

LIPOPROTEINI

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Prenos lipidov po krvi

MK- proste.....vezava na albumin

MK v obliki TAG.....kot lipoproteini (hilomikroni in VLDL)

steroidni hormoni.....vezava na albumin in specifične proteine

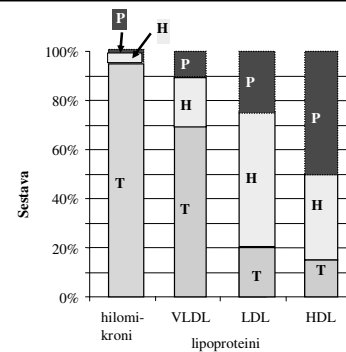
holesterol.....kot lipoproteini (hilomikroni in LDL)

ketonska telesca.....topna!!

Prenos lipidov po krvi

Lipoproteini so sestavljeni iz:

- *lipidnega dela (TAG, holesterol in holesterolni estri ter fosfolipidi)
- *proteinskega dela (apolipoproteini)

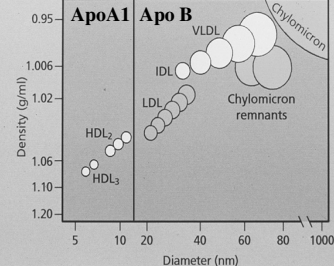


Glavne vrste lipoproteinov in odstotek triacilglicerolov (T) , holesterola (H) in proteinov (P) .

