OLD HOUSE DETAIL
IOANNINA

# ΘΕΡΑΠΕΥΤΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΕΤΕΡΟΖΥΓΗΣ ΚΑΙ ΟΜΟΖΥΓΗΣ ΟΙΚΟΓΕΝΟΥΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑΣ: ΠΑΡΟΝ ΚΑΙ ΜΕΛΛΟΝ

ΜΩΥΣΗΣ ΕΛΙΣΑΦ, ΚΑΘΗΓΗΤΗΣ
ΠΑΘΟΛΟΓΙΑΣ ΙΑΤΡΙΚΗΣ ΣΧΟΛΗΣ
ΠΑΝΕΠΙΣΤΗΜΙΟΥ ΙΩΑΝΝΙΝΩΝ

# LDL-C Clinical targets

- There are no current European guidelines for the management of HoFH
- ESC/EAS Guideline recommendations for LDL-C clinical targets in patients with HeFH[1]

| Recommendations | Class of evidence | Level of evidence |
|---|---|---|
| Treatment is aimed as reaching the LDL-C goals for high risk subjects **(<2.5 mmol/L, less than 100mg/dL) or in the presence of CVD of very high risk subjects (1.8 mmol/L less than 70mg/dL).** If targets cannot be reached, maximal reduction in LDL-C should be considered using appropriate drug combinations in tolerated doses | IIa | C |

In patients receiving apheresis these *"levels will only postpone rather than prevent CV disease but advances in adjuvant therapy such as microsomal triglyceride transfer protein and anti-sense apoB may enable more radical reductions in LDL-C in the future"*[2]

1. Adapted from Catapano et al. Atherosclerosis 2011, 217S; S1-S44. 2. Thompson et al. Atherosclerosis 2012, 208: 317-321

# ΣΤΟΧΟΙ ΥΠΟΛΙΠΙΔΑΙΜΙΚΗΣ ΑΓΩΓΗΣ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ FH

ΣΤΟΧΟΣ LDL CHOL <135 mg/dl σε παιδιά

ΣΤΟΧΟΣ LDL CHOL <100mg/dl ΜΟΝΟΘΕΡΑΠΕΙΑ Ή ΣΥΝΔΥΑΣΜΟΙ (+EZETIMIBE-COLESEVELAM)

ΣΤΟΧΟΣ LDL CHOL <70mg/dl ΣΕ ΑΤΟΜΑ ΜΕ ΕΓΚΑΤΕΣΤΗΜΕΝΗ ΑΓΓΕΙΑΚΗ ΝΟΣΟ

Consensus Statement of the European Atherosclerosis Society, 2013

# ΒΑΣΙΚΕΣ ΑΡΧΕΣ ΑΓΩΓΗΣ ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ FH

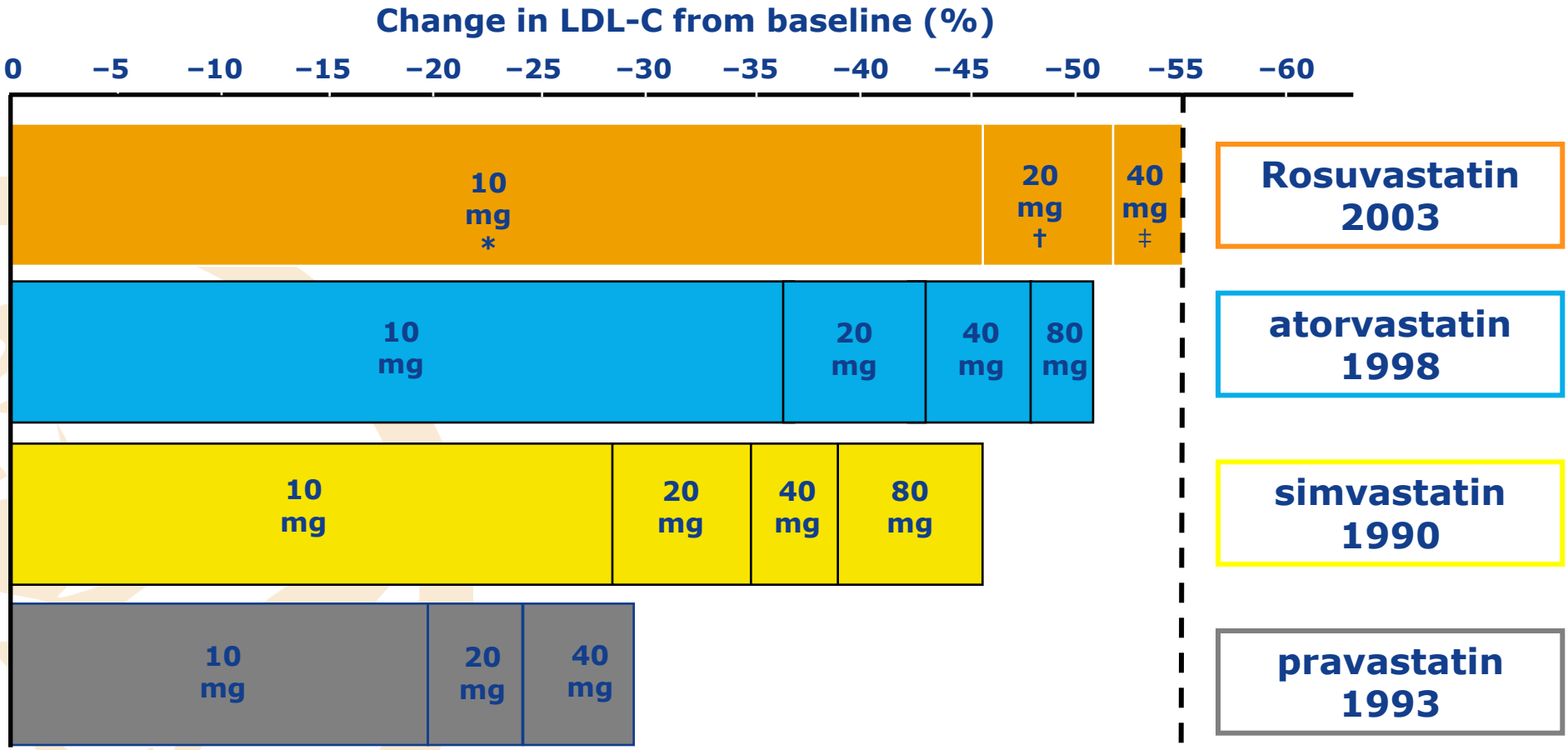
- Διακοπή καπνίσματος
- Δίαιτα (+ ΦΥΤΙΚΕΣ ΣΤΕΡΟΛΕΣ)
- Άσκηση
- ΦΑΡΜΑΚΑ
  - Στατίνες+,++ (μέγιστες ανεκτές δόσεις)
  - Ezetimibe
  - Colesevelam

+ Atorva 80mg/d, Rosuva 40mg/d, Pita 4mg/d

++ >8-10 έτη

- LIPID APHERESIS

# Statin development: Evolution towards more powerful molecules




*p<0.002 vs atorvastatin 10 mg; simvastatin 10, 20, 40 mg; pravastatin 10, 20, 40 mg
†p<0.002 vs atorvastatin 20, 40 mg; simvastatin 20, 40, 80 mg; pravastatin 20, 40 mg
‡p<0.002 vs atorvastatin 40 mg; simvastatin 40, 80 mg; pravastatin 40 mg

Adapted from Jones PH et al. *Am J Cardiol* 2003;92:152–160

## ΠΕΡΙΟΡΙΣΜΟΙ ΤΗΣ ΜΟΝΟΘΕΡΑΠΕΙΑΣ ΜΕ ΣΤΑΤΙΝΕΣ

ROSUVA 40mg/d: ↓ LDL CHOL ΚΑΤΑ 51-55%

ATORVA 80mg/d: ↓ LDL CHOL ΚΑΤΑ 51-55%

ΕΤΟΙΜΟΣ ΣΤΑΘΕΡΟΣ ΣΥΝΔΥΑΣΜΟΣ

INEGY (10+40mg/d): ↓ LDL CHOL ΚΑΤΑ 55%

*Genetic and environmental factors affecting the response to statin therapy in patients with molecularly defined familial hypercholesterolemia*

Miltiadous G. et al: Pharmacogenetics and Genomics 2005;15: 219-225

# MATERIAL

- 49 unrelated patients with heterozygous FH in whom the genetic defect of LDLR gene was previously detected

- 28 patients carried the G1646A and C858A mutations, which are class II mutations

- 21 patients were heterozygous for the G1775A mutation, which is a class V mutation

Administration of atorvastatin 20mg/d

# RESULTS

| Parameters | Baseline Values | Values after treatment | % decrement | p |
|---|---|---|---|---|
| LDL CHOL (mg/dl) | 287±70 | 178±38 | 37±11 | 0.001 |
| Apo B (mg/dl) | 191±58 | 132±28 | 36±22 | 0.001 |

# Genetic and environmental factors affecting the response to statin therapy (atorvastatin 20mg/day) in patients with molecularly defined familial hypercholesterolaemia

| Type of the LDLR mutation | n | -LDL-C% mean±SD | Covariate baseline LDL-C | p* |
|---|---|---|---|---|
| II | 28 | 34±9 | 297 | 0.001 |
| V | 21 | 49±9 | 254 | |

