Myeloid cell heterogeneity in the cardio-cerebrovascular disease

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Myeloid cell heterogeneity is caused by switching the cell sources from local tissue-res ident macrophage proliferation to circulating cell recruitment, and/or macrophage phenot ypic plasticity. While long-lived tissue-resident macrophages support tissue homoeostasi s, recruited cells may promote destruction of the arterial wall, leading to organ ischemi a including acute stroke and myocardial infarction (MI). Here, we identified a new type of microglia associated with stroke in the I/R injured brain. Single-cell RNA sequencing (scRNA-seq) was used to assess transcriptional changes of microglia and immune cells in the contralateral (CL) and ipsilateral (IL) hemispheres after transient middle cerebral artery occlusion (tMCAO) surgery to mimic ischemic stroke. We classified a unique type of microglia with enhanced antioxidant function and markers similar to those of disease-associated microglia (DAM), designated them as stroke-associated microglia (SAM). Moreover, as a result of scRNA-seq in ischemic heart (MI) of *Pcsk9* k/o mice, we found that PCSK9 mediates macrophage heterogeneity in MI. $CCR2^{-}Lyve1^{+}$ cardiac macrophages increased in deficient PCSK9 MI hearts and stimulated anti-inflammation against cardiac damage. Therefore, deficient PCSK9 in myeloid cells alleviated cardiac dysfunction after myocardial injury and the BDNF pathway was activated in the cardiac ischemic state to improve cell survival and wound healing compared to the control. Collectively, our data suggest that myeloid cell heterogeneity is regulated by specific genes in the cardiovascular diseases thereby affecting pathogenesis of stroke and MI.