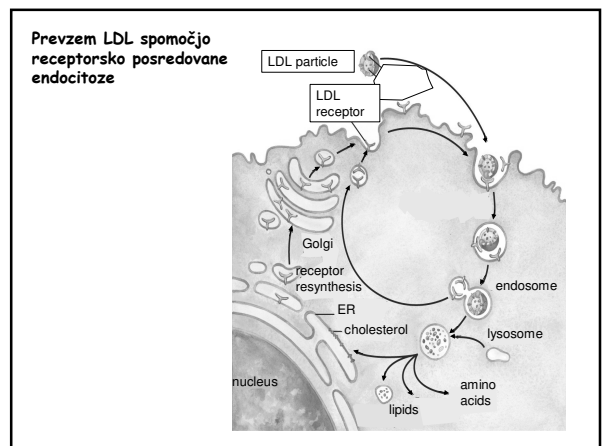
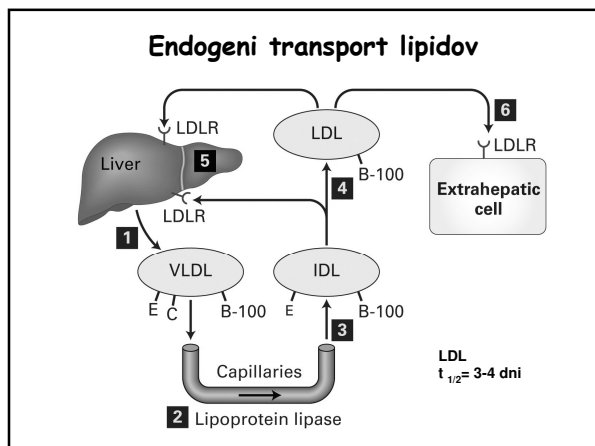
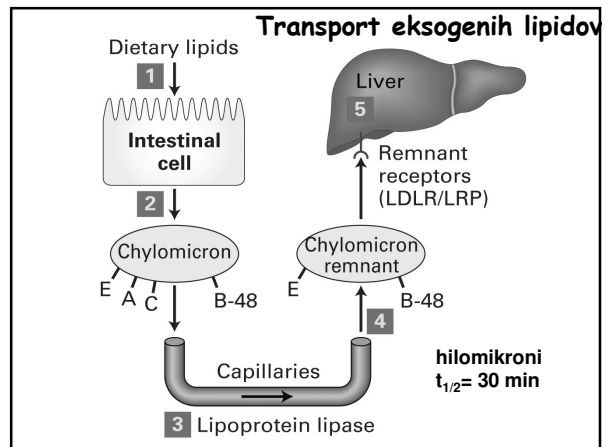
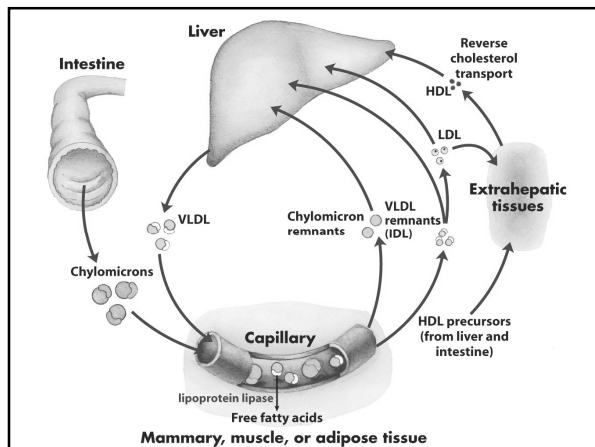
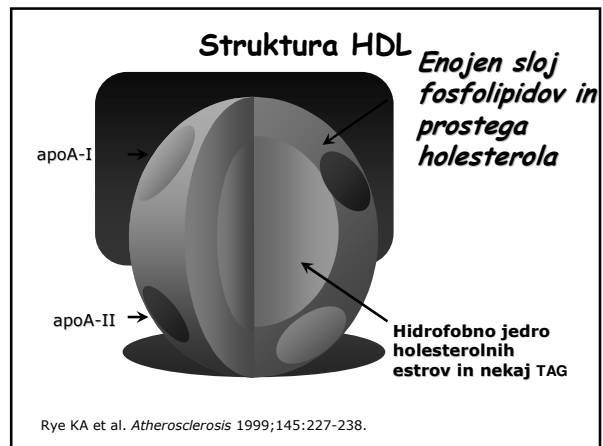
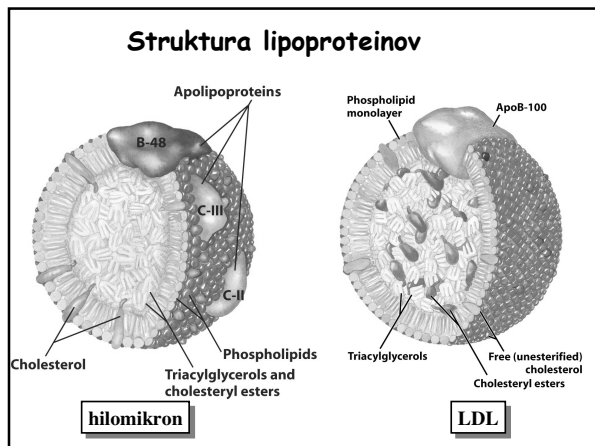
Vloga apolipoproteinov

- interagirajo z lipidnim delom in pomagajo pri njegovi solubilizaciji
- encimski aktivatorji ali inhibitorji
- omogočajo vezavo na receptorje
- za HDL značilni apoA1, za LDL apoB100, za hilomikrone Apo B48

