Summary

CD26/DPP IV can be considered a moonlighting protein because it is a multifunctional protein that exerts its different functions depending on cell type and intra- or extracellular conditions in which it is expressed. In the present review, we summarize all its known functions in relation to physiological and pathophysiological conditions. The protein is a proteolytic enzyme, receptor, costimulatory protein, and is involved in adhesion and apoptosis. The CD26/DPP IV protein plays a major role in immune response. Abnormal expression is found in the case of autoimmune diseases, HIV-related diseases and cancer. Natural substrates for CD26/DPP IV are involved in immunomodulation, psycho/neuronal modulation and physiological processes in general. Therefore, targeting of CD26/DPP IV and especially its proteolytic activity has many therapeutic potentials. On the other hand, there are homologous proteins with overlapping proteolytic activity, which thus may prevent specific modulation of CD26/DPP IV. In conclusion, CD26/DPP IV is a protein present both in various cellular compartments and extracellularly where it exerts different functions and thus is a true moonlighting protein.