* by ancova

Miltiadous G. et al: Pharmacogenetics and Genomics 2005;15:219-225

# Factors affecting the statin LDL-C lowering effect in patients with heterozygous FH

| PARAMETER | beta | P-value* |
|---|---|---|
| CLASS OF THE LDLR GENE MUTATION II vs V | 0.60 | 0.00 |
| APOE POLYMORPHISM | 0.07 | 0.60 |
| CETP POLYMORPHISM | -0.15 | 0.41 |
| SEX | 0.00 | 0.98 |
| AGE | 0.06 | 0.66 |
| TOBACCO | 0.16 | 0.30 |
| BMI | 0.27 | 0.09 |
| BASELINE LDL-C LEVELS | 0.69 | 0.001 |

*multiple regression analysis (n=49)

# EZETIMIBE ADDED TO ONGOING STATIN THERAPY (META-ANALYSIS)

## EZETIMIBE / STATIN VS PLACEBO/STATIN

LDL CHOL: -23.6%, p<0.0001

HDL CHOL: +1.7%, p<0.0001

D. Mikhailidis et al: CMRO 2007;23: 2009-2026

# ROSUVASTATIN 40mg + EZETIMIBE 10mg

↓ LDL CHOL κατά 69,8%

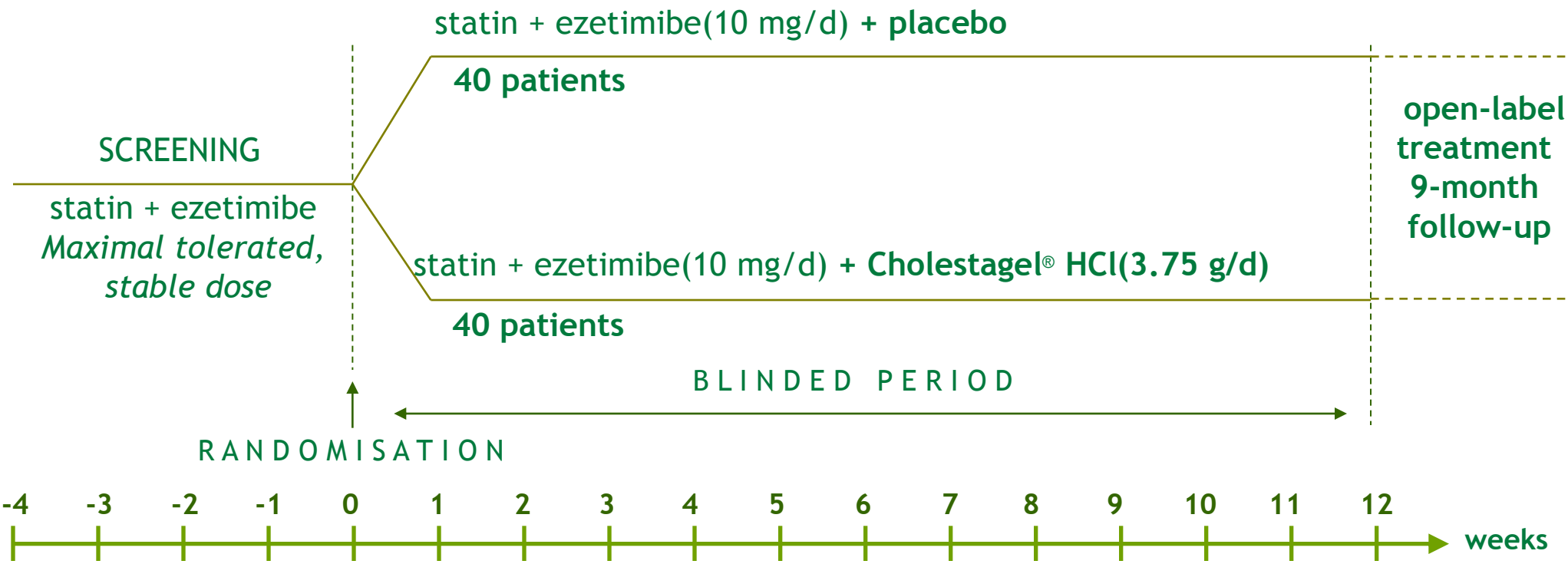
↓ TRG κατά 35%

↑ HDL CHOL κατά 11%

EXPLORER STUDY: Am J Cardiol 2007;99:673-680

# Triple Design

- **Phase 4 randomised, double-blind, placebo-controlled, parallel-group, multicentre study of Cholestagel® as add-on therapy in patients with FH with LDL-C > 100mg/dL (2.5 mmol/l)**



# ΤΡΙΠΛΗ ΥΠΟΛΙΠΙΔΑΙΜΙΚΗ ΑΓΩΓΗ ΣΕ ΕΝΗΛΙΚΑ ΑΤΟΜΑ

Ασθενείς με FH υπό αγωγή με ΣΤΑΤΙΝΗ + EZETIMIBE

Τυχαιοποίηση σε COLESEVELAM (3.8g/d) vs placebo

Δ LDL CHOL: -18.5%, 6 εβδομάδες

-12%, 12 εβδομάδες

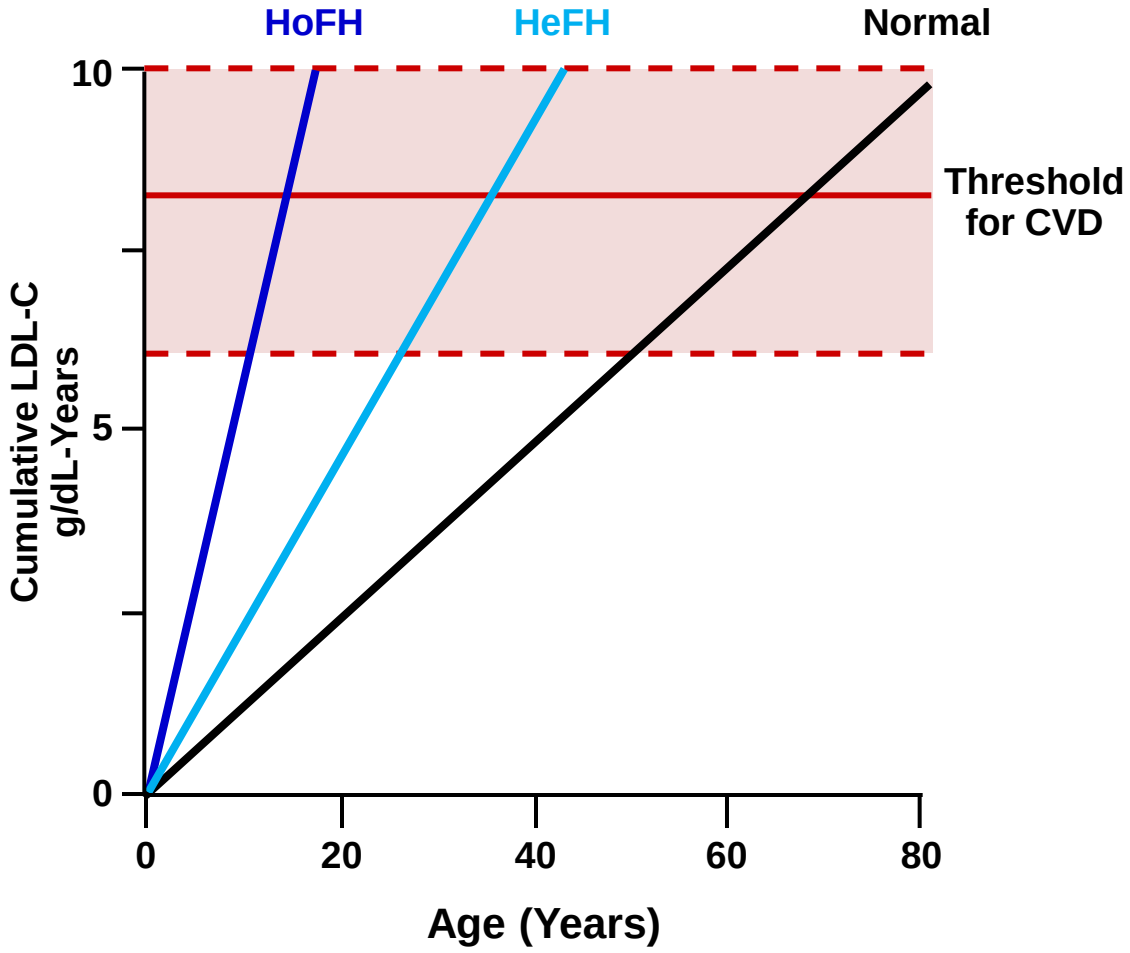
Δ HDL CHOL: +3.3%, 12 εβδομάδες

Δ ApoB/Apo$A_1$: -12.2%, 12 εβδομάδες

Clin Ther 2010;32: 615-625

# Elevated LDL-C is the cause of cardiovascular disease in HoFH

- LDL-C is a causal factor in the development of CVD
- Patients with HoFH typically develop cardiovascular disease before the age of 20years[1]
- Even with currently existing therapies, the mean age of death is 33 years[2]




1. Goldstein, J. L., H. H. Hobbs, et al. (2001). *The Metabolic and Molecular Basis of Inherited Disease*.
2. Raal J, et al. *Circulation*. (2011).
3. Adapted from Horton et al. *J Lipid Res*. 2009;50:S172-S177