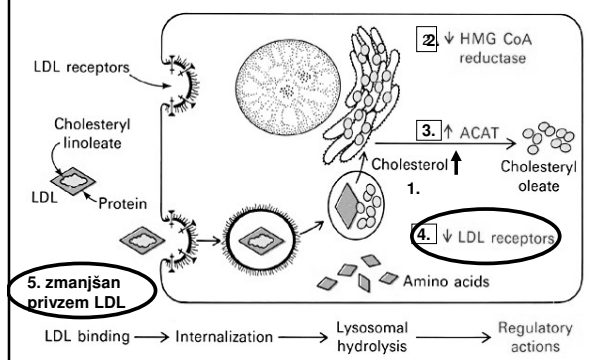
The lipoprotein particle family



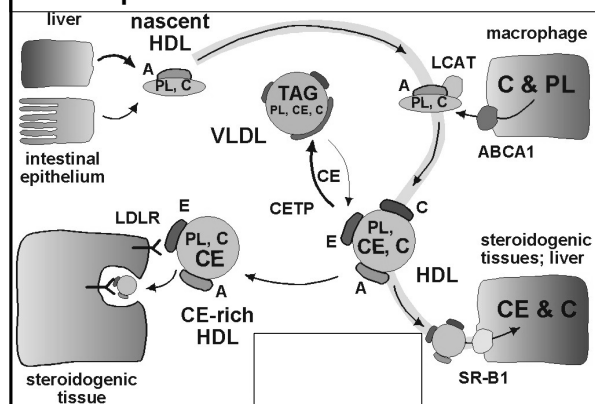
Ločimo jih glede na:
velikost
gostota
potovanje v električnem polju itd.



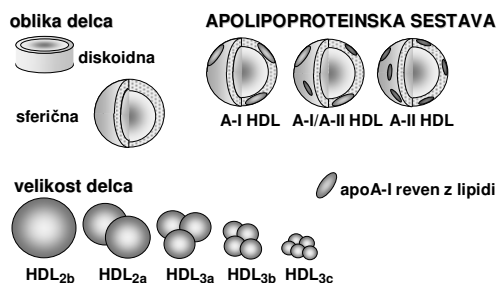
Kakšni bodo učinki sproščenega holesterola v celici?



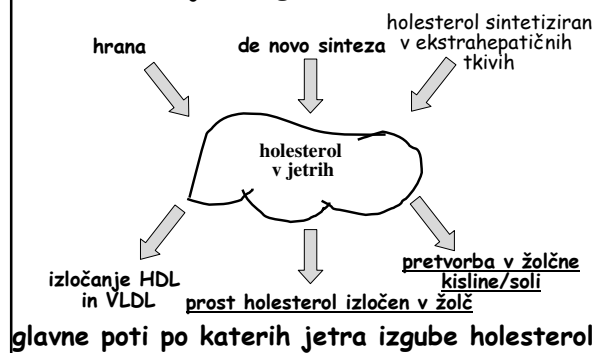
Obratni prenos holesterola- metabolizem HDL



HDL (in drugi lipoproteini) niso enotni



Homeostaza holesterola v organizmu viri jetrnega holesterola



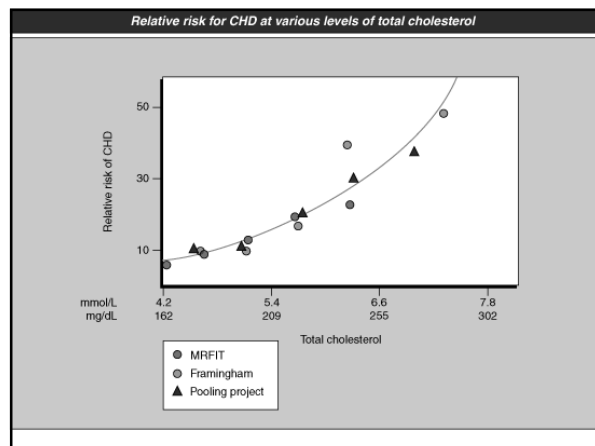
Nekateri rizični dejavniki za razvoj ateroskleroze

spremenljivi

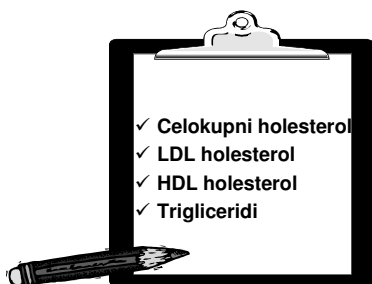
- kajenje
- dislipidemija**
- diabetes
- hipertenzija
- debelost
- telesna aktivnost

