ApoB tərkibli lipoproteinlər - rolu, metabolizmi, tənzimlənməsi

Kardiyo Mekteb -1 «Lipid ve AF» 29-30 Aprel 2023, Baku

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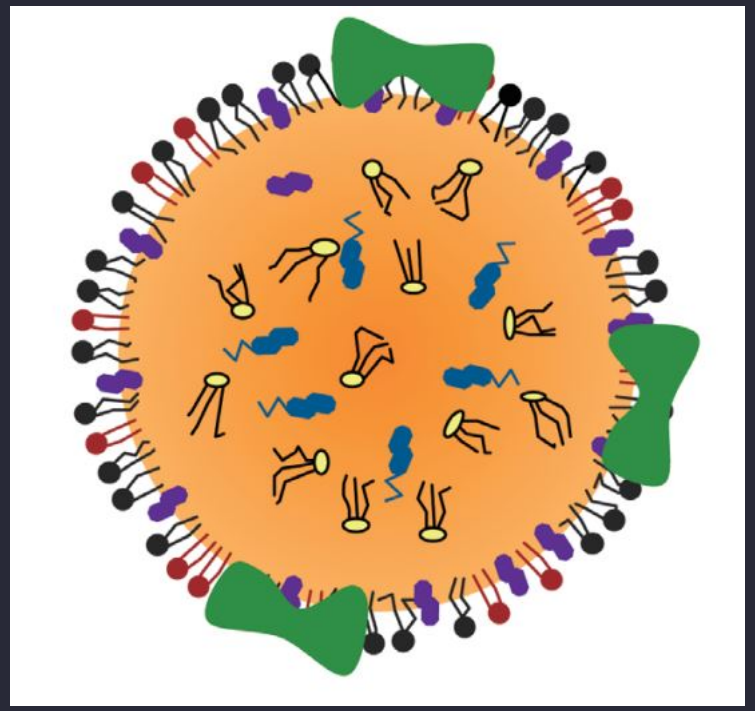
Sunum Planı

- ApoB içeren lipoproteinler
  - Şilomikron, VLDL, IDL, LDL, Lp(a)
- Yapıları
- Metabolizması
- Sınıflandırması

Lipoproteinler

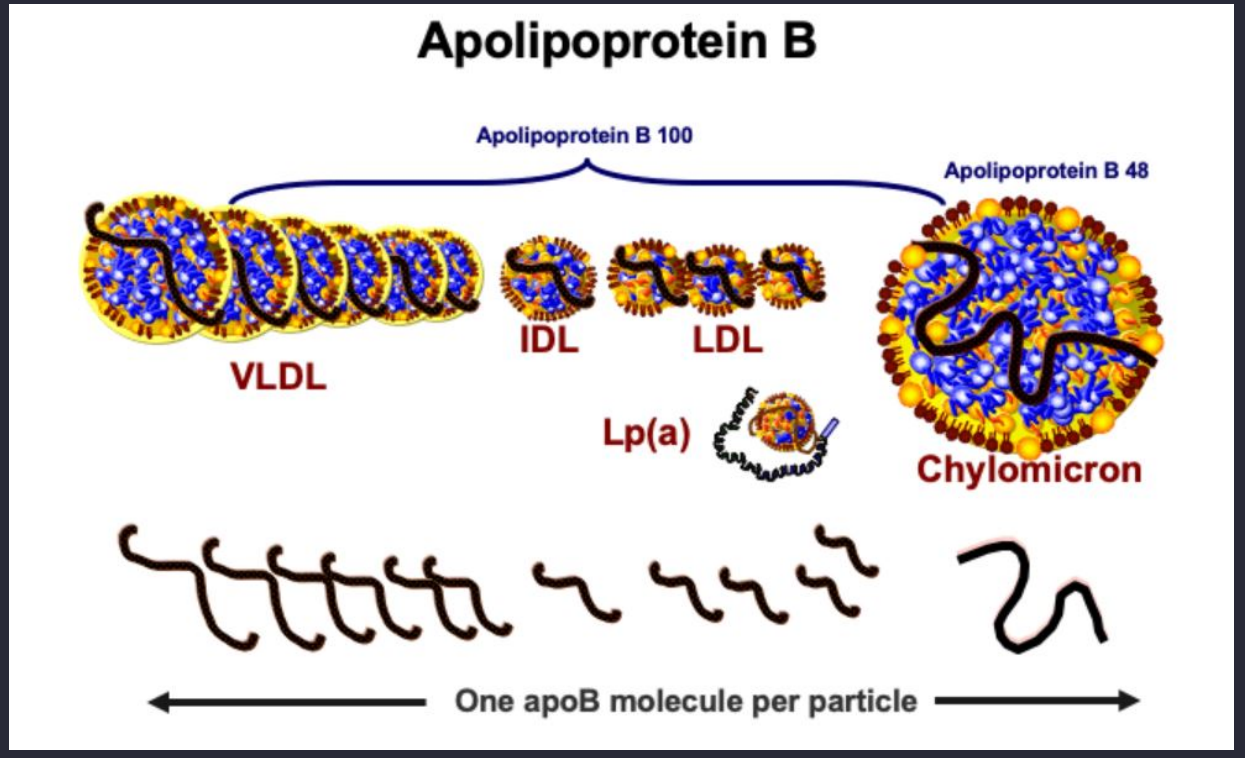


- Merkezde hidrofobik trigliserit ve kolesterol esterleri
- Yüzeyde fosfolipid ve serbest kolesterol
- Apolipoprotein

Morita SY. Metabolism and Modification of Apolipoprotein B-Containing Lipoproteins Involved in Dyslipidemia and Atherosclerosis. Biol Pharm Bull. 2016;39(1):1-24.