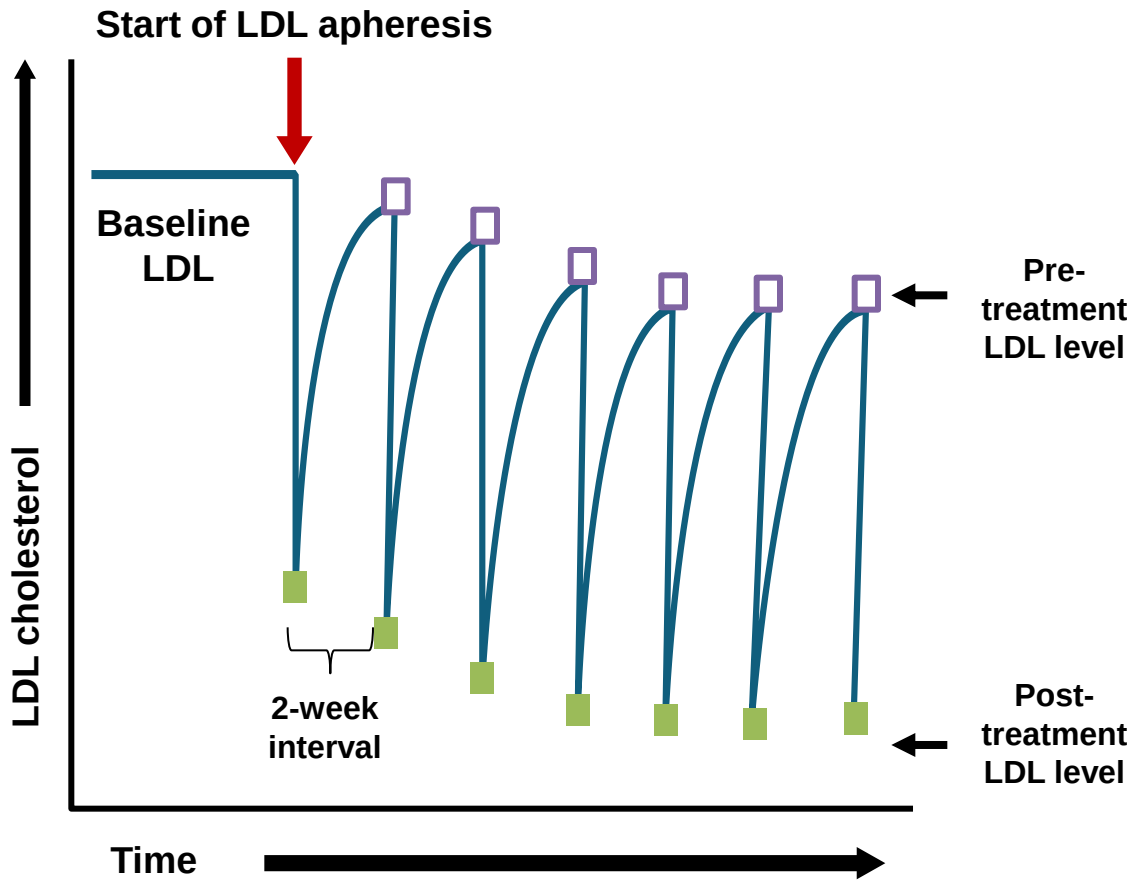
# Current cholesterol lowering drugs are insufficient in HoFH

| Class | Major Effect | Typical LDL-C-Lowering Response |
|---|---|---|
| **Statins (e.g. atorvastatin, rosuvastatin)** | **↑ LDLR activity** | **<10 to 25%** |
| **Bile acid sequestrants (e.g. cholestyamine, colestipol)** | **↑ LDLR activity** | **<10%** |
| **Cholesterol absorption inhibitors (e.g. ezetimibe )** | **↑ LDLR activity** | **<10%** |
| **Nicotinic acid (i.e. niacin)** | **Unknown** | **<10%** |

Rader DJ, et al. *J Clin Invest.* 2003;111:1796-1803. Konrad RJ, et al. *Lipids Health Dis.* 2011;10:38.

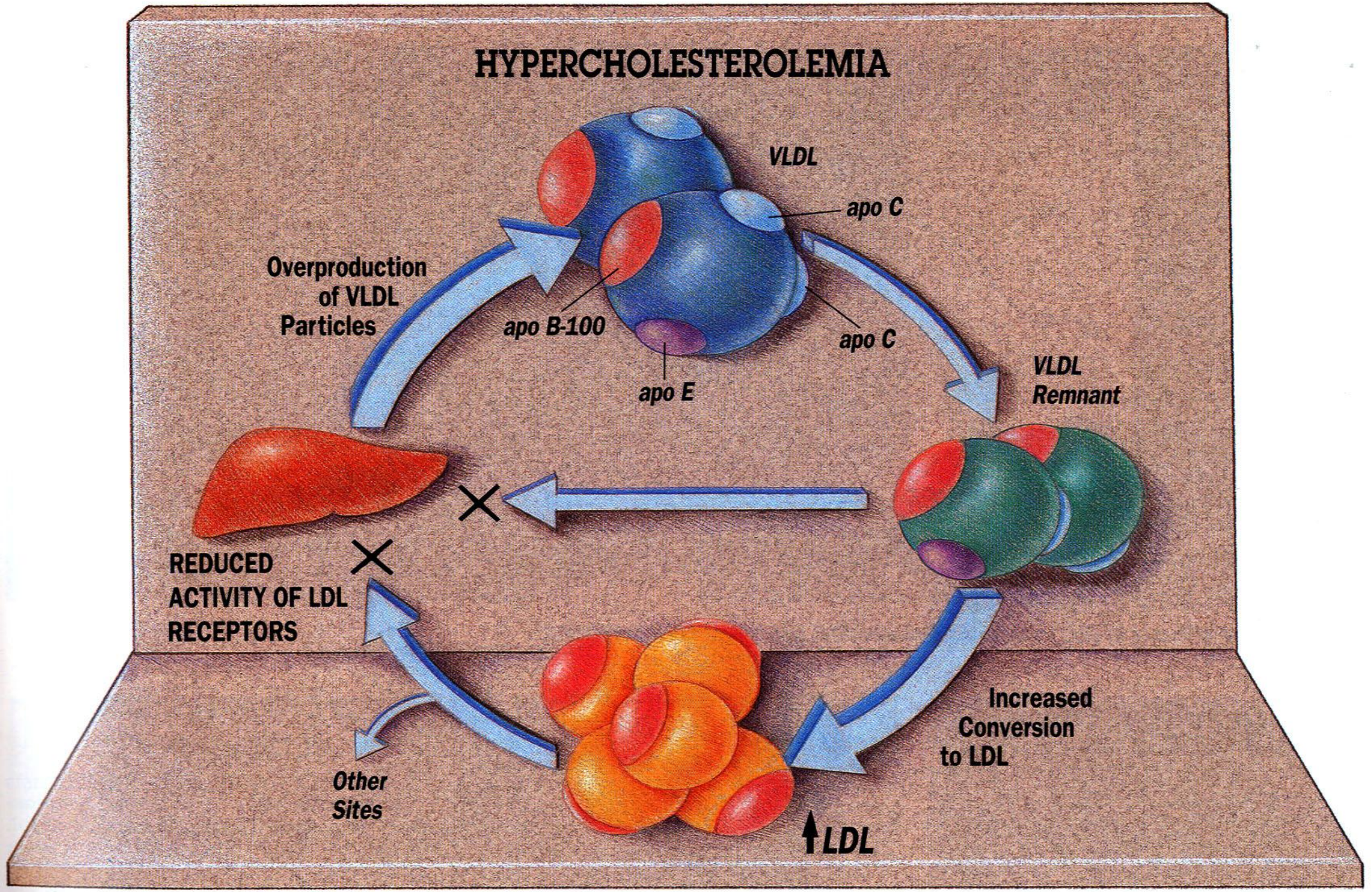
# LDL apheresis is current standard of care for HoFH

# LDL-C Levels acutely decrease and then rebound following apheresis

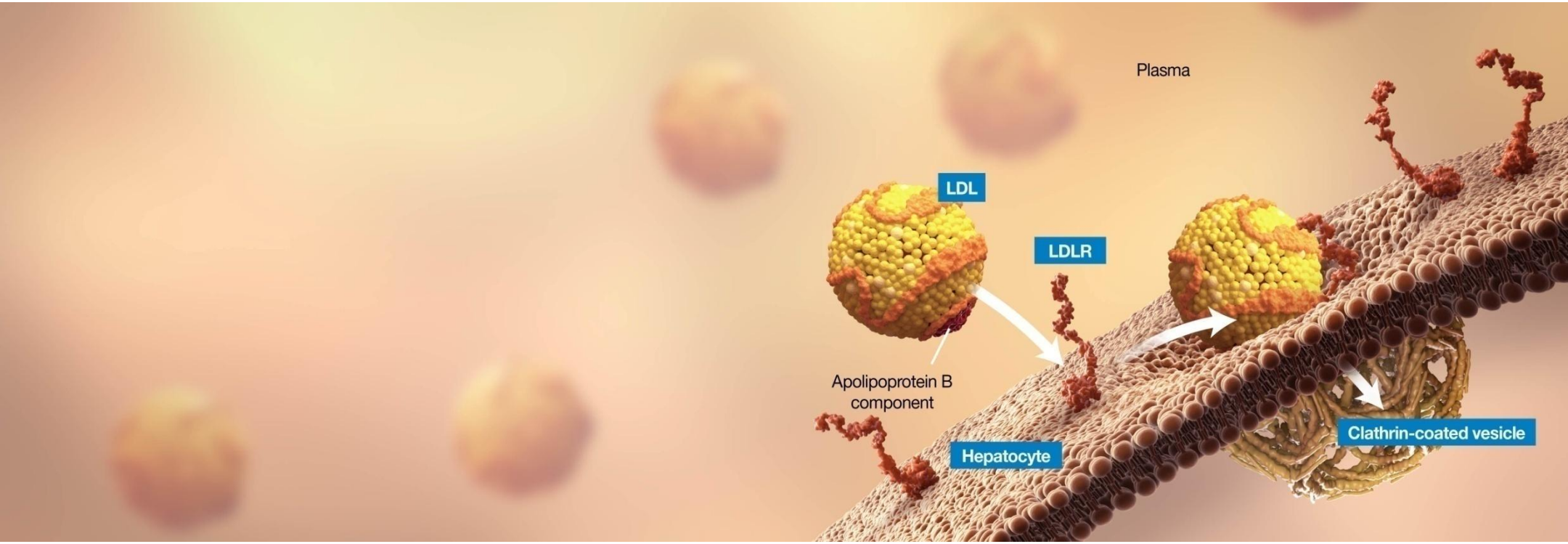



- In a cohort of 7 patients with HoFH, lipid lowering therapies and once weekly apheresis reduced LDL-C to
  - Pre-apheresis - 5.1 mmol/l
  - Post apheresis - 2.2 mmol/l
  - Mean interval - 4.2 mmol/l