nespremenljivi

- starost
- spol
- družinska zgodovina



Lipoproteinski profil

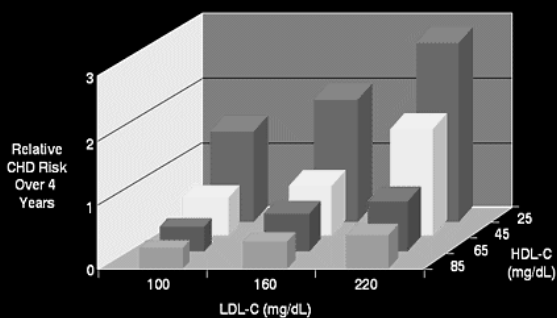


Razmerje LDL/HDL in bolezen srca in ožilja

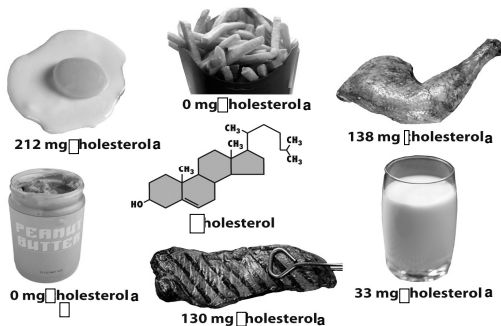
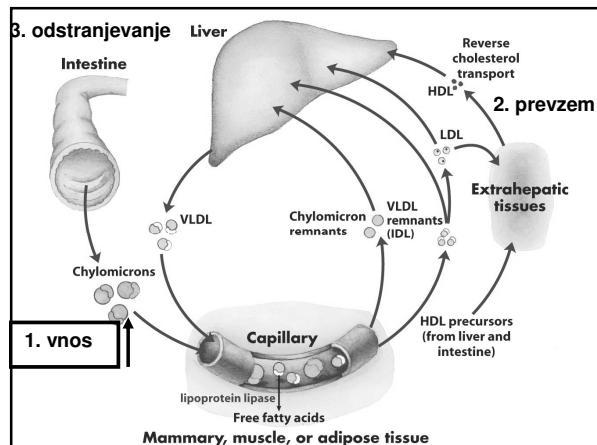
- LDL = "slabi holesterol"
- HDL = "dobri holesterol", ima zaščitno vlogo
- pomembno je razmerje LDL/HDL



High LDL-C and Low HDL-C: Increased Risk of CHD



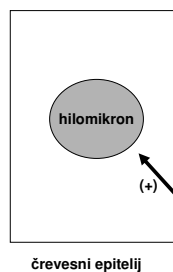
Castelli WP et al. Can J Cardiol. 1986;4(suppl A):5A-10A.



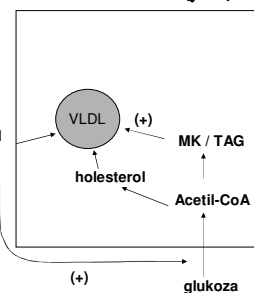
Holesterol najdemo v hrani živalskega izvora

