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KLOTHO polymorphisms in the elderly population from the Sao Paulo Ageing & Health Study

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The KLOTHO gene was discovered in 1997 when its defective expression in mice led to a syndrome that resembles human ageing, including a short lifespan, arteriosclerosis, and osteoporosis[1]. Its byproduct exists as a secreted protein[2] and as a transmembrane protein expressed predominantly in the distal tubules of the kidney, choroid plexus, and pituitary gland[1], having unknown function in humans. The secreted form suppresses oxidative stress and growth factor signaling, including insulin/IGF-1 signaling, which is associated with longer life span. In fact, studies in human populations attempted to show associations between a functional variant of Klotho, called ''KL-VS'', which has six polymorphisms in linkage disequilibrium, and aging/longevity[3].

At this moment, at least 10 mutations and single-nucleotide polymorphisms (SNPs) were described in humans; 395 G>A and 1818 C>T are the most common SNPs[4]. Nonetheless, the effects of each SNP in human ageing is still obscure.

Associations between specific KLOTHO SNPs and age-related outcomes were demonstrated in different populations. The 395 G>A polymorphism was associated with blood pressure levels in Korean women, and the 1818 C>T polymorphism with fasting plasma glucose in the same population[5]. In Japanese men, both SNPs correlated to body-fat ratio and to HDL cholesterol levels; and in Japanese women, to fasting glucose, bone mineral density and systolic blood pressure[6].

In Brazilian population there are no studies regarding KLOTHO polymorphisms and age-related comorbidities. Hence, our group seeks to evaluate three KLOTHO gene polymorphisms in an elderly population from the Sao Paulo Ageing & Health Study (SPAH) and their potential association with the prevalence of senility-related outcomes.

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