In a recent issue of this journal \(^1\) it was concluded that lipoprotein(a) has an independent prothrombotic role through inhibition of fibrinolysis and by allowing an increased substrate for both platelet aggregation and thrombin, respectively. Accordingly, high levels of both lipoprotein(a) and fibrinogen, in addition to age and insulin, would be considered important risk factors for cardiovascular disease in the elderly. This conclusion apparently clashes with the results of several previous epidemiological surveys, concluding that elevated plasma lipoprotein(a) concentration is a rather frequent finding in centenarians.\(^2,^6\) This apparent paradox has engaged the minds of several scientists for many years, trying to find a reliable bridge between the cardiovascular potential of elevated concentrations of this elusive lipoprotein and human longevity.\(^7,^8\) Apolipoprotein(a), which characterizes lipoprotein(a), is constituted by an inactive protease domain, a single copy of the plasminogen kringle V and multiple repeats of domains homologous to the plasminogen kringle IV. The kringle domains, protein motifs arranged in a triple loop tertiary structure stabilized by three disulfide bridges, are highly conserved conformational regions hidden in the structure of a variety of members of the prothrombin gene family, including prothrombin, plasminogen, apolipoprotein(a), hepatocyte growth factor, urokinase, factor XII, tissue plasminogen activator.\(^4\) Reliable studies on animal models have recently demonstrated that proteolytic break-down products of plasminogen, apolipoprotein(a) and other kringle-containing proteins endorse anti-angiogenic and antitumoral properties both \textit{in vitro} and \textit{in vivo}. In particular, apolipoprotein(a) fragments cleaved from the native protein by naturally occurring enzymes and specific tumour reductases, can maintain metastases in a dormant state and shrink primary tumors by blocking neo-vascularization and tumor growth \textit{in vivo}, allowing prolonged survivals of animals bearing primary human malignancies.\(^9-13\) This outstanding evidence would attribute to lipoprotein(a) an otherwise unexpected beneficial role beside its unfavourable cardiovascular potency and it would finally provide a reliable explanation for the historical paradox of elevated lipoprotein(a) levels associated with longevity.

References

1. Marongiu F. High levels of lipoprotein (a) and fibrinogen: are they a dangerous association in the elderly? Haematologica 2006;91:1584.