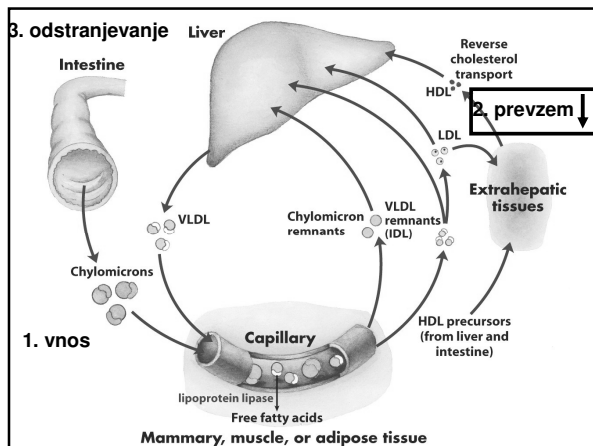
Hrana in biosinteza lipoproteinov

Sinteza hilomikronov



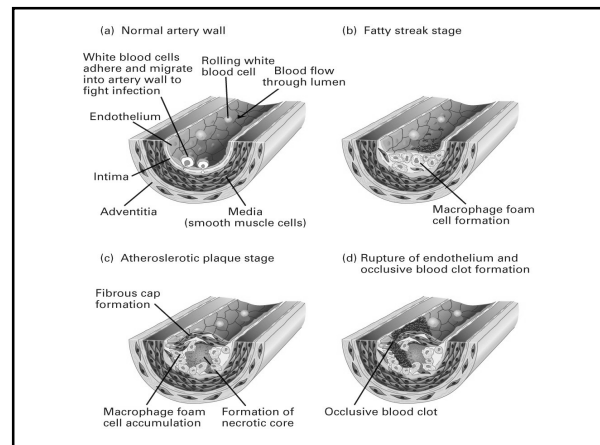
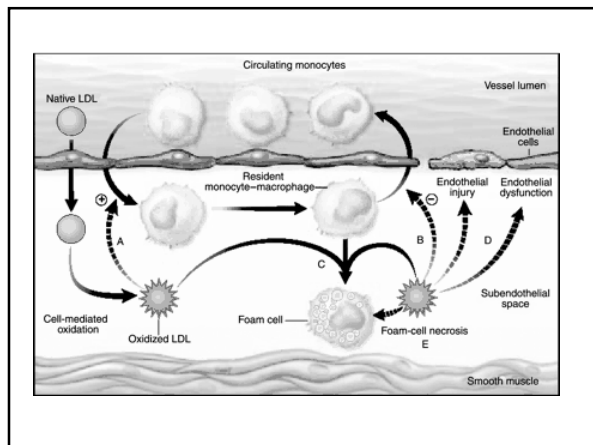
Sinteza VLDL (jetra)





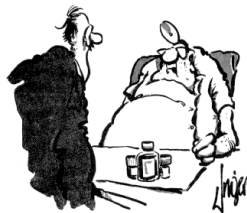
Družinska hiperholesterolemija

- okvarjen gen za LDL receptor (90%) ali apo B 100 (10%)
- zgoden pojav bolezn srca in ožilja
- 1 / 500 prebivalstva (heterozigotna oblika bolezni)
- povišan celokupni and LDL holesterol
- pozitivna družinska zgodovina
- večina bolnikov s homozigotno obliko bolezni (1/miljon) umre v otroštvu

