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Macrophage Polarization in Tissue Inflammation and Fibrosis

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Editorial

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Abbreviations: AKI: Kidney Injury; CKD: Chronic Kidney Disease; ECM: Extracellular Matrix.

Editorial

Macrophages are mononuclear phagocytic cells, which have varied phenotypes and perform diverse intricate functions ranging from inflammation to their role in onset and progression of fibrotic diseases [1-3]. After development and differentiation of myeloid progenitor cells in the bone marrow, monocytes are released into the bloodstream and these monocytes infiltrate into tissue during inflammation and mediate tissue repair [4]. Macrophages are present in all tissues of human body and depending on tissue microenvironments, they develop into specialized cells like osteoclasts (bone), microglial cells (brain), kupffer cells (liver), Langerhans cells (skin) and macrophage derived dendritