=212–4&doi=10.1016/j.mehy.2015.04.027&pmid=25956736)

24. Giralt M, Villarroya F. White, brown, beige/brite: different adipose cells for different functions? *Endocrinology* (2013)154 (9): 2992–3000. doi: 10. 1210/en. 2013-1403

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=23782940) | [CrossRef Full Text](http://dx.doi.org/10.1210/en.2013-1403) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=White,+brown,+beige/brite:+different+adipose+cells+for+different+functions?&author=M.+Giralt&author=F.+Villarroya&journal=Endocrinology&publication_year=2013&volume=154&pages=2992–3000&doi=10.1210/en.2013-1403&pmid=23782940)

25. Madonna R, Petrov L, Teberino MA, Manzoli L, Karam JP, Renna FV, et al. Transplantation of adipose tissue mesenchymal cells conjugated with VEGF-releasing microcarriers promotes repair in murine myocardial infarction. *Cardiovasc Res* (2015)108 (1): 39–49. doi: 10. 1093/cvr/cvv197

[PubMed Abstract](http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=26187727) | [CrossRef Full Text](http://dx.doi.org/10.1093/cvr/cvv197) | [Google Scholar](http://scholar.google.com/scholar_lookup?title=Transplantation+of+adipose+tissue+mesenchymal+cells+conjugated+with+VEGF-releasing+microcarriers+promotes+repair+in+murine+myocardial+infarction&author=R.+Madonna&author=L.+Petrov&author=M.+A.+Teberino&author=L.+Manzoli&author=J.+P.+Karam&author=F.+V.+Renna&journal=Cardiovasc+Res&publication_year=2015&volume=108&pages=39–49&doi=10.1093/cvr/cvv197&pmid=26187727)