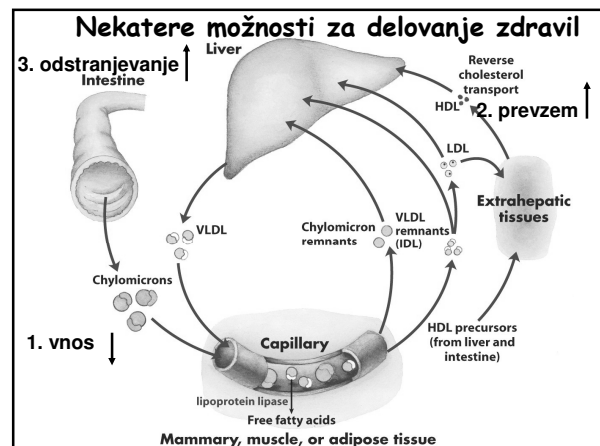


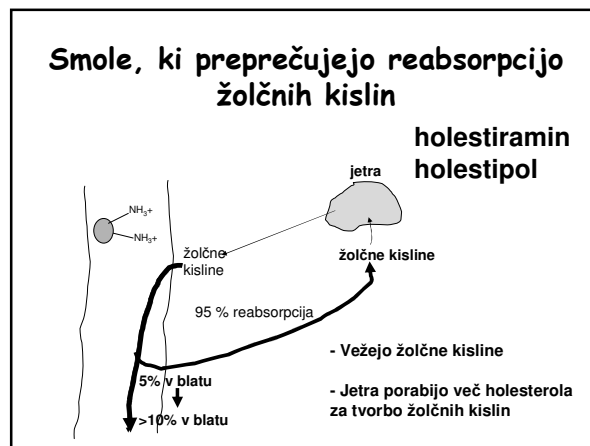
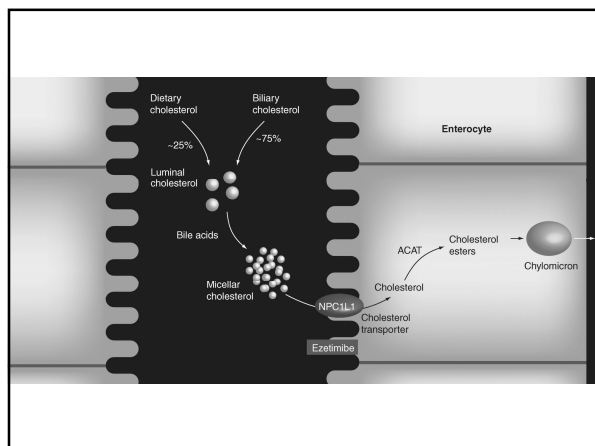
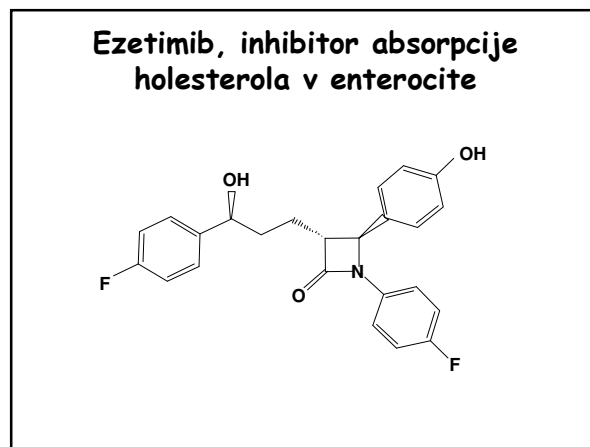
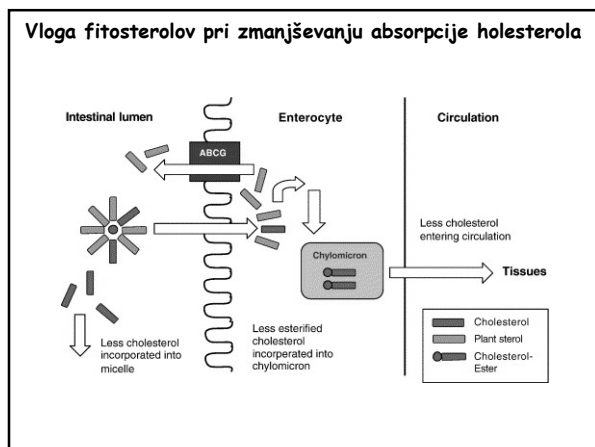
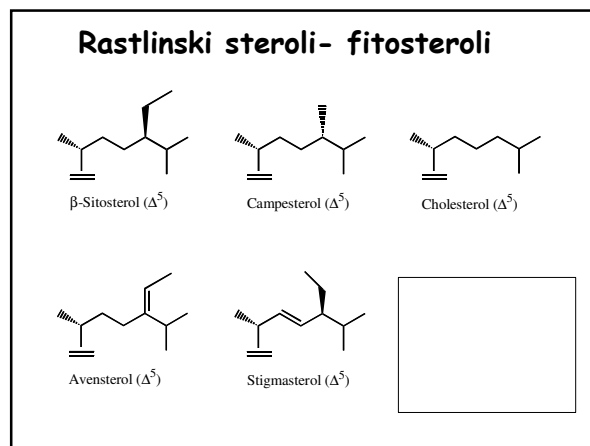
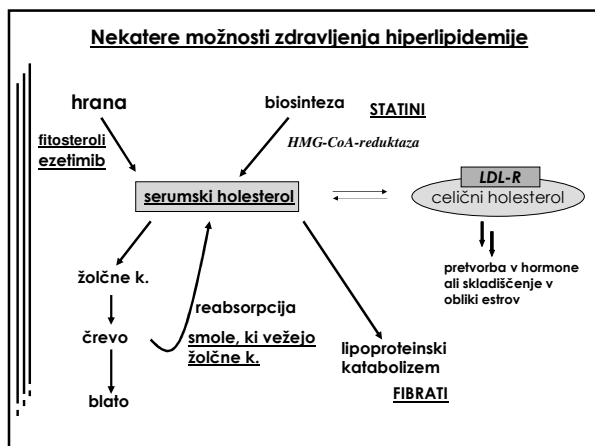
Nekaj dejavnikov vpliva na koncentracijo holesterola in TAG v krvi

- zdrava prehrana
- fizična aktivnost
- hujšanje
- zdravila



"I want you to walk two miles a day ... and take my dog with you."



