Low-density lipoprotein (LDL) has a role in aging process, including vascular senescence. However, not all LDL particles are pathogenic, and the culprit LDL entity remains to be identified. In our search for the culprit LDL, we have isolated a highly electronegative entity, L5, from human plasma LDL subfractions (L1-L5) resolved by using anion-exchange chromatography. From evidence based on in vitro, in vivo, and human studies, we have demonstrated L5’s pro-senescent, inflammatory, atherosclerotic, and thrombotic properties, which are not seen in L1-L4. Chemical analysis has revealed that L5 carries excessive apolipoproteins (apoE, A1, CII, CIII, (a), J) in addition to apoB100, which is the only protein in the least electronegative LDL, L1. Further analysis has shown consistent glycosylation on certain residues of both apoE and apoB100 in L5 particles. The associated conformational changes result in hindrance of L5 docking to the normal LDL receptor, forcing an increased residence time of the L5 particles in circulation. The apoB100 molecule in L5 also possesses a prominent SMase-like activity. Consequently, L5 is not only a ceramide-rich lipoprotein but can also induce excessive ceramide production in ECs through SMase-like activity. Additionally, our preliminary studies suggest that L5 is able to glycosylate transmembrane receptors, such as STRA6 (stimulated by retinoic acid 6). Because of STRA6’s role in transducing retinoic acid (vitamin A) signaling, its glycosylation by L5 impedes normal cellular function, adding to complications in disease patterns, as in type 2 diabetes. Thus, L5 is both a glycan receiver and glycan donor/catalyzer. Glycan-lipid interactions are likely to have important biological and clinical implications. Extensive investigations are warranted to delineate the underlying mechanisms to advance our understanding of lipid-associated diseases and to disclose new targets for treatment.