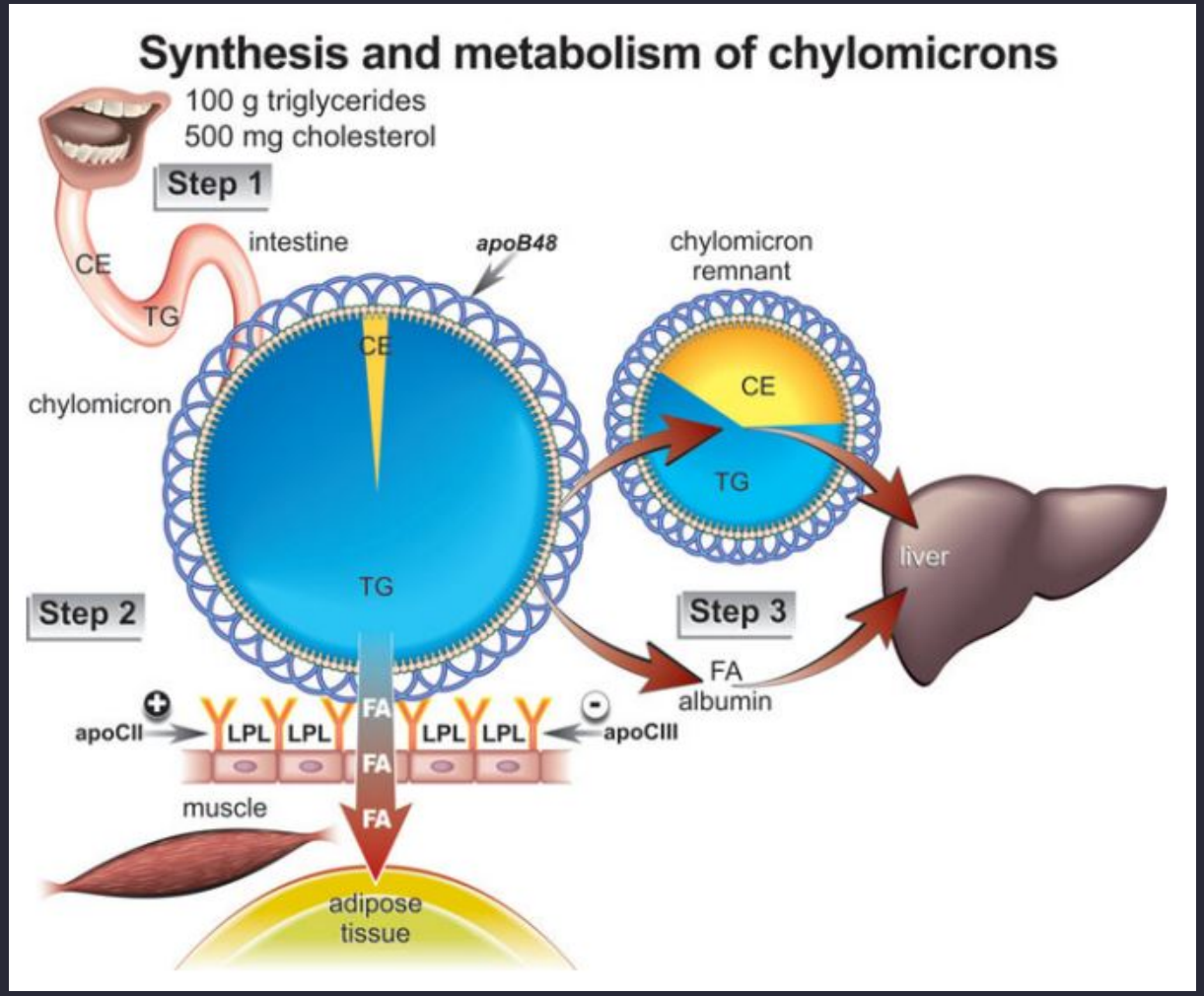
Apolipoprotein B

- ApoB48 İnce barsakta sentezlenir
- ApoB100 Karaciğerde sentezlenir



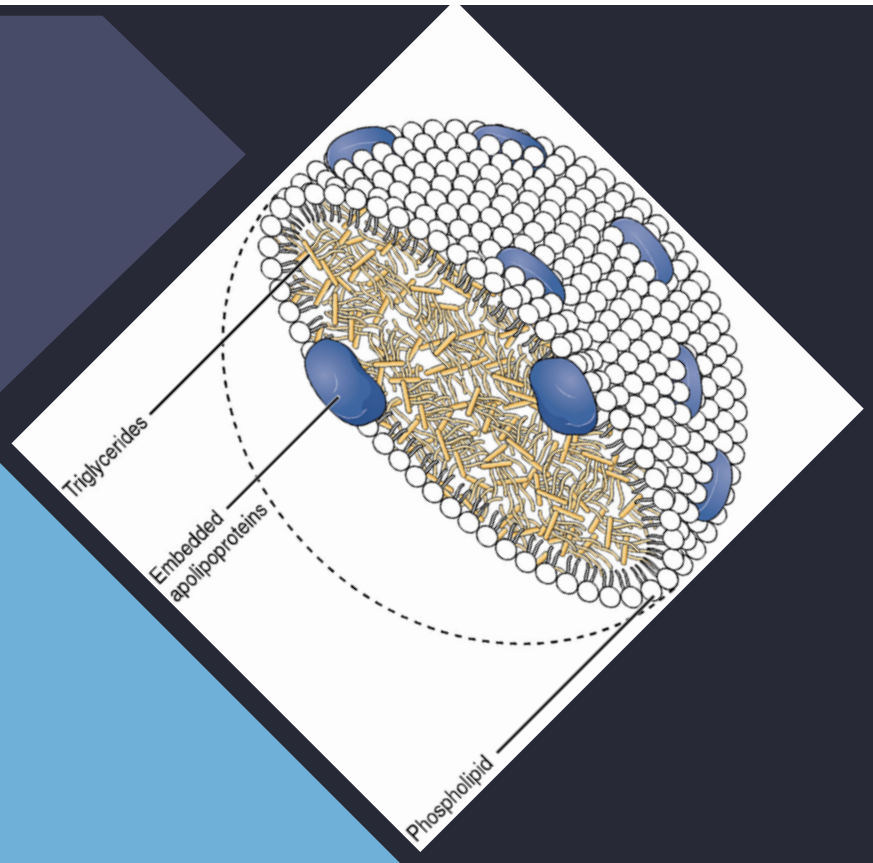
ApoB48

Ağızdan alınan lipidler şilomikronları oluşturur



Şilomikronlar LPL aracılığıyla parçalanır, artıklar KC tarafından alınır

De Graaf J, Couture P, Sniderman AD. *ApoB in Clinical Care*. Bohn Stafleu van Loghum; 2015

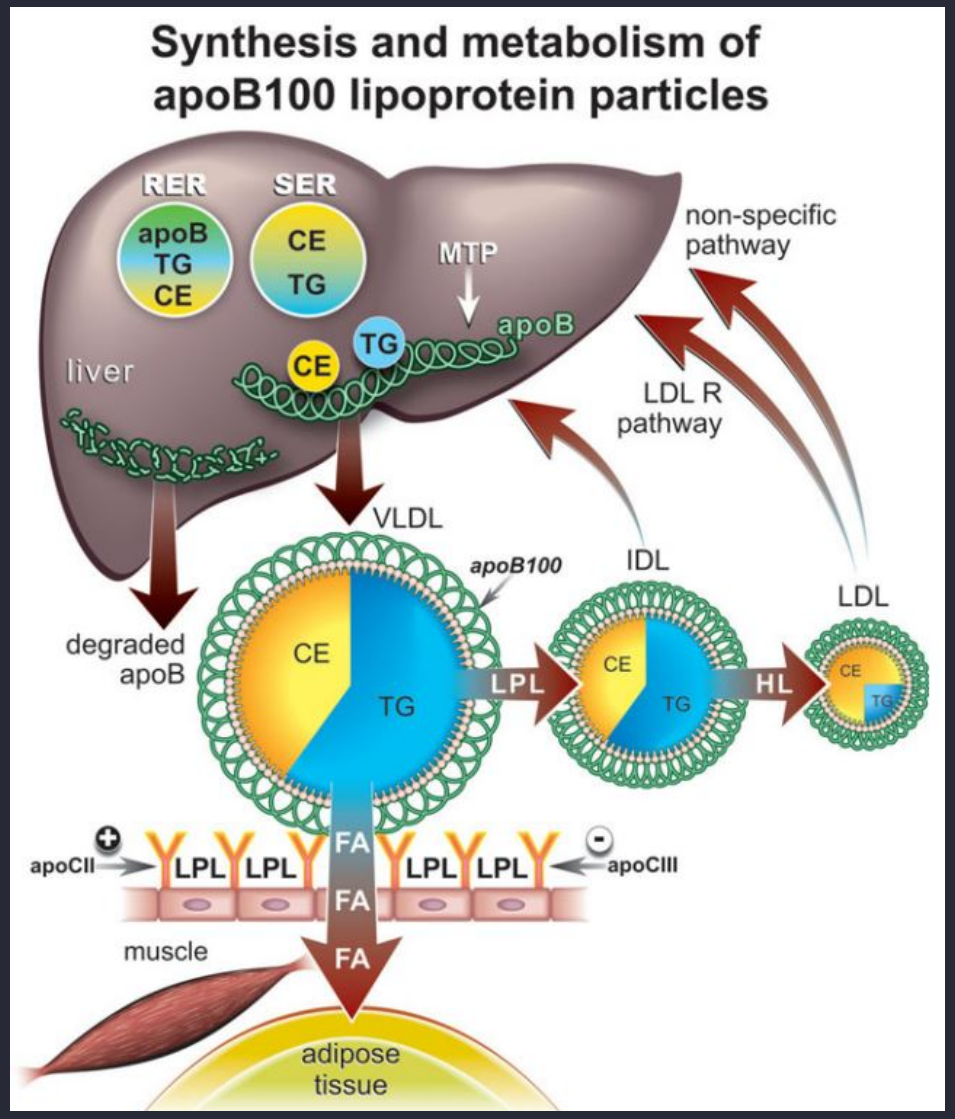


Şilomikron ve Şilomikron Kalıntıları

- Şilomikronlar büyük oldukları için endoteli geçemez bu nedenle aterojenik olmadıkları kabul edilir
- LPL şilomikronları hidrolize eder
- Apo CII LPL aktive eder Apo CIII inhibe eder
- Serbest yağ asitleri yağ ve kas dokusu tarafından alınır
- Yağ dokuya girişte sorun varsa karaciğere yönelir ve VLDL üretimini arttırır
- Şilomikron ve şilomikron kalıntıları hızlıca karaciğere alınır

ApoB100

- ApoB100 KC, ER de sentezlenir
- TG ve kolesterol ER de ApoB100 e yüklenerek VLDL oluşur
- VLDL, LPL ve HPL ile hidrolize olarak IDL ve sonrasında LDL ye dönüşür