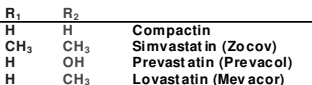


Kaj bomo dosegli s preprečevanjem absorpcije holesterola oz. reabsorpcije žolčnih kislin???

Inhibitorji HMG-CoA reduktaze

mevalonat

R_1	R_2	
H	H	Compactin
CH_3	CH_3	Simvastatin (Zocov)
H	OH	Prevastatin (Prevacol)
H	CH_3	Lovastatin (Mevacor)



Kakšni so učinki inhibicije holesterola v celici?

The diagram illustrates the metabolic pathways and regulatory mechanisms of cholesterol within a cell. It shows the following components and processes:

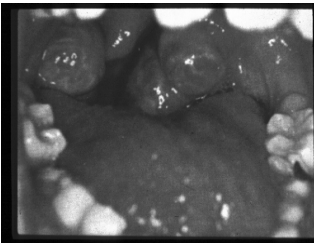
- LDL receptors**: Located on the cell membrane, they bind to **LDL** (Low-Density Lipoprotein) particles, which consist of a **Protein** and **Cholesteryl linoleate**.
- 5. omogočen prevzem LDL**: This step indicates that the binding of LDL to its receptor is facilitated or enabled.
- Internalization**: The LDL-receptor complex is internalized into the cell via endocytosis.
- Lysosomal hydrolysis**: The internalized LDL is broken down in the lysosomes, releasing **Amino acids** and **Cholesterol**.
- Cholesterol metabolism**:
 - 1. ↓ HMG CoA reductase**: Inhibition of this enzyme leads to a decrease in cholesterol synthesis.
 - 2. ↓**: A general decrease in cholesterol levels.
 - 3. ↓ ACAT**: Inhibition of Acyl-CoA:cholesterol acyltransferase leads to a decrease in **Cholesteryl oleate** synthesis.
 - 4. ↑ LDL receptors**: An increase in the number of LDL receptors on the cell membrane, which is a compensatory mechanism to maintain cholesterol levels when synthesis is inhibited.
- Regulatory actions**: The final outcome of these metabolic changes, leading to a regulation of cholesterol levels within the cell.

Kakšni so učinki delovanja statinov in ezetimiba???

Kako dobro poznamo metabolizem lipoproteinov???

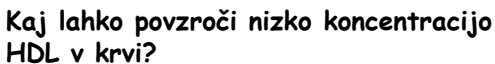
Tangier-ska bolezen

Hipertrofirani oranžno obarvani mandeljni
Zelo nizka konc. HDL v krvi
Povečana jetra in vranica
Zgoden razvoj boleznih srca in ožilja



Kaj lahko povzroči nizko koncentracijo HDL v krvi?

Hipertrofirani oranžno
obarvani mandeljni
Zelo nizka konc. HDL v krvi
Povečana jetra in vranica
Zgoden razvoj bolezni srca
in ožilja



Ali veste

- zakaj se holesterol (TAG) po krvi prenaša v obliki lipoproteinov
- kakšna je vloga apolipoproteinov
- kakšna je vloga posameznih lipoproteinov
- kako lahko posamezni lipoproteini predajo svoj lipidni “tovor” celicam
- zakaj določamo konc. holesterola in posameznih lipoproteinov v krvi
- kako statini omogočijo znižanje konc. holesterola (LDL) v krvi

- 7



Se še spomnite

- kako so sestavljeni lipoproteini
- kaj je receptorsko posredovana endocitoza
- kako se po krvi prenašajo proste maščobne kisline
- kakšna je topnost ketonskih spojin