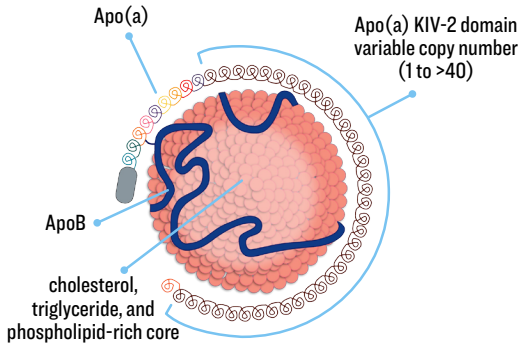
# Lipoprotein(a): An Independent Driver of Cardiovascular Risk

Lipoprotein(a) [Lp(a)] is a lifelong genetic risk factor for ASCVD, independent of other lipids[1-3]

Elevated Lp(a) affects **~1 in 5** individuals[4]

## Structure of Lp(a)[3,5-7]

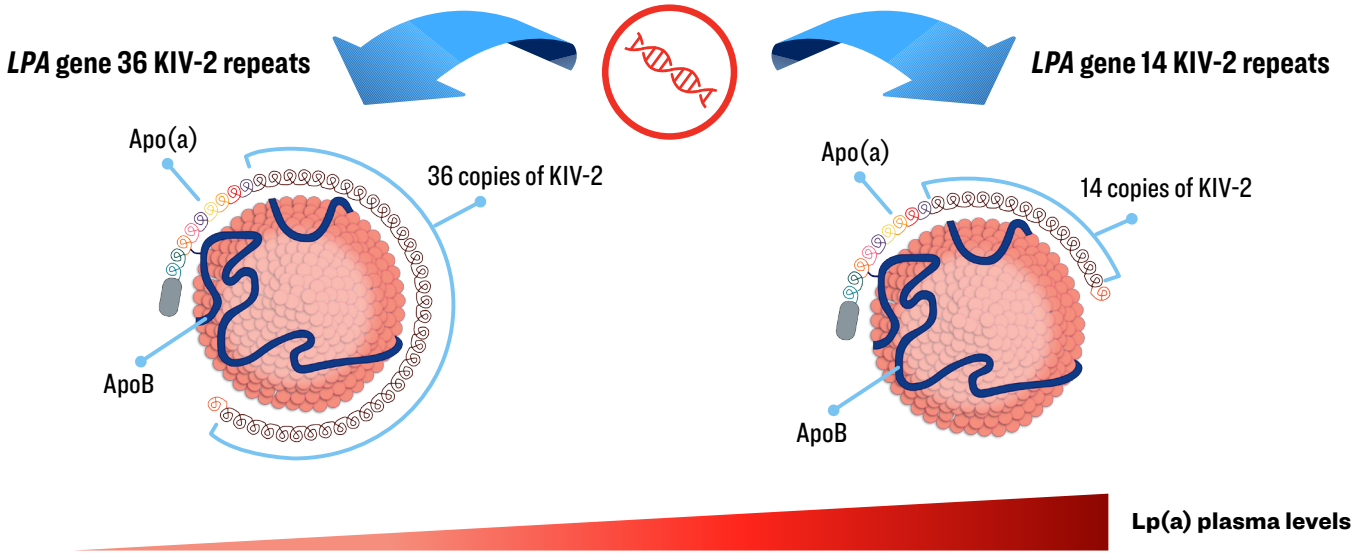



- Lp(a) is composed of a cholesterol-rich particle containing apoB, which is covalently attached to apo(a) via a disulfide bond[1,3,8]
- Apo(a) is specific to Lp(a) and shares structural homology with plasminogen[1,3]

## 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]



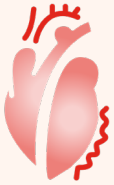
## Apo(a) isoforms are genetically determined (cont.)

- 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

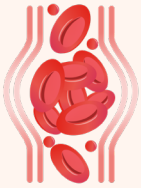
**1 Accelerates plaque buildup**

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 stable clots[2,8]

**Elevated Lp(a) can result in up to a 4-fold increase in ASCVD risk[10]**

## 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.