1. Thomson et al. Atherosclerosis 2010, 208: 317-321. 2. Graesdal et al. J Clin Lipidology 2012, 6:331-339

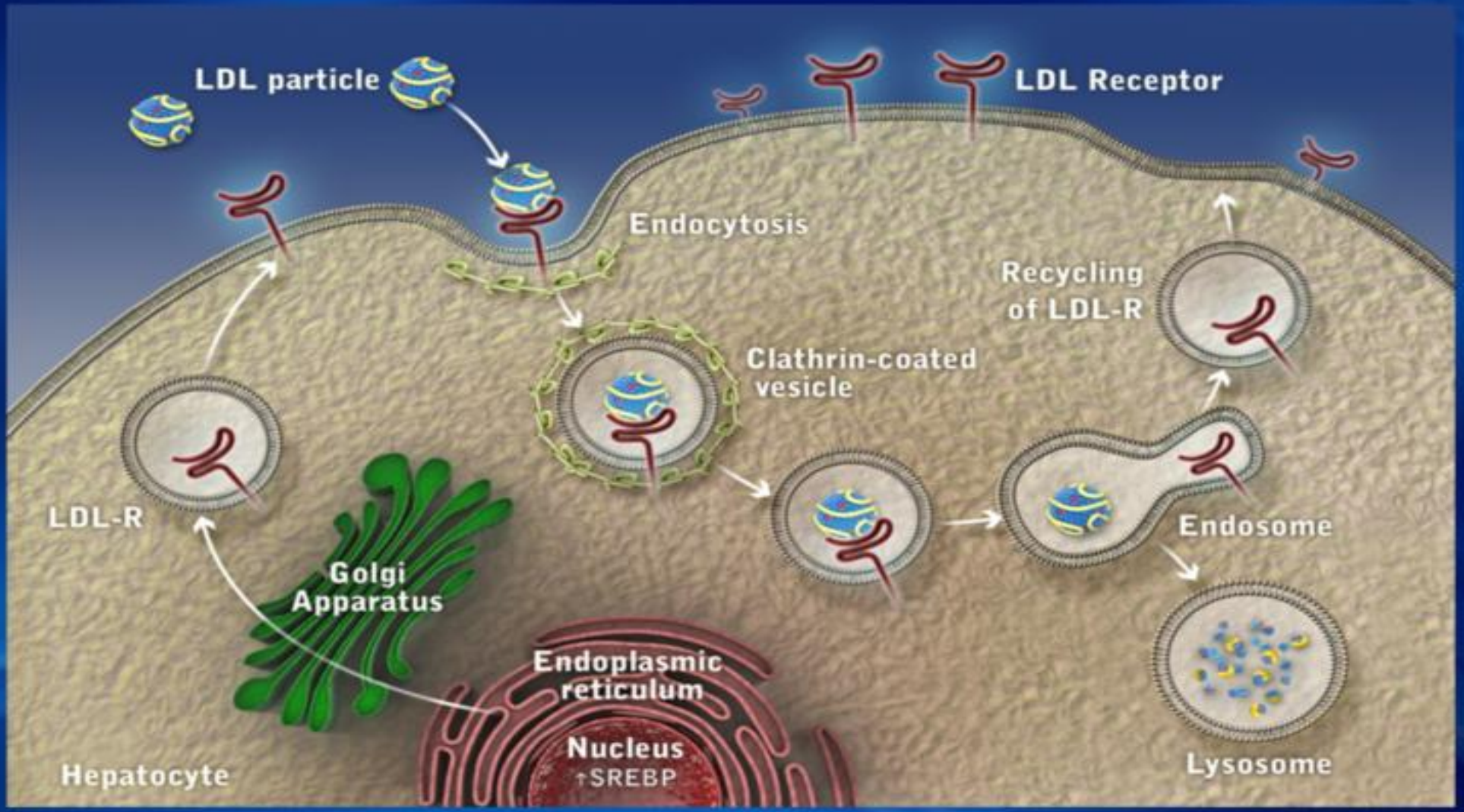

HYPERCHOLESTEROLEMIA
VLDL
apo C
Overproduction of VLDL Particles
apo B-100
apo C
apo E
VLDL Remnant
REDUCED ACTIVITY OF LDL RECEPTORS
Increased Conversion to LDL
Other Sites
LDL

# Hepatic LDLRs Play a Central Role in Cholesterol Homeostasis

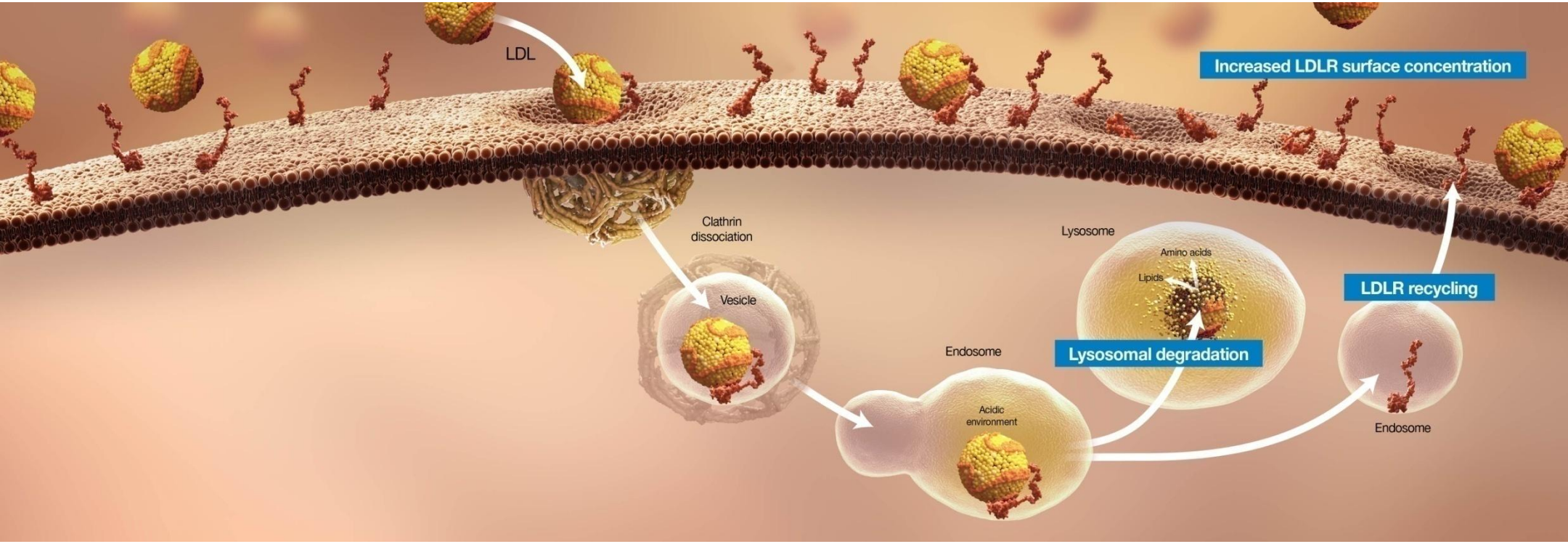



1. Brown MS, et al. *Proc Natl Acad Sci* 1979;76:3330-3337.
2. Qian YW, et al. *J Lipid Res*. 2007;48:1488-1498.
3. Steinberg D, et al. *Proc Natl Acad Sci U S A.* 2009;106:9546-9547.

# LDL Receptor Function and Life Cycle



# Recycling of LDLRs Enables Efficient Clearance of LDL-C Particles




1. Brown MS, et al. *Proc Natl Acad Sci U S A*. 1979;76:3330-3337.
2. Steinberg D, et al. *Proc Natl Acad Sci U S A*. 2009;106:9546-9547.
3. Goldstein JL, et al. *Arterioscler Thromb Vasc Biol*. 2009;29:431-438.

