Molecular variants of soluble guanylyl cyclase affecting cardiovascular risk.

Soluble guanylyl cyclase (sGC) is the physiological receptor for nitric oxide (NO) and NO-releasing drugs, and is a key enzyme in several cardiovascular signaling pathways. Its activation induces the synthesis of the second messenger cGMP. cGMP regulates the activity of various downstream proteins, including cGMP-dependent protein kinase G, cGMP-dependent phosphodiesterases and cyclic nucleotide gated ion channels leading to vascular relaxation, inhibition of platelet aggregation, and modified neurotransmission. Diminished sGC function contributes to a number of disorders, including cardiovascular diseases. Knowledge of its regulation is a prerequisite for understanding the pathophysiology of deficient sGC signaling. In this review we consolidate the available information on sGC signaling, including the molecular biology and genetics of sGC transcription, translation and function, including the effect of rare variants, and present possible new targets for the development of personalized medicine in vascular diseases.