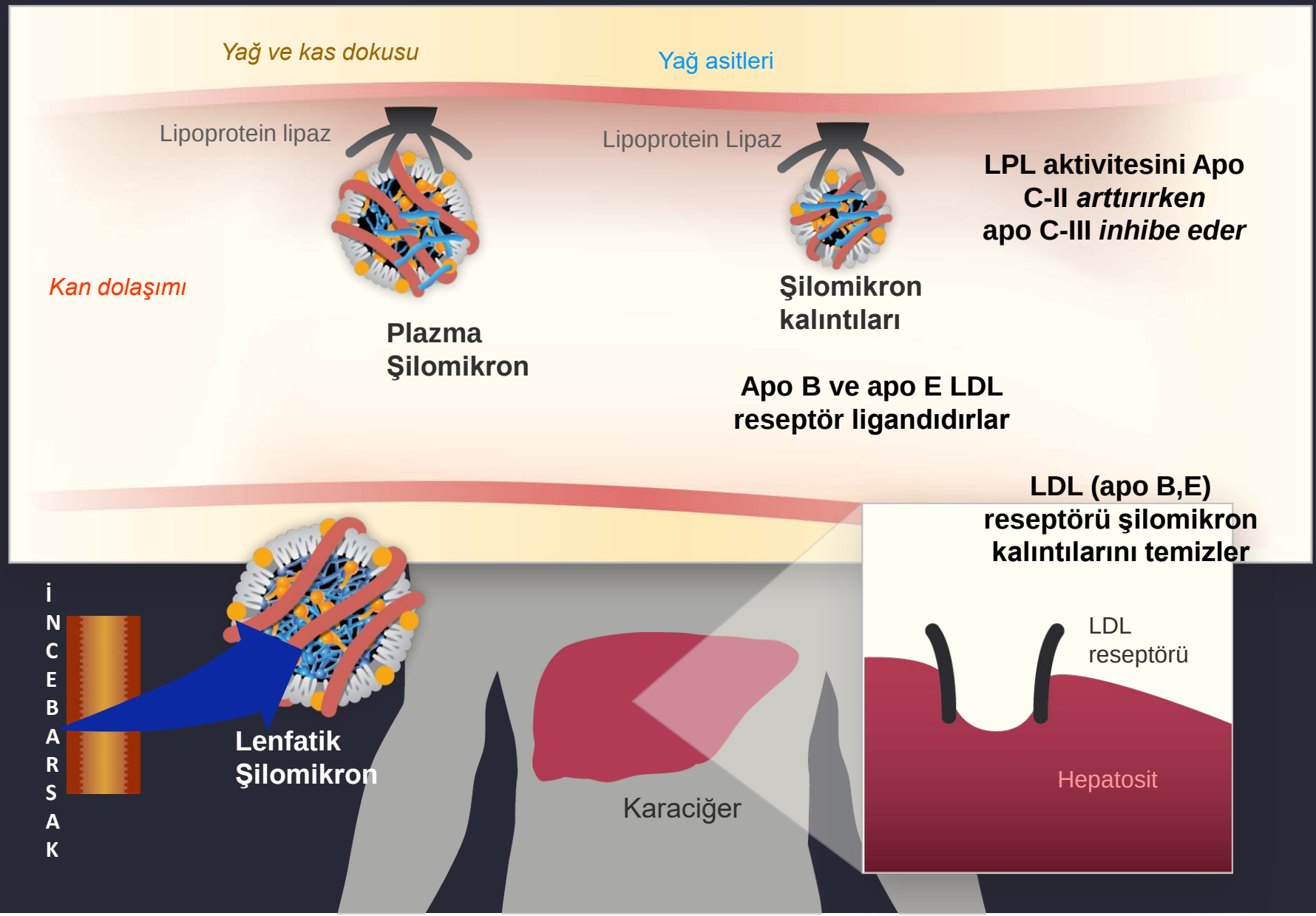


De Graaf J, Couture P, Sniderman AD. *ApoB in Clinical Care*. Bohn Stafleu van Loghum; 2015

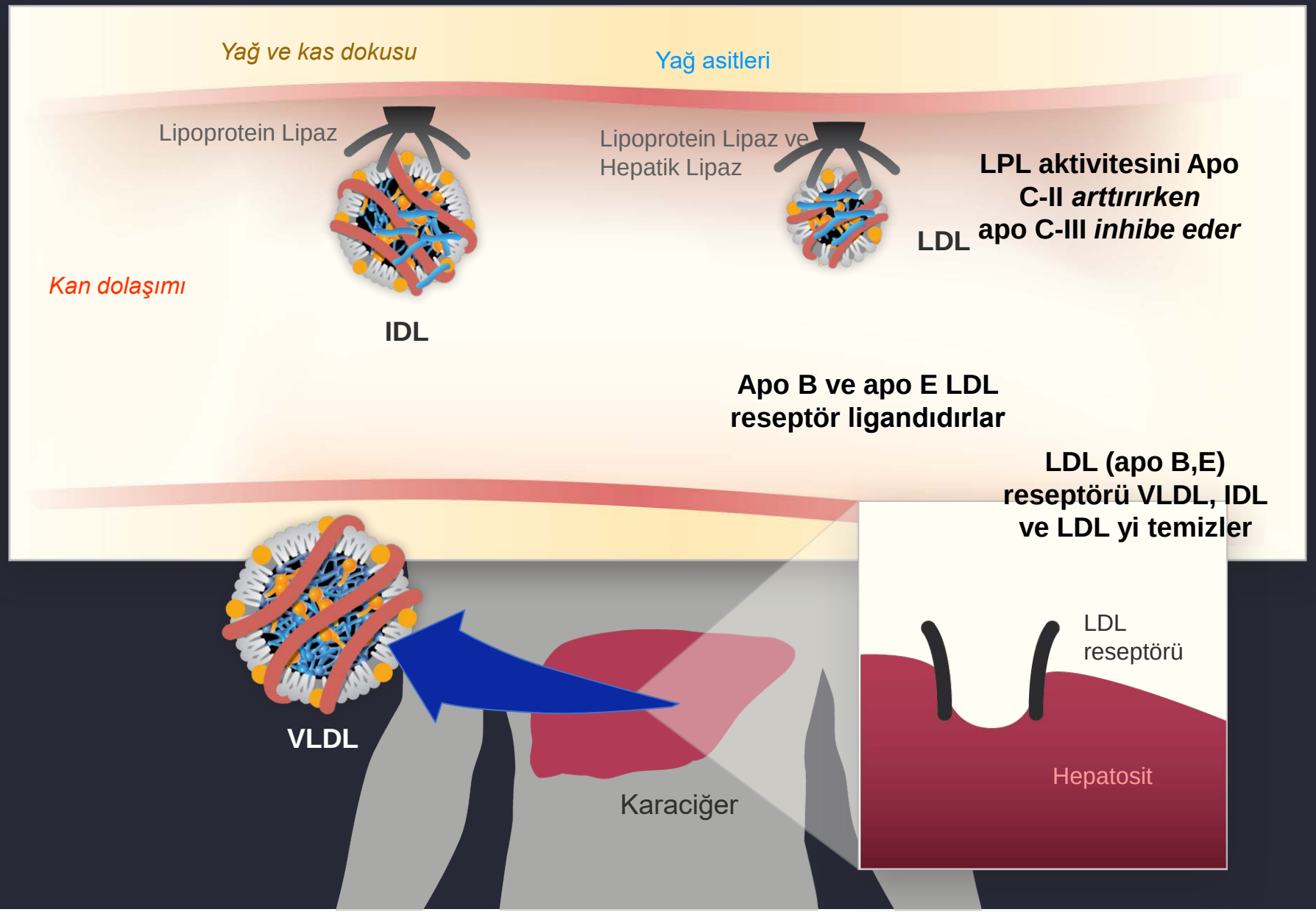
VLDL

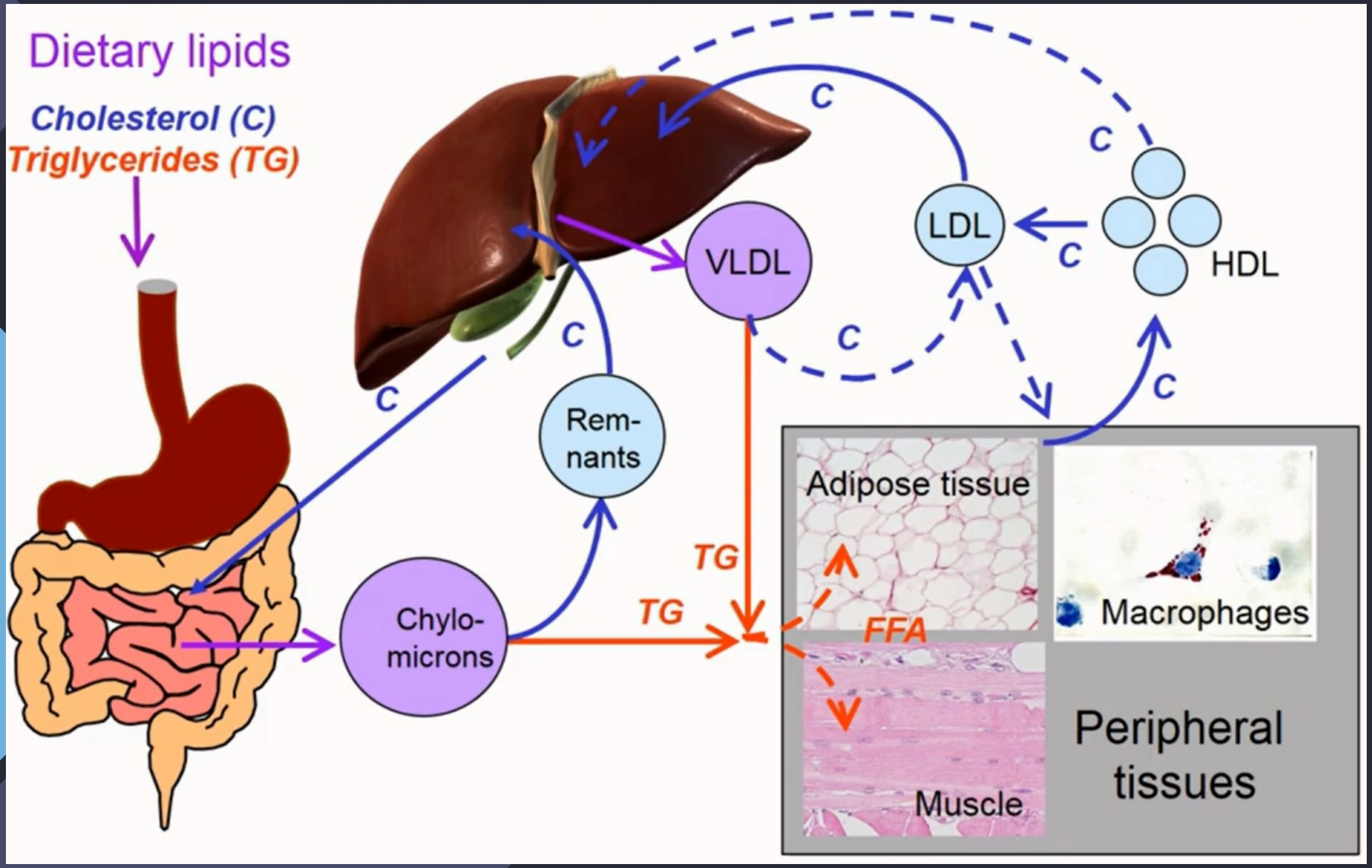
- VLDL karaciğerde ApoB100 e trigliserit ve kolesterol eklenmesiyle oluşur
- VLDL periferde LPL ile hidrolize olur ve trigliserid içeriği azalır
- Kolesterol içeriği artan VLDL, IDL ye dönüşür

