

Lipoprotein(a): An Independent Driver of Cardiovascular Risk

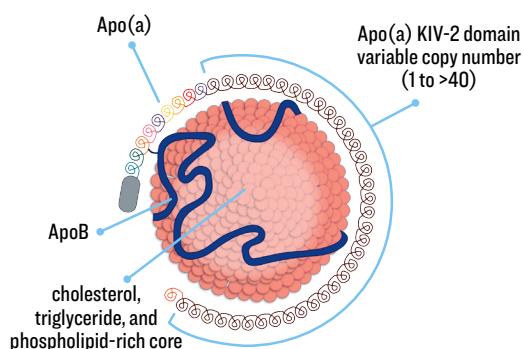


Lipoprotein(a) [Lp(a)] is a lifelong genetic risk factor for ASCVD, independent of other lipids¹⁻³

Elevated Lp(a) affects **~1 in 5** individuals⁴



Structure of Lp(a)^{3,5-7}

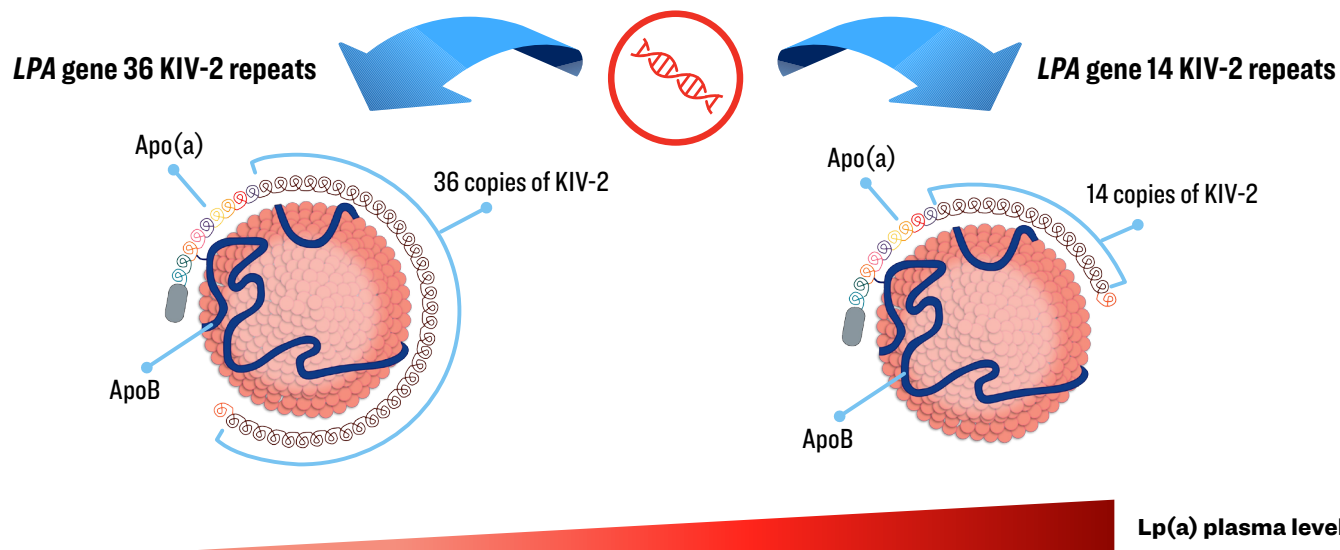


- Lp(a) is composed of a cholesterol-rich particle containing apoB, which is covalently attached to apo(a) via a disulfide bond^{1,3,8}
- Apo(a) is specific to Lp(a) and shares structural homology with plasminogen^{1,3}

Apo(a) isoforms are genetically determined

- Apo(a) isoform size, defined by varying kringle IV type 2 (KIV-2) repeats, is a major genetic determinant of Lp(a) concentration^{2,3}
- More than 40 apo(a) isoforms exist, typically with 1 to >40 KIV-2 repeats^{1,3,5}

Smaller isoforms correlate with higher Lp(a) plasma concentrations and increased ASCVD risk^{2,3,8}



Apo(a) isoforms are genetically determined (cont.)



- Lp(a) concentration is mostly genetically determined by variation at the *LPA* gene locus and is inherited through autosomal codominant transmission.^{3,10}
- Levels are generally established in childhood and remain similar over time, with minimal influence from diet or lifestyle.^{1-3,10}

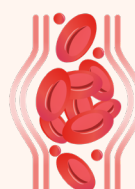
Lp(a) contributes to cardiovascular disease risk through 3 mechanisms



- 1** Accelerates plaque buildup
Promotes cholesterol deposition and Lp(a) retention in the arterial wall, contributing to plaque progression^{7,9}



- 2** Promotes inflammation
Oxidized phospholipids (OxPLs) on Lp(a) activate inflammatory pathways within the vessel wall^{1,2}



- 3** Increases thrombosis risk
Structural homology of apo(a) to plasminogen interferes with fibrinolysis, leading to more unstable clots^{2,8}

Elevated Lp(a) can result in up to a 4-fold increase in ASCVD risk¹⁰

Priority Actions

Measure Lp(a) once in a lifetime

Given its high prevalence, genetic basis, generally stable levels over time, and independent role in ASCVD, **measure Lp(a) at least once in a lifetime for all adults to accurately characterize risk.**^{1,3,4,10}

Standardize Lp(a) testing and reporting

When possible, **use isoform-insensitive assays**, which minimize the impact of apo(a) size variation, and **report Lp(a) in nmol/L** to reflect particle concentration and support consistent interpretation.^{2,8,10}

Apo(a)=apolipoprotein(a); ApoB=apolipoprotein B; ASCVD=atherosclerotic cardiovascular disease; *LPA*=Lipoprotein(a) gene.

1. Tsimikas S. *J Am Coll Cardiol*. 2017;69(6):692-711. 2. Enas EA, et al. *Indian Heart J*. 2019;71(2):99-112. 3. Nordestgaard BG, Langsted A. *Lancet*. 2024;404(10459):1255-1264. 4. Tsimikas S, Marcovina SM. *J Am Coll Cardiol*. 2022;80(9):934-946. 5. Jawi MM, et al. *J Lipids*. 2020;2020:3491764. 6. Kim K, Choi SH. *J Lipid Atheroscler*. 2022;11(3):250-261. 7. Filtz A, et al. *Eur Cardiol*. 2026;21:e07. 8. Iannuzzo G, et al. *Biomedicines*. 2021;9(7):838. 9. Reyes-Soffer G, et al. *Am J Prev Cardiol*. 2024;18:100651. 10. Blumenthal RS, et al. *J Am Coll Cardiol*. 2026;87(19):2624-2757.