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Sommario/riassunto

Cardiovascular disease (CVD) is the most common cause of morbidity and mortality worldwide, putting a major burden on life quality and social health care systems. Type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) have been identified as important risk factors for CVD, severely increasing the risk on e.g. myocardial infarction, and cardiovascular complications constitute the main cause of death in patients presenting with T2DM, CKD or a combination of both. As these pathologies are expected to rise alarmingly in the next decades, a better understanding of molecular and cellular mechanisms contributing to T2DM, CKD and CVD is required to improve prevention and treatment of these diseases. Furthermore, insight into the interplay between these pathologies and identification of molecular players interconnecting these comorbidities is of tremendous importance for optimal health management in the future. This Research Topic will focus on the chemokine receptor CXCR4 and its ligands CXCL12/SDF-1a and macrophage migration inhibitory factor (MIF) in the context of CVD and its link with T2DM and CKD, as well as address dipeptidyl peptidase-4 (DPP4) as an important protease destabilizing CXCL12. Chemokines and their receptors are important mediators of cell mobilization, recruitment and arrest, and also more broadly induce cell activation by triggering various intracellular signalling tracks. They control homeostatic conditions, but are also critically involved in inflammatory and pathological processes. Genome-wide association

studies revealed single nucleotide polymorphisms connecting CXCL12 as well as MIF with CVD, and a role for both chemokines in T2DM and CKD has also been reported. In this review collection, current knowledge on molecular aspects of the CXCR4 ligand/receptor family and associated signalling pathways will be discussed. The physiological roles of CXCR4, CXCL12, MIF and DPP4 will be summarized, and recent findings on their function in pathological conditions of CVD, T2DM and CKD will be highlighted. This is combined with an extensive introduction providing insight into the pathologies of CVD, T2DM and CKD, discussing clinical features and common pathological aspects of these comorbidities on cellular and molecular level. Also, an overview of available animal models to study these diseases will be provided. This way, this Research Topic summarizes latest knowledge on this crucial molecular axis and its relationship with cardiovascular pathologies for both specialists and interested non-specialists and aims to stimulate further initiatives to unravel the mechanistic involvement of the CXCR4 ligand/receptor family in these morbidities, potentially paving the way for new therapeutical initiatives in the future.