Ekzojen Lipid Metabolizması

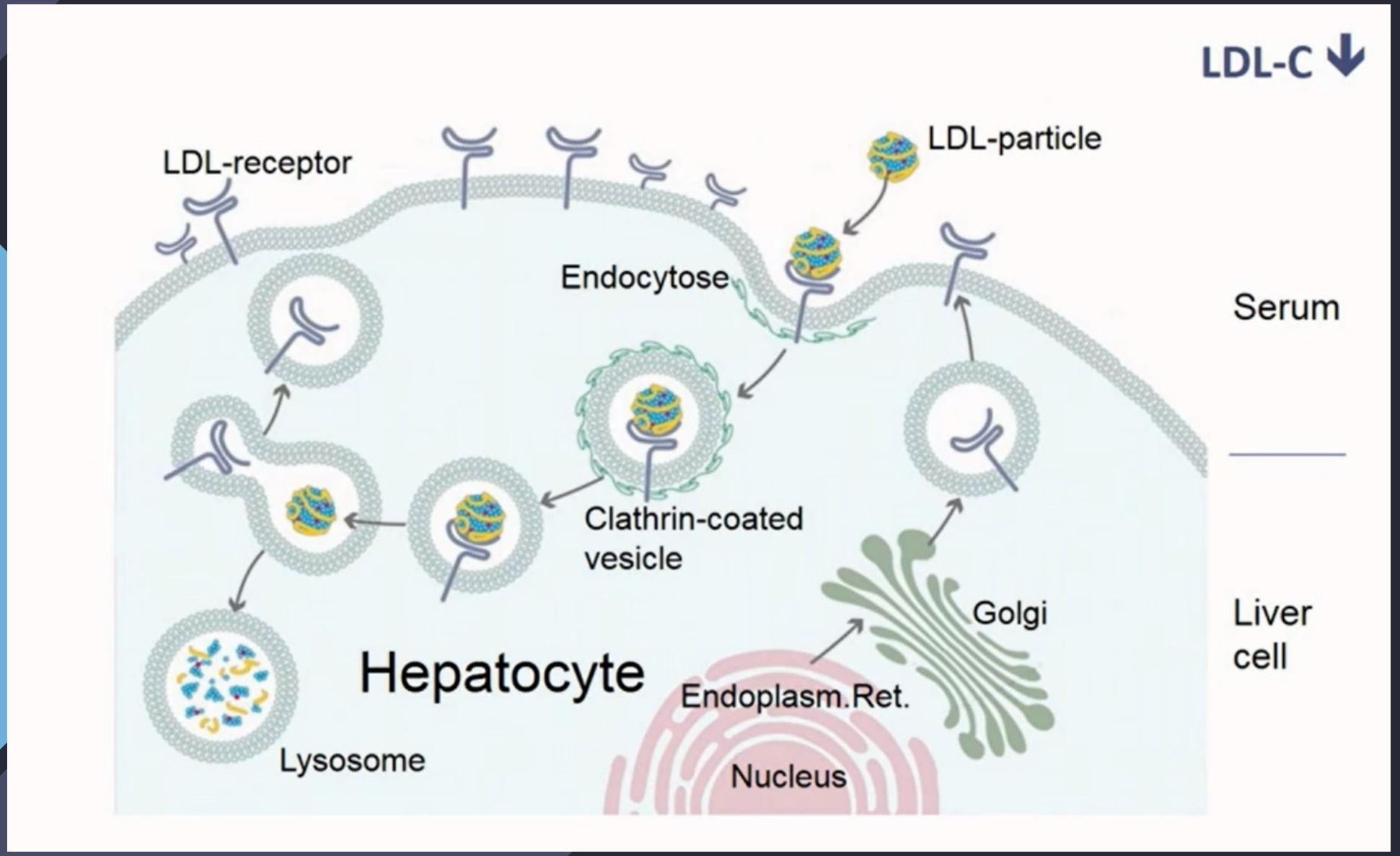


Endojen Lipid Metabolizması

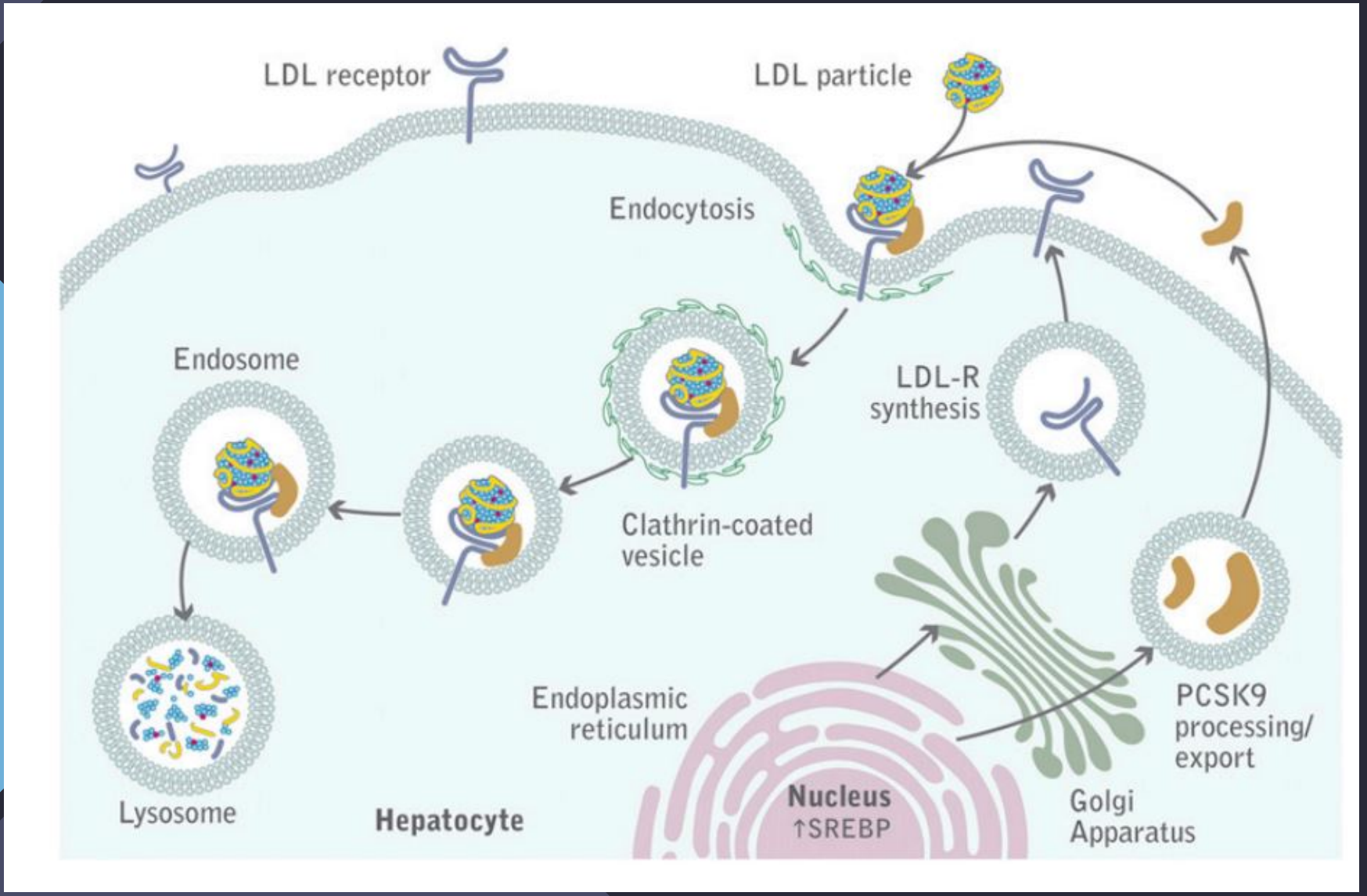



Dietary lipids
Cholesterol (C)
Triglycerides (TG)
C
C
C
C
C
C
VLDL
LDL
HDL
Rem-
nants
Chylo-
microns
TG
TG
FFA
Adipose tissue
Macrophages
Muscle
Peripheral
tissues