# PCSK9

- Ένζυμο που συνδέεται με τους LDL υποδοχείς και αυξάνει την αποδόμηση τους
- Γλυκοπρωτεϊνη (692 αμινοξέα) που ανήκει στην οικογένεια των πρωτεασών της σερίνης που ονομάζονται proprotein convertase (PC)
- Το γονίδιο που κωδικοποιεί την πρωτεΐνη βρίσκεται στο χρωμόσωμα 1 (1P32)
- Εκφράζεται σε πολλά όργανα-κυρίως όμως στο ήπαρ

PCSK9

Σύνδεση με τους LDL υποδοχείς

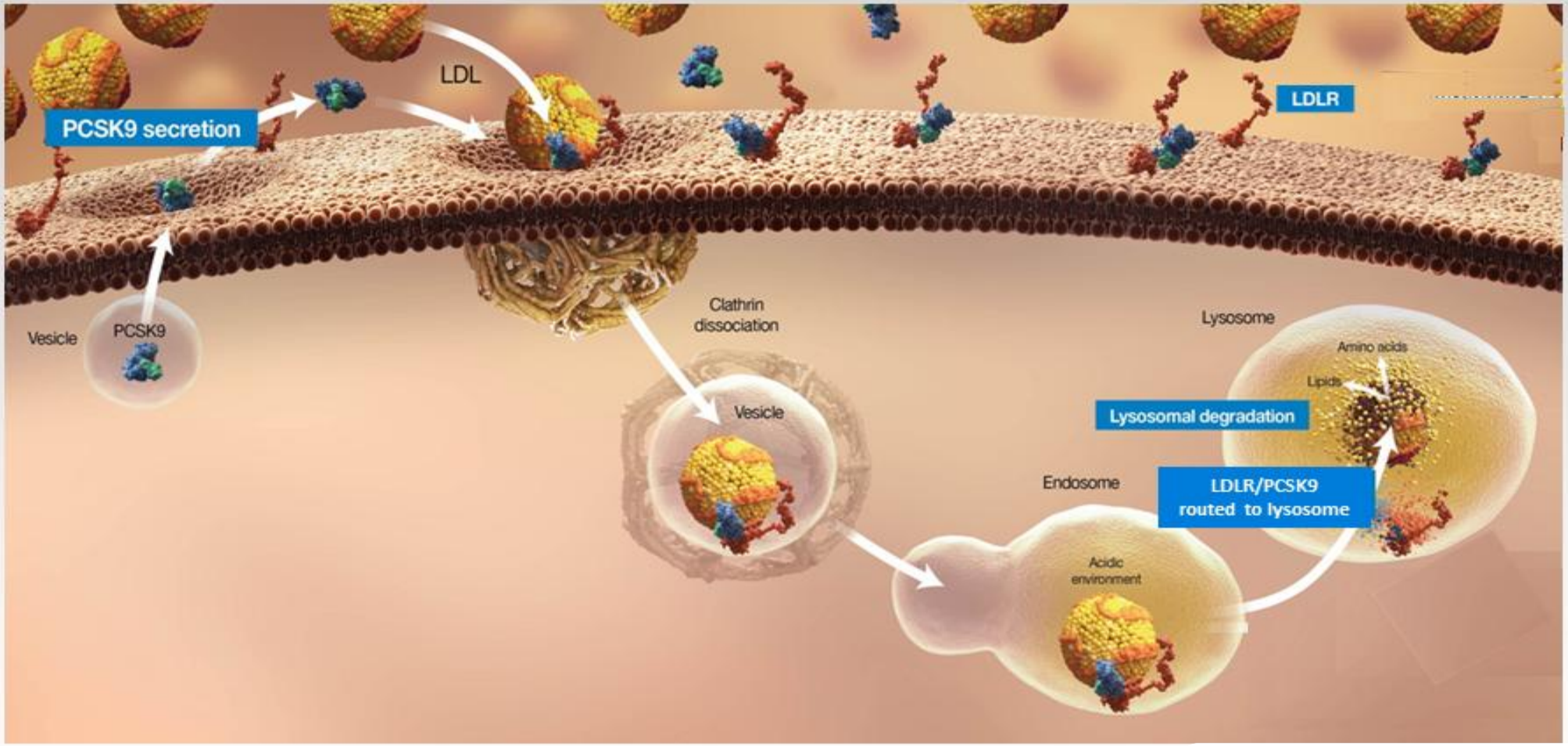
Σύμπλοκο PCSK9 / LDLR

Αποδόμηση στα λυσοσώματα

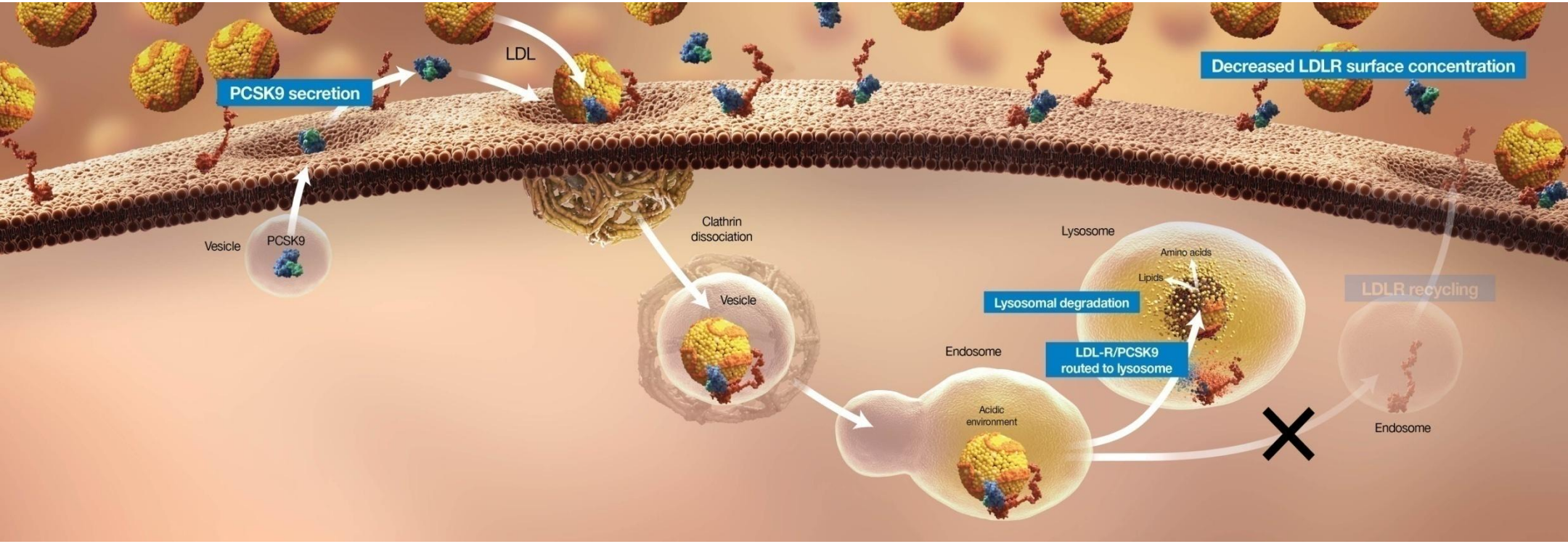
↓ LDL-R

↑ LDL CHOL

# PCSK9 Regulates Surface LDLRs by Increasing Their Lysosomal Degradation



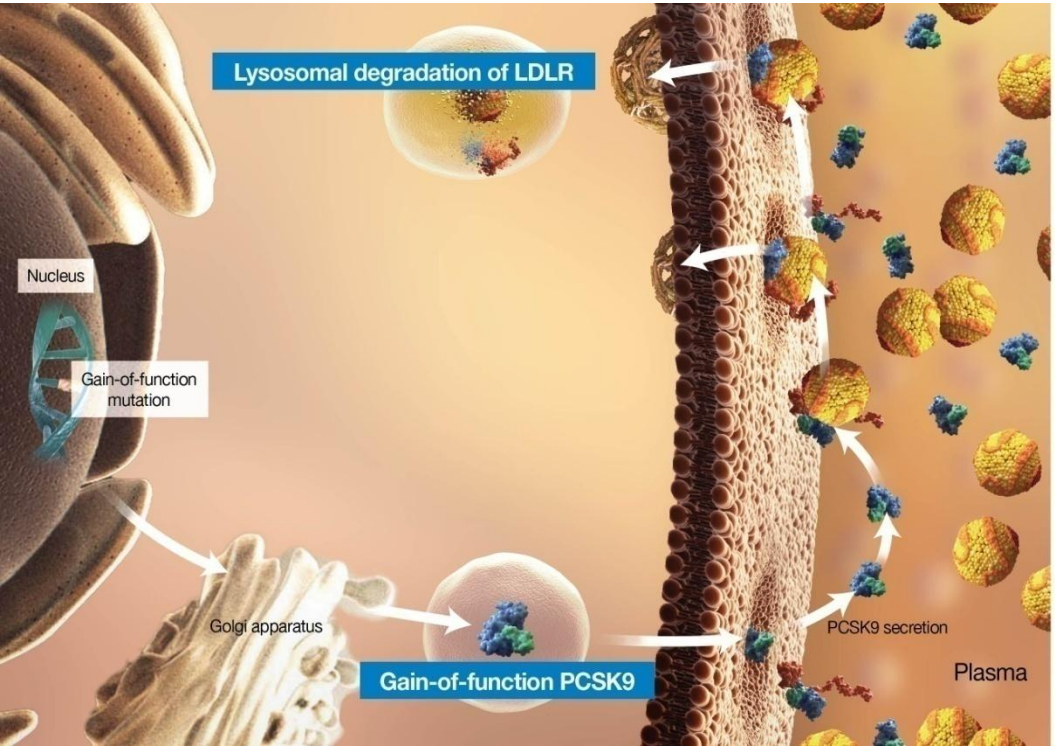
# PCSK9 Regulates the Surface Expression of LDLRs by Targeting for Lysosomal Degradation



