

Charakterisierung intermediärer Monozyten als eigenständige proinflammatorische Zellpopulation

Abstract (Zusammenfassung in englischer Sprache):

Compared to individuals from the general population, patients with chronic kidney disease (CKD) suffer from a dramatically increased mortality, which is mainly due to accelerated atherosclerosis and subsequent elevated cardiovascular morbidity. As central cellular components of the immune system, monocytes may contribute to accelerated atherosclerosis in CKD patients. Three monocyte subsets are characterized *via* flow-cytometry: classical CD14⁺⁺CD16⁻, intermediate CD14⁺⁺CD16⁺ and nonclassical CD14⁺CD16⁺⁺ monocytes. Recent studies revealed a central role of intermediate monocytes in CKD-associated atherosclerosis. Accordingly, high cell counts of intermediate monocytes predicted cardiovascular events in dialysis patients.

The present thesis first extends findings from epidemiological studies in dialysis patients, characterizing intermediate monocytes as predictors of cardiovascular events in cohorts of non-dialysis CKD patients and even in patients without overt CKD. Secondly, experimental analyses provided a detailed characterization of the three monocyte subsets, revealing subset-specific proinflammatory characteristics of intermediate monocytes. Finally, dysregulated epigenetic mechanisms were found in CKD patients, which may contribute to the shift in monocyte subsets and to accelerated atherosclerosis in these patients.

In summary, these results allow a better characterization of monocyte heterogeneity and broaden the pathophysiological understanding of the high cardiovascular morbidity of CKD patients. Based on these results, intermediate monocytes are currently discussed as potential targets for prevention and treatment of CKD-associated cardiovascular disease.