LDL

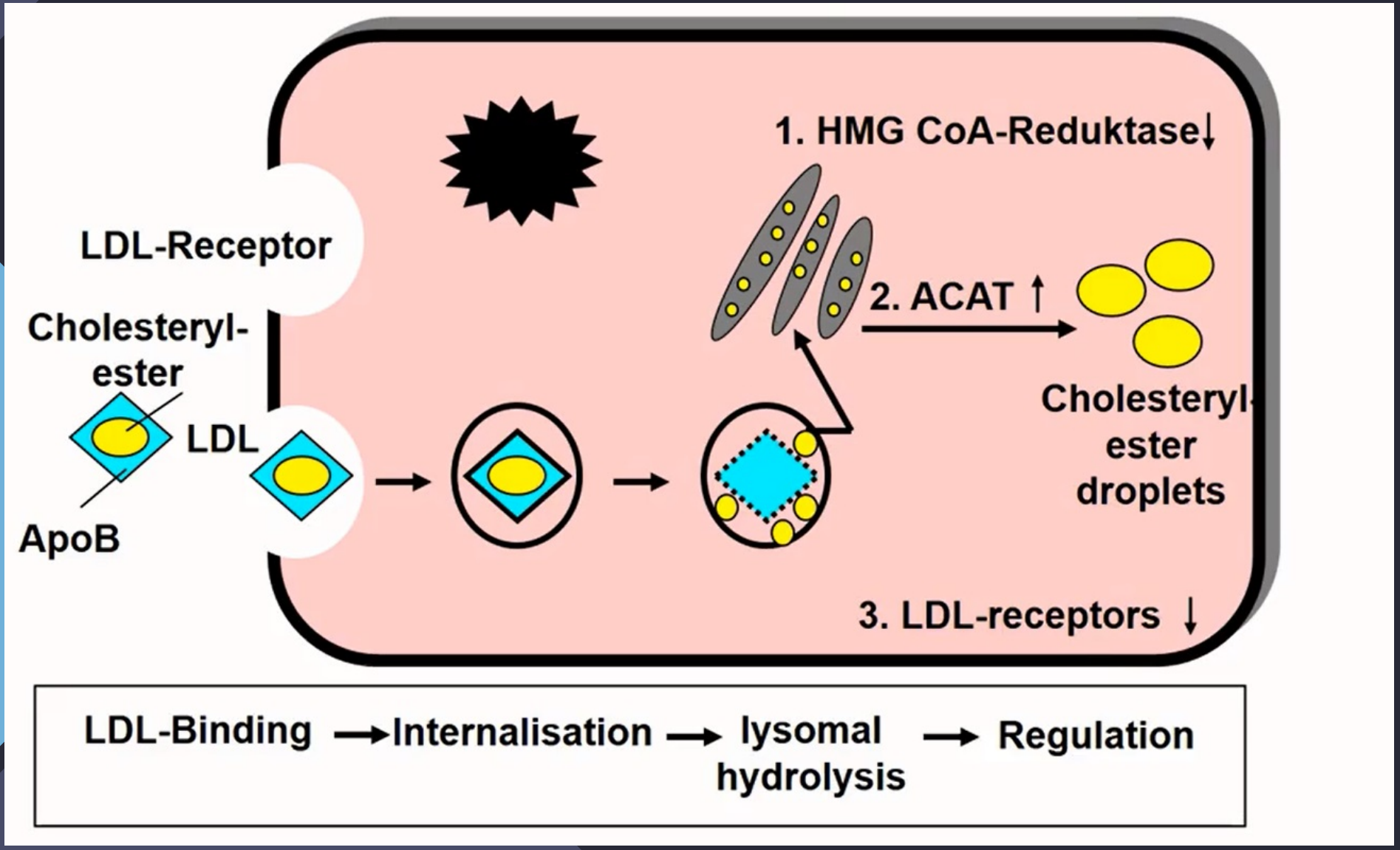

LDL-C
LDL-receptor
LDL-particle
Endocytose
Serum
Clathrin-coated
vesicle
Golgi
Liver
cell
Hepatocyte
Endoplasm.Ret.
Lysosome
Nucleus

LDL



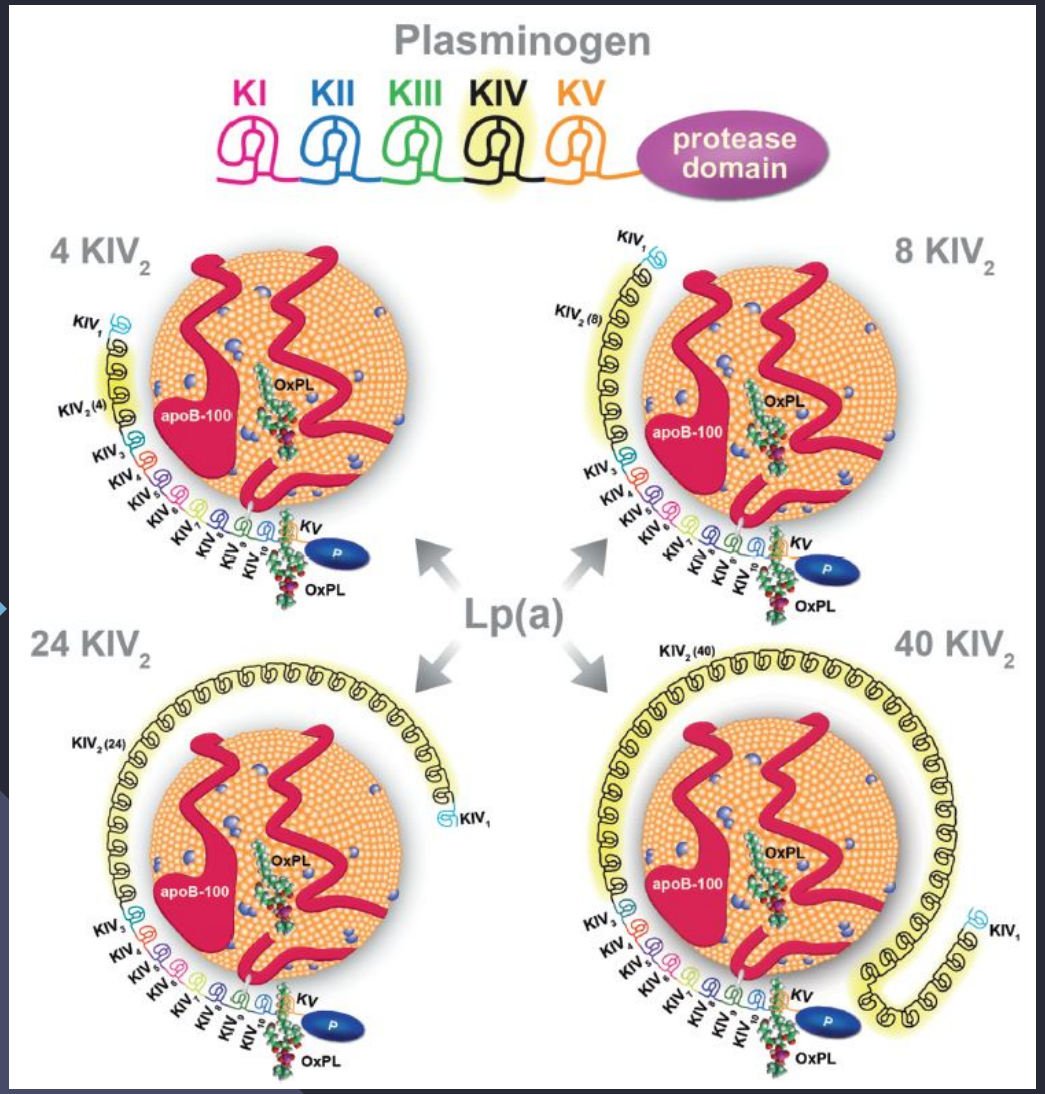
Lambert G, Sjouke B, Choque B, Kastelein JJ, Hovingh GK. The PCSK9 decade. J Lipid Res. 2012 Dec;53(12):2515-24.

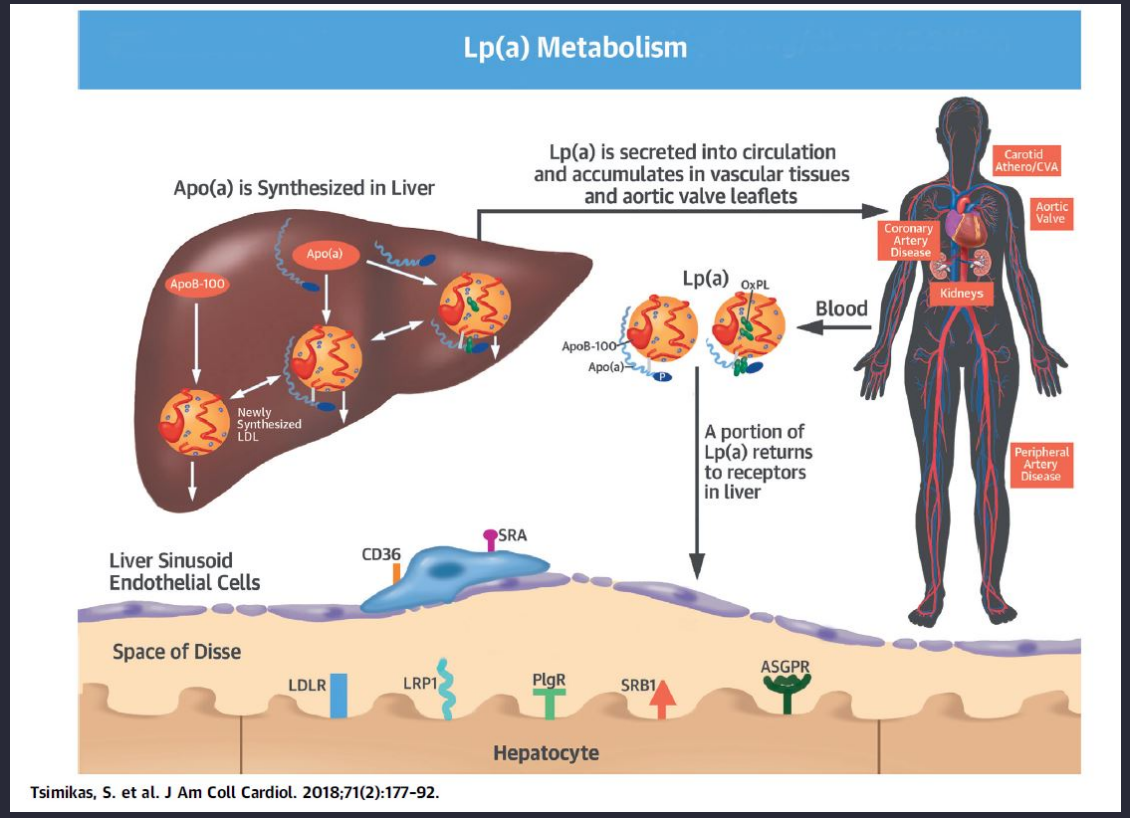
LDL



Lambert G, Sjouke B, Choque B, Kastelein JJ, Hovingh GK. The PCSK9 decade. J Lipid Res. 2012 Dec;53(12):2515-24.