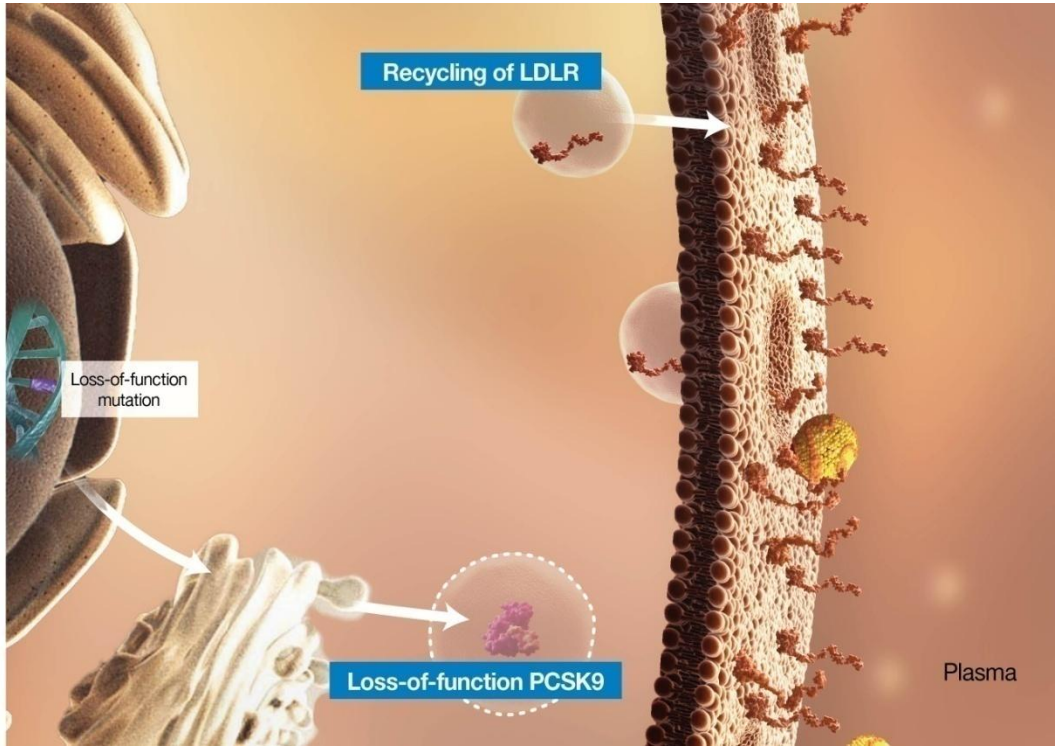


1. Qian YW, et al. *J Lipid Res*. 2007;48:1488-1498.
2. Horton JD, et al. *J Lipid Res*. 2009;50:S172-S177.
3. Zhang DW, et al. *J Biol Chem.* 2007;282:18602-18612.

# Genetic Variants of PCSK9 Demonstrate Its Importance in Regulating LDL Levels




**PCSK9 Gain of Function = Less LDLRs**




**PCSK9 Loss of Function = More LDLRs**

# Gain-of-Function Mutations in PCSK9 Cause Autosomal-Dominant Hypercholesterolemia* (ADH)

| *PCSK9* Variant | Population | Clinical Characteristics |
|---|---|---|
| D374Y | British, Norwegian families, 1 Utah family | Premature CHD<br>Tendon xanthomas<br>Severe hypercholesterolemia |
| S127R | French, South African, Norwegian families | Tendon xanthomas; CHD, early MI, stroke |
| R215H | Norwegian family | Brother died at 31 from MI; strong family history of CVD |

- Associated with:
  - High serum LDL-C[2]
  - Premature CHD and MI[2]
  - In vitro testing in many identified mutations show decreased levels of LDLRs[3]

1. Abifadel M, et al. *Hum Gen*. 2009;30:520-529.
2. Horton JD, et al. *J Lipid Res*. 2009;50:S172-S177.
3. Cameron J, et al. *Hum Mol Genet.* 2006;15:1551-1558.

**For a full list of ADH mutations, please see refer to Abifadel reference.*

# Loss-of-Function Mutations in PCSK9 Are Associated With Decreased LDL-C and CHD Risk

| *PCSK9* Variant | Population | LDL-C | CHD Risk |
|---|---|---|---|
| R46L | ARIC, DHS | ↓ 15%[1] | ↓ 47%[1] |
| Y142X or C679X | ARIC, DHS | ↓ 28%-40%[1,2] | ↓ 88%[1] |
| R46L | CGPS | ↓ 11%[3] | ↓ 46%[3] |

- Heterozygous LOF mutations found in 1% to 3% of population[1]
- Associated with
  - Lower serum LDL-C[1]
  - Lower incidence of coronary heart disease[1]
- PCSK9 null individual identified (compound heterozygote for two inactivating mutations)
  - No detectable circulating PCSK9 with strikingly low LDL-C (14 mg/dL)[4]
  - Healthy and fertile college graduate in apparent good health[4]
- Inhibiting LDLR/PCSK9 interaction may lower plasma LDL-C levels[5]

LOF = loss of function.


1. Cohen JC, et al. *N Engl J Med.* 2006;354:1264-1272.
2. Cohen J, et al. *Nat Genet.* 2005;37:161-165.
3. Benn M, et al. *J Am Coll Cardiol*. 2010;55:2833-2842.
4. Zhao et al. *Am Journal of Hum Gen*. 2006;79:514-534.
5. Steinberg D, et al. *Proc Natl Acad Sci U S A.* 2009;106:9546-9547.

ΣΤΑΤΙΝΕΣ

↓ ενδοκυττάριας σύνθεσης χοληστερόλης

↑ δραστηριότητας των LDL υποδοχέων

↑ καταβολισμού των LDL

↓ LDL CHOL

↑ έκφρασης της PCSK9

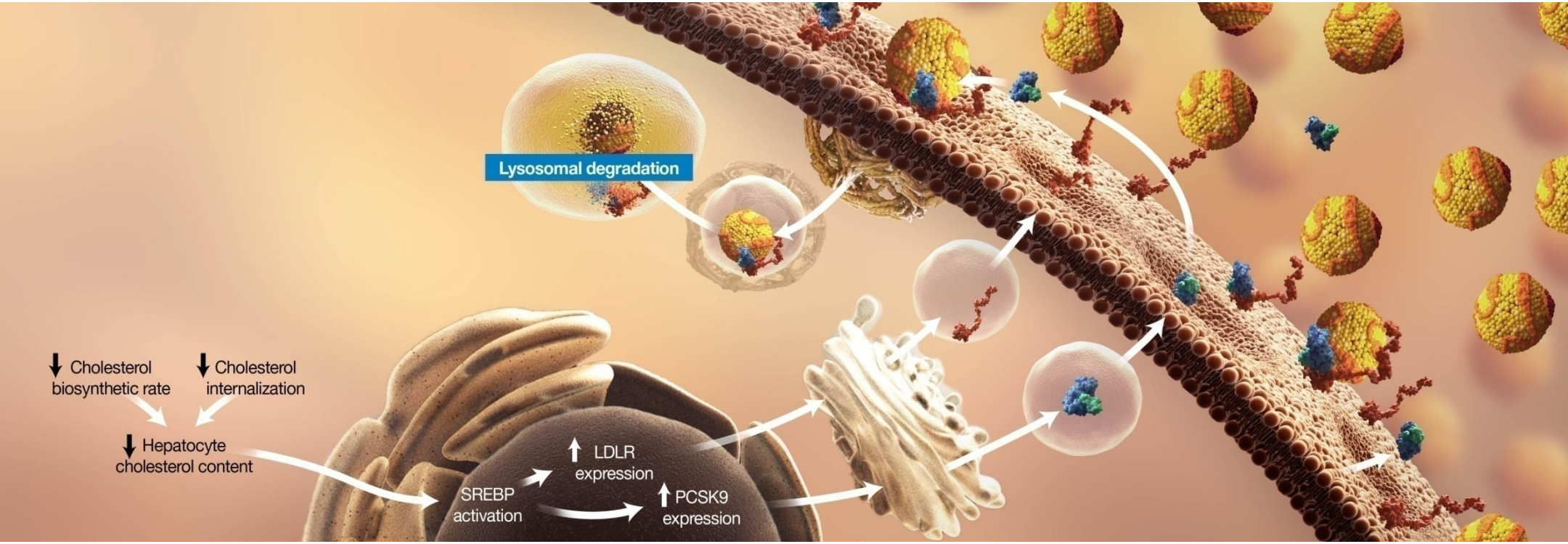
↑ αποδόμησης των LDL υποδοχέων στα λυσοσώματα

↓ LDL υποδοχέων

↑ LDL CHOL

Μείωση της δυνατότητας των στατινών να μειώσουν τα επίπεδα της LDL CHOL

# LDLR and PCSK9 Expression Are Both Upregulated When Intercellular Cholesterol Levels Are Low




*[SREBP] = sterol regulatory element-binding protein.