Lp(a)

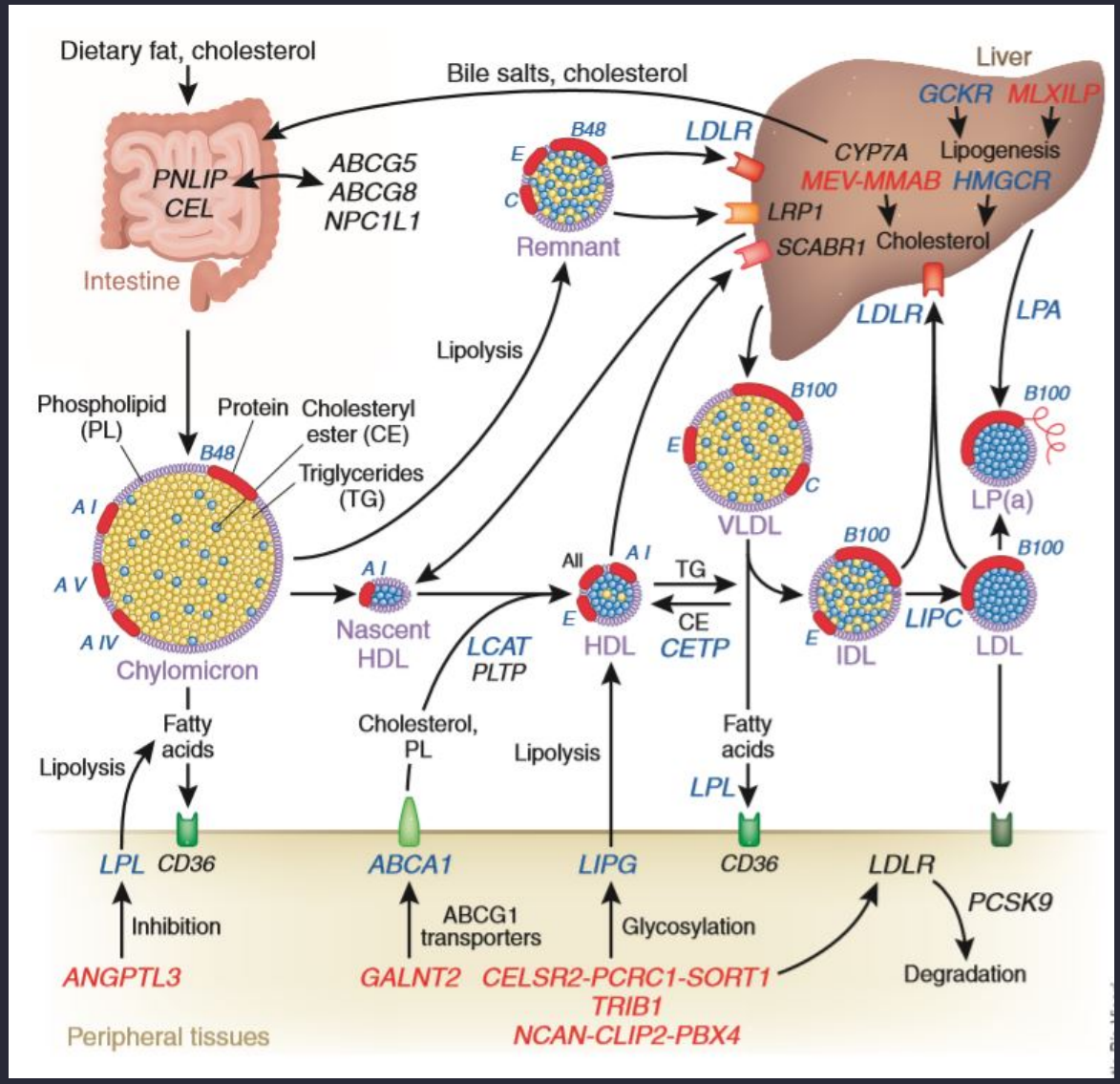




Tsimikas, S. et al. J Am Coll Cardiol. 2018;71(2):177-92.

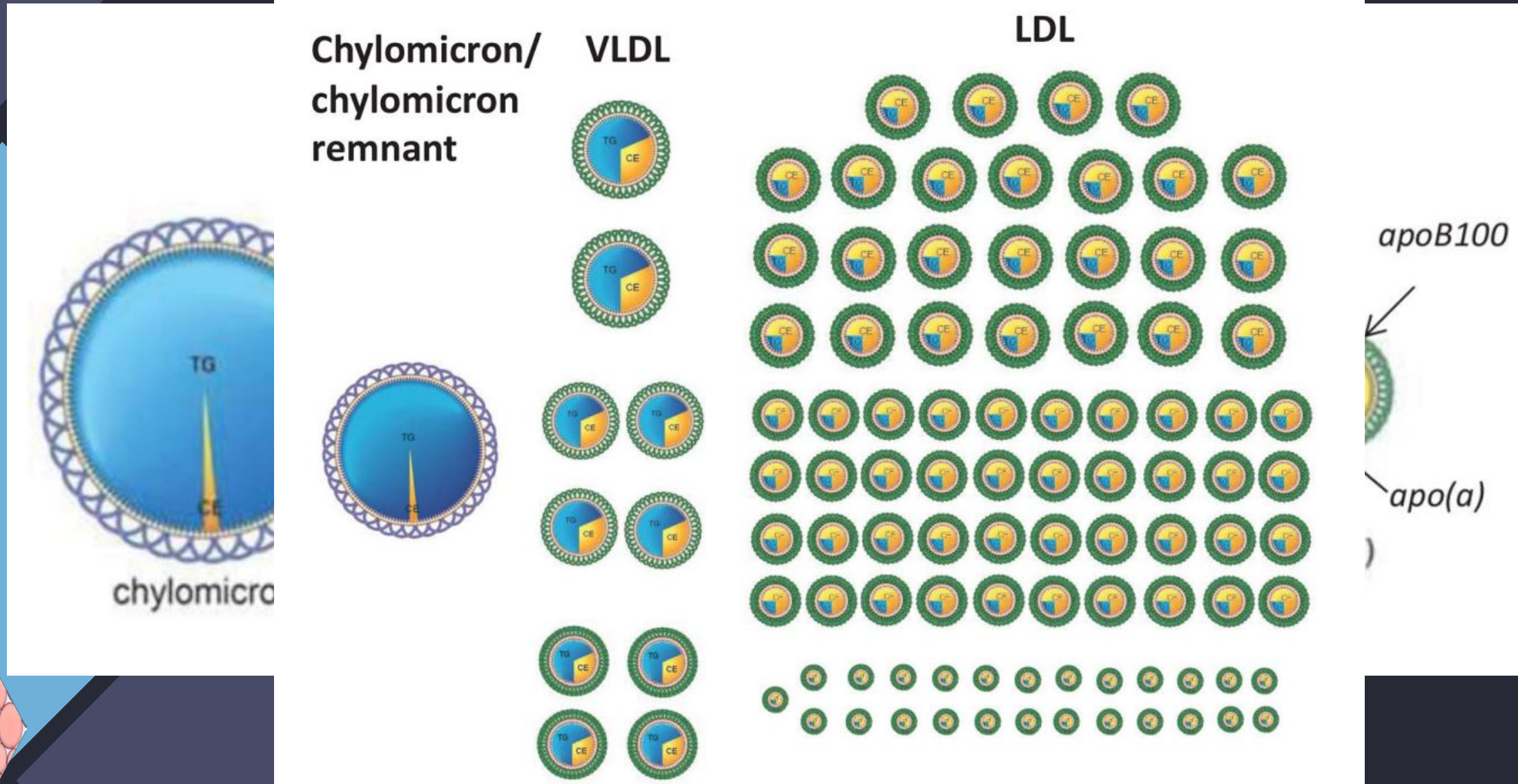
Tsimikas Lipoprotein(a) JACC VOL. 69, NO. 6, 2017 F E B R U A R Y 1 4 , 2 0 1 7 : 6 9 2 – 7 1 1

Lipoprotein Metabolizması



Aldons J Lusis & Päivi Pajukanta A treasure trove for lipoprotein biology nature genetics | volume 40 | number 2 | february 2008

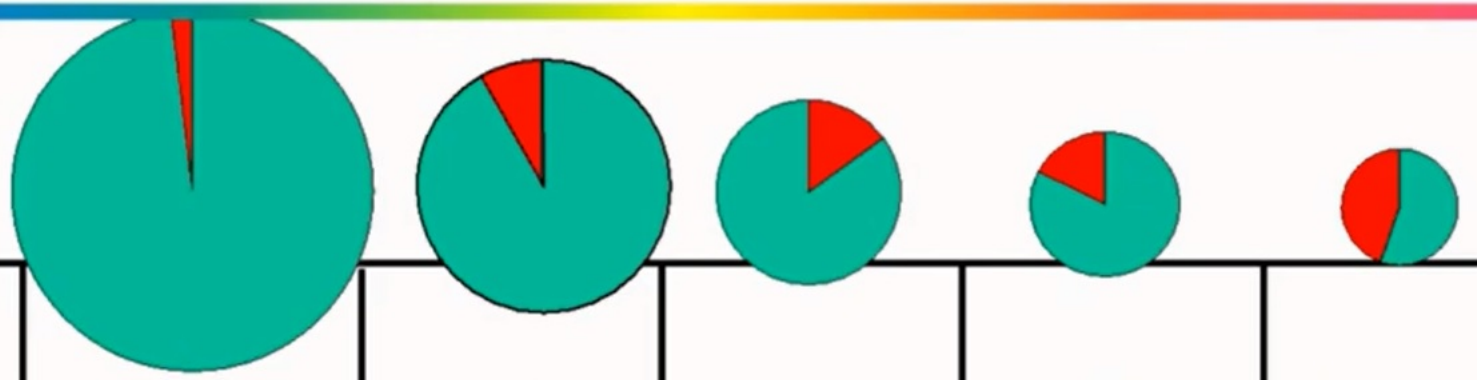
ApoB İçeren Lipoproteinler



JAMA Cardiol. 2019 December 01; 4(12): 1287–1295.

Plasma Lipoproteins

Lipids
Proteins



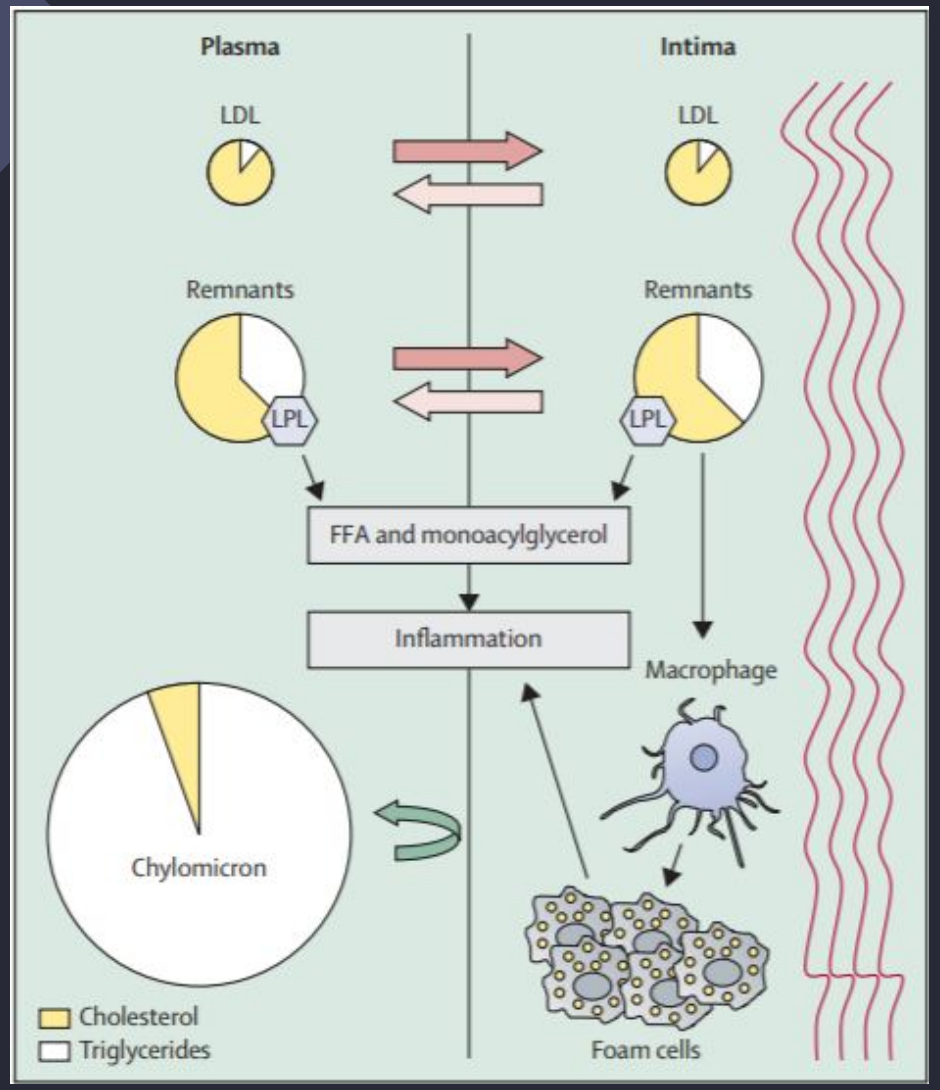
	Chylo-microne	VLDL	IDL	LDL	HDL
Density (kg/L)	< 0.995	< 1.006	< 1.019	< 1.063	< 1.21
% Lipids	98-99	90-95	84-88	74-78	< 55
Main apolipo-proteins	A-I, A-IV B-48 (Cs, E)	B-100 Cs, E (A-I)	B-100 Cs, E	B-100	A-I, A-II A-IV Cs, E

Table 6 **Physical and chemical characteristics of human plasma lipoproteins**

	Density (g/mL)	Diameter (nm)	TGs (%)	Cholesteryl esters (%)	PLs (%)	Cholesterol (%)	Apolipoproteins	
							Major	Others
Chylomicrons	<0.95	80–100	90–95	2–4	2–6	1	ApoB-48	ApoA-I, A-II, A-IV, A-V
VLDL	0.95–1.006	30–80	50–65	8–14	12–16	4–7	ApoB-100	ApoA-I, C-II, C-III, E, A-V
IDL	1.006–1.019	25–30	25–40	20–35	16–24	7–11	ApoB-100	ApoC-II, C-III, E
LDL	1.019–1.063	20–25	4–6	34–35	22–26	6–15	ApoB-100	
HDL	1.063–1.210	8–13	7	10–20	55	5	ApoA-I	ApoA-II, C-III, E, M
Lp(a)	1.006–1.125	25–30	4–8	35–46	17–24	6–9	Apo(a)	ApoB-100

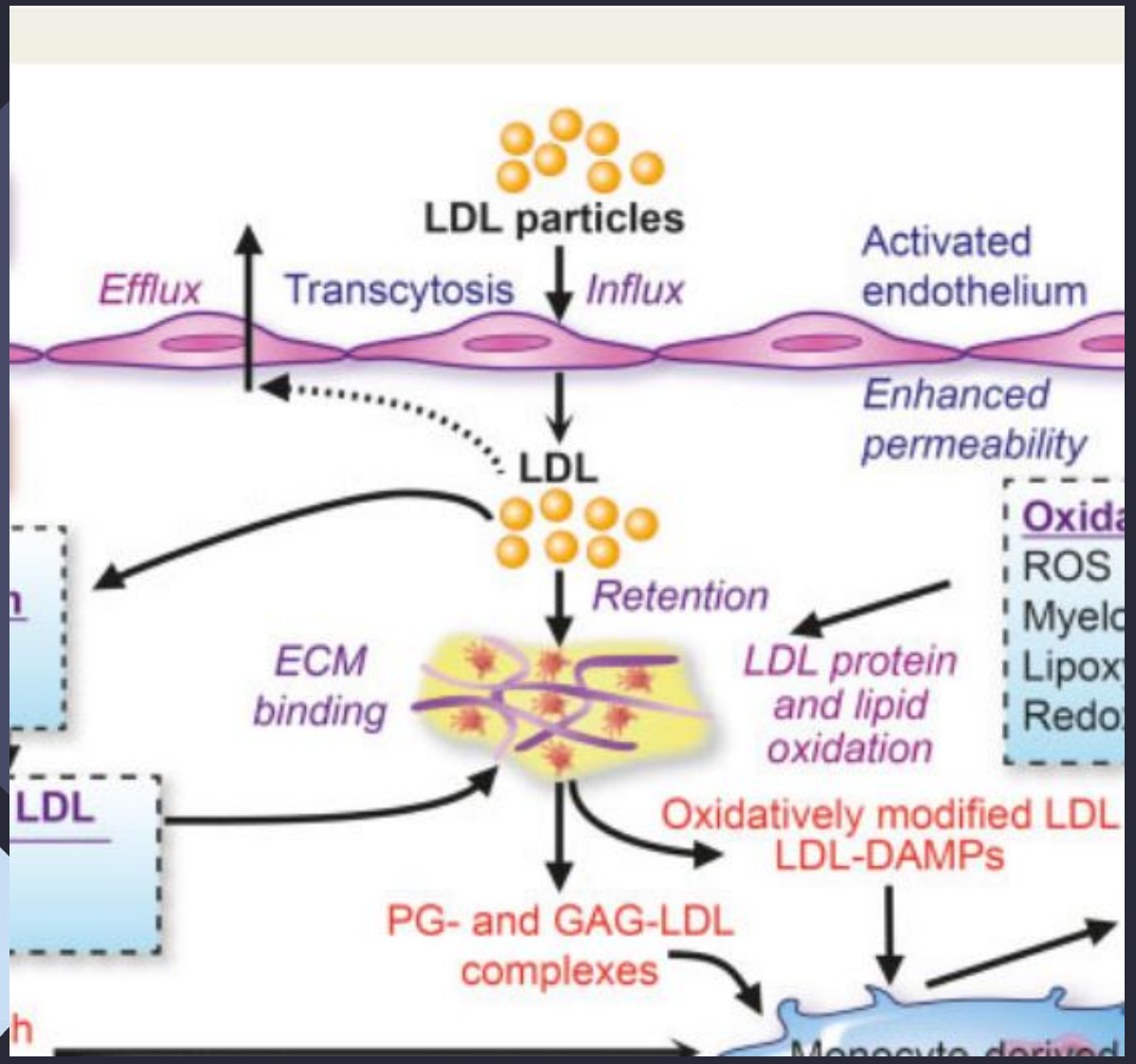
Apo = apolipoprotein; HDL = high-density lipoprotein; IDL = intermediate-density lipoprotein; LDL = low-density lipoprotein; Lp(a) = lipoprotein(a); PLs = phospholipids; TGs = triglycerides; VLDL = very low-density lipoprotein.