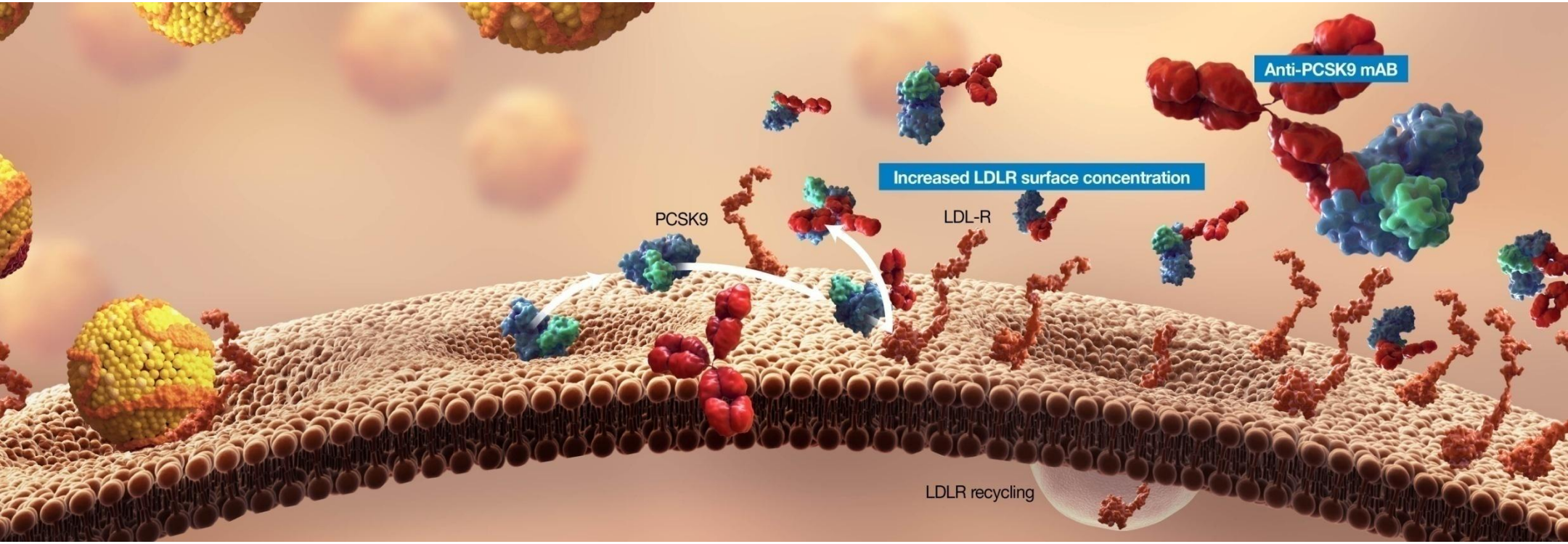
1. Goldstein JL, et al. *Arterioscler Thromb Vasc Biol.* 2009;29:431-438.
2. Dubuc G, et al. *Arterioscler Thromb Vasc Biol.* 2004;24:1454-1459.

Οι στατίνες επιτυγχάνουν το στόχο της υπολιπιδαιμικής αγωγής σε ένα σχετικά μικρό ποσοστό ασθενών υψηλού κινδύνου – ανάγκη χορήγησης υψηλών δόσεων – δοσοεξαρτώμενες ανεπιθύμητες ενέργειες τους

# ΓΙΑ ΤΗΝ ΕΠΙΤΕΥΞΗ ΤΩΝ ΣΤΟΧΩΝ ΤΗΣ ΥΠΟΛΙΠΙΔΑΙΜΙΚΗΣ ΑΓΩΓΗΣ

**Ανάγκη χορήγησης υποχοληστερολαιμικών φαρμάκων με διαφορετικό μηχανισμό δράσης**

# Blockade of PCSK9/LDLR Interaction May Lower LDL Levels

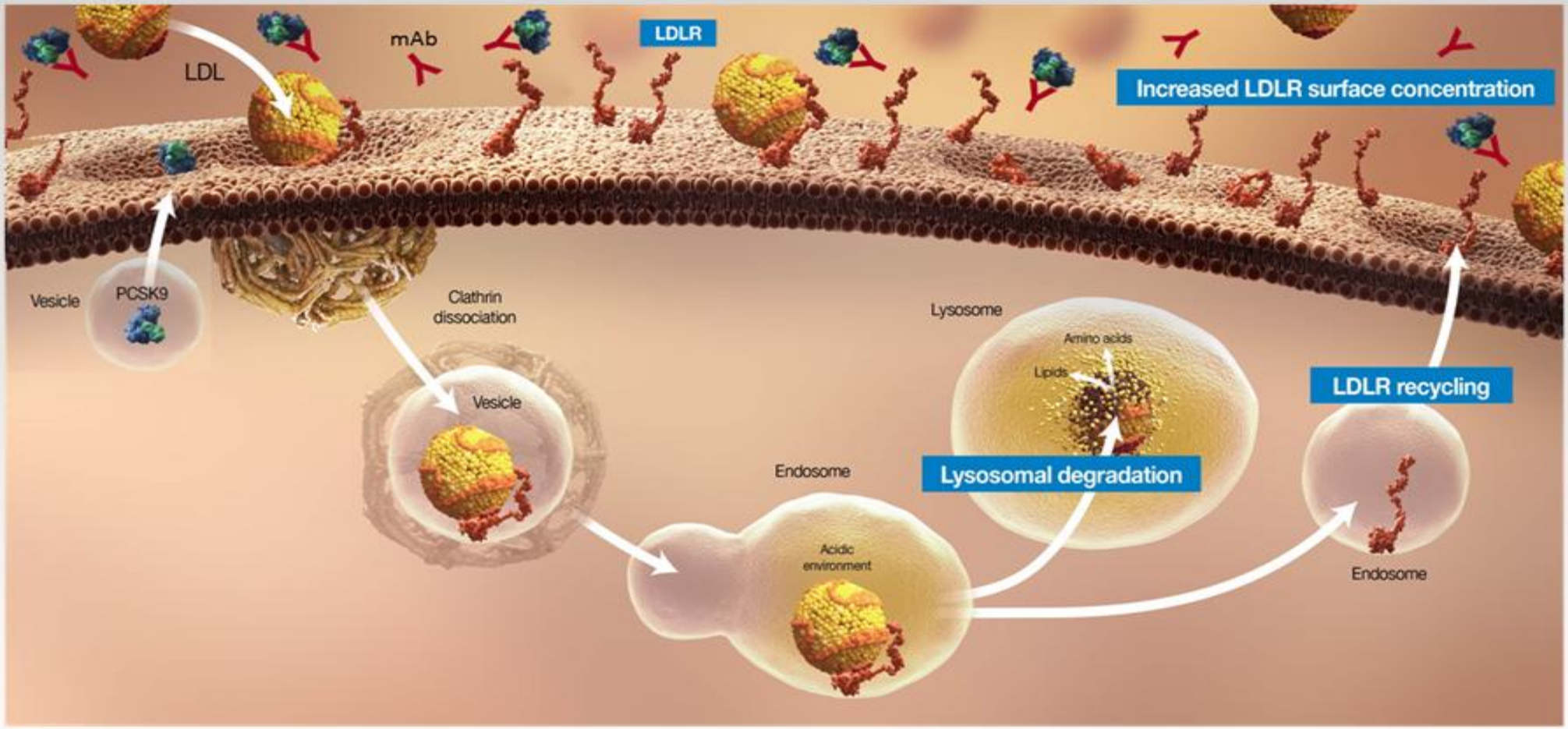



1. Chan JC, et al. *Proc Natl Acad Sci U S A.* 2009;106:9820-9825.

# PCSK9 INHIBITORS

Μονοκλωνικά αντισώματα που εμποδίζουν την αλληλεπίδραση της PCSK9 (proprotein convertase subtilisin/kexin 9) με τον LDL υποδοχέα

# Impact of PCSK9 Monoclonal Antibodies on LDL Receptor Surface Concentrations



# ΕΠΙΤΕΥΞΗ ΤΩΝ ΣΤΟΧΩΝ ΤΗΣ ΥΠΟΛΙΠΙΔΑΙΜΙΚΗΣ ΑΓΩΓΗΣ

PCSK9 inhibitors

+

ΣΤΑΤΙΝΗ

# EVOLOCUMAB VS EZETIMIBE IN HYPERCHOLESTEROLEMIC SUBJECTS UNABLE TO TOLERATE EFFECTIVE STATINS DOSES GAUSS-2 TRIAL (n=307)

Evolocumab 140mg/2 εβδομάδες ή evolocumab 420mg/4 εβδομάδες vs ezetimibe 10mg

Evolocumab: ↓ LDL CHOL κατά 53-56%

Δ με ezetimibe κατά 37-39%

Muscle adverse events: evolocumab 12% vs ezetimibe 23%

JACC 2014;63: 2541-2548

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# A 52-Week Placebo-Controlled Trial of Evolocumab in Hyperlipidemia

Dirk J. Blom, M.D., Ph.D., Tomas Hala, M.D., Michael Bolognese, M.D., Michael J. Lillestol, M.D., Phillip D. Toth, M.D., Lesley Burgess, M.B., B.Ch., M.Med., Ph.D., Richard Ceska, M.D., Ph.D., Eli Roth, M.D., Michael J. Koren, M.D., Christie M. Ballantyne, M.D., Maria Laura Monsalvo, M.D., Kate Tsirtsonis, M.Sc., Jae B. Kim, M.D., Rob Scott, M.D., Scott M. Wasserman, M.D., and Evan A. Stein, M.D., Ph.D., for the DESCARTES Investigators*

This article was published on March 29, 2014, at NEJM.org.