ApoB içeren lipoproteinler – Ateroskleroz



Børge G Nordestgaard, Anette Varbo Triglycerides and cardiovascular disease Vol 384 August 16, 2014

Klinik Önemi – Ateroskleroz



European Heart Journal (2020) 41, 2313–2330

ApoB Kardiyovasküler riski daha iyi gösterebilir

Journal of the American Heart Association

Volume 11, Issue 20, 18 October 2022

https://doi.org/10.1161/JAHA.122.025858

American Heart Association.

BASIC SCIENCE FOR CLINICIANS

Physiological Bases for the Superiority of Apolipoprotein B Over Low-Density Lipoprotein Cholesterol and Non–High-Density Lipoprotein Cholesterol as a Marker of Cardiovascular Risk

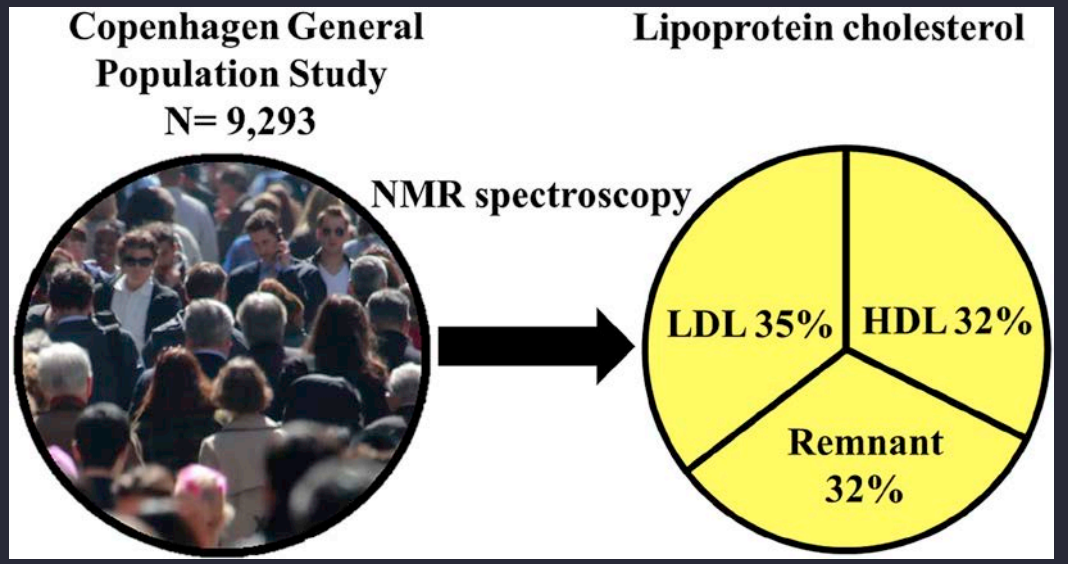
Tamara Glavinovic, MD ; George Thanassoulis, MD ; Jacqueline de Graaf, MD; Patrick Couture, MD; Robert A. Hegele, MD *; Allan D. Sniderman, MD *

Glavinovic T et al. Physiological Bases for the Superiority of Apolipoprotein B Over Low-Density Lipoprotein Cholesterol and Non-High-Density Lipoprotein Cholesterol as a Marker of Cardiovascular Risk. J Am Heart Assoc. 2022 Oct 18;11(20):e025858.

ApoB Kardiyovasküler riski daha iyi gösterebilir

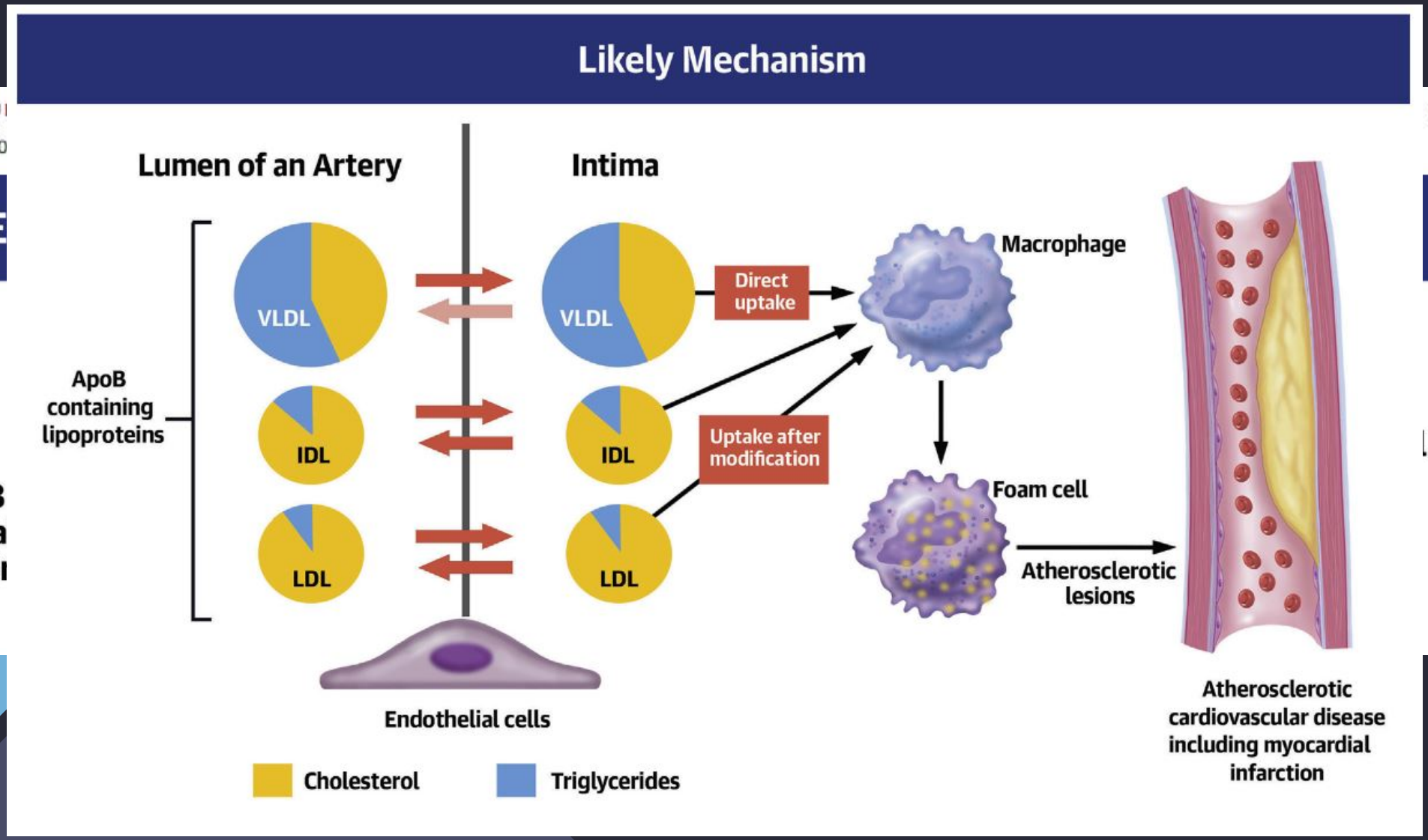
› Atherosclerosis. 2019 Jul;286:97-104. doi: 10.1016/j.atherosclerosis.2019.05.011. Epub 2019 May 9.

A third of nonfasting plasma cholesterol is in remnant lipoproteins: Lipoprotein subclass profiling in 9293 individuals



Balling M et al. A third of nonfasting plasma cholesterol is in remnant lipoproteins: Lipoprotein subclass profiling in 9293 individuals. Atherosclerosis. 2019 Jul;286:97-104.

ApoB Kardiyovasküler riski daha iyi gösterebilir



Balling M et al. VLDL Cholesterol Accounts for One-Half of the Risk of Myocardial Infarction Associated With apoB-Containing Lipoproteins. J Am Coll Cardiol. 2020 Dec 8;76(23):2725-2735.

ESC European Society of Cardiology

European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

2016	2019
Lipid analyses for CVD risk estimation	**Lipid analyses for CVD risk estimation**
ApoB should be considered as an alternative risk marker whenever available, especially in individuals with high TG.	ApoB analysis is recommended for risk assessment, particularly in people with high TG, DM, obesity or metabolic syndrome, or very low LDL-C. It can be used as an alternative to LDL-C, if available, as the primary measurement for screening, diagnosis, and management, and may be preferred over non-HDL-C in people with high TG, DM, obesity, or very low LDL-C.

Use of ApoB in risk stratification. ApoB may be a better measure of an individual's exposure to pro atherogenic lipoproteins, and hence its use may be particularly helpful for risk assessment in people where measurement of LDL-C underestimates this burden, such as those with high TG, DM, obesity, or very low LDL-C.

Sonuç

- Lipoproteinler suda çözünemeyen lipidlerin taşınmasında görev alır.
- Gerek diyetle alınan gerekse sentezlenen lipidler temel olarak enerji metabolizmasının düzenlenmesinde görev alır.
- Kanda HDL haricindeki lipoproteinler ApoB içerir.
- ApoB her lipoproteinde 1 adet bulunur.
- ApoB içeren lipoproteinlerden <70 nm olanları aterojeniktir
- Kanda ApoB içeren temel lipoprotein LDL dir.
- LDL ile ApoB partikül sayısı genelde koreledir.
- TG yüksek, DM veya obeiztesi olan LDL düşük hastalarda ApoB kardiyovasküler riski daha iyi gösterebilir.

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