Ασθενείς υπό αγωγή με ATORVA (10 ή 80mg/d) ή συνδυασμό ATORVA (80mg/d) + ezetimibe (10mg/d)
Evolocumab vs placebo
(420mg/4 εβδομάδες), n=901

↓ LDL CHOL κατά 57%, p<0.001

Ανεπιθύμητες ενέργειες: ρινοφαρυγγίτιδα, οσφυαλγία, γριπώδης συνδρομή

N Engl J Med 2014;370: 1809-1819

# REDUCTION IN LIPOPROTEIN (a) WITH PCSK9 MONOCLONAL ANTIBODY EVOLOCUMAB (AMG 145)

## n=1359 άτομα

**Evolocumab (140mg/2 weeks) ⇨ ⬇ Lp(a) κατά 29.5%**

**Evolocumab (420mg/4weeks) ⇨ ⬇ Lp(a) κατά 24.5%**

**Η μείωση της Lp(a) συσχετίζονται με τις ποσοστιαίες μειώσεις της LDL CHOL**

JACC 2014;63: 1278-1288

# EVOLOCUMAB (AMG 145) ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ (ΜΕΛΕΤΗ OSLER)

Μια μελέτη 52 εβδομάδων , n=1104, 420mg /4 εβδομάδες

⬇ LDL CHOL κατά 52.3%
ΑΠΟΤΕΛΕΣΜΑΤΙΚΗ ΚΑΙ ΑΣΦΑΛΗΣ ΑΓΩΓΗ

CIRCULATION, 2014;129: 2034-2043

# ΕΠΙΤΕΥΞΗ ΣΤΟΧΟΥ ΥΠΟΛΙΠΙΔΑΙΜΙΚΗΣ ΑΓΩΓΗΣ ΣΕ ΑΤΟΜΑ ΥΨΗΛΟΥ ΚΙΝΔΥΝΟΥ

## LAPLACE-TIMI 57 TRIAL

**>90% των ασθενών πέτυχε το στόχο LDL CHOL <70mg/dl**

J Am Coll Cardiol 2014;63: 430-3

# ΜΟΝΟΘΕΡΑΠΕΙΑ ΜΕ EVOLOCUMAB ςΕ ΑςΘΕΝΕΙς ΜΕ ΥΠΕΡΧΟΛΗςΤΕΡΟΛΑΙΜΙΑ

## ΜΕΛΕΤΗ MENDEL-2

n=614 , EVOLOCUMAB 120mg /2 εβδομάδες ή 420 mg / 4 εβδομάδες:

⬇ LDL CHOL κατά 55-57% vs placebo

⬇ LDL CHOL κατά 38% vs ezetimibe

JACC 2014;63: 2531-40

# EVOLOCUMAB OR EZETIMIBE + STATIN THERAPY ΣΕ ΑΣΘΕΝΕΙΣ ΜΕ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ

## LAPLACE -2 Randomized clinical trial

Evolocumab:

- ⬇ LDL CHOL κατά 66%-75% / 2 εβδομάδες
- ⬇ LDL CHOL κατά 63%-75% / 4 εβδομάδες

JAMA 2014;311: 1870-1882

# AMG-145: A PCSK9 INHIBITOR

- Χορηγείται υποδόρια κάθε 2/4 εβδομάδες
- Αποτελεσματική μείωση της LDL CHOL σε ασθενείς με ή χωρίς FH, ακόμα και σε ασθενείς με ομόζυγη FH
- Ιδιαίτερα αποτελεσματικό φάρμακο σε συνδυασμό με στατίνες (± ezetimibe)

European Heart Journal Advance Access published July 22, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu274

REVIEW

*Clinical update*

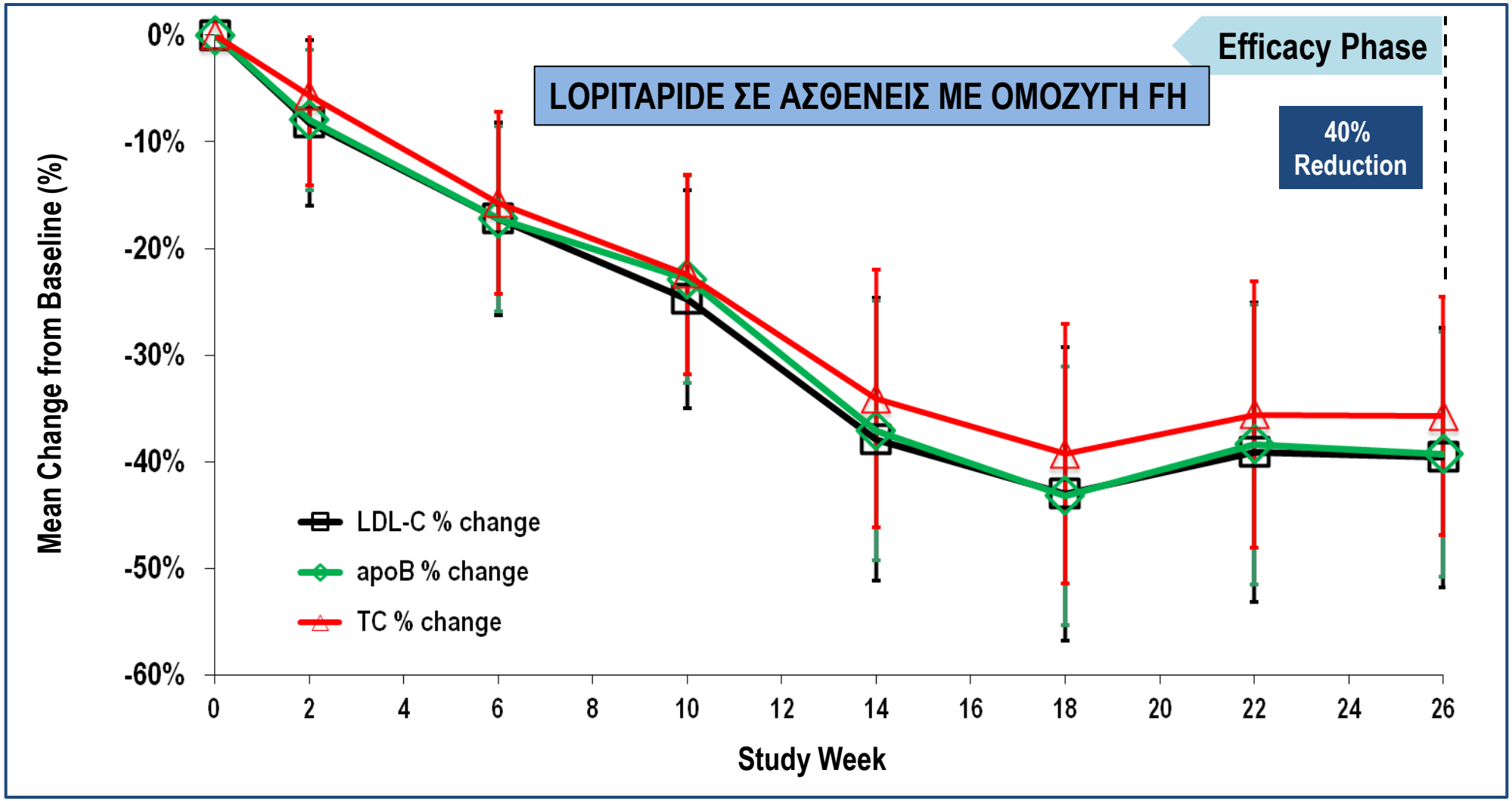
# Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society

**Marina Cuchel*, Eric Bruckert, Henry N. Ginsberg, Frederick J. Raal, Raul D. Santos, Robert A. Hegele, Jan Albert Kuivenhoven, Børge G. Nordestgaard, Olivier S. Descamps, Elisabeth Steinhagen-Thiessen, Anne Tybjærg-Hansen, Gerald F. Watts, Maurizio Averna, Catherine Boileau, Jan Borén, Alberico L. Catapano, Joep C. Defesche, G. Kees Hovingh, Steve E. Humphries, Petri T. Kovanen, Luis Masana, Päivi Pajukanta, Klaus G. Parhofer, Kausik K. Ray, Anton F. H. Stalenhoef, Erik Stroes, Marja-Riitta Taskinen, Albert Wiegman, Olov Wiklund, and M. John Chapman, for the European Atherosclerosis Society Consensus Panel on Familial Hypercholesterolaemia†**

Institute for Translational Medicine and Therapeutics, University of Pennsylvania, 8039 Maloney Building, 3600 Spruce Street, Philadelphia, PA 19104, USA

*Received 13 March 2014; revised 19 May 2014; accepted 13 June 2014*

# Mean % Change in TC, LDL-C, and Apo B Through the Efficacy Phase (ITT, LOCF)




Rader DJ. J Clin Lipid. 2012:6(3): 282-3; Data on File, Aegerion Pharmaceuticals

# Lomitapide should be approved for HoFH in Europe, EMA advised

**LOJUXTA, Aegerion Pharmaceuticals**

**London, UK** - The **Committee for Medicinal Products for Human Use** (CHMP) of the **European Medicines Agency** (EMA) has recommended that the **lomitapide** preparation Lojuxta (Aegerion Pharmaceuticals) be approved "as an adjunct to a low-fat diet and other lipid-lowering medicinal products with or without low-density-lipoprotein apheresis in adult patients with homozygous familial hypercholesterolemia (HoFH)" [1]. Such recommendations are usually adopted officially by the EMA.

The "positive opinion" rendered by the CHMP follows **FDA approval of the same company's lomitapide preparation** Juxtapid for the same indication in December 2012, as reported by **heartwire**. The FDA's advisory panel had **recommended its approval** by a vote of 13 to 2.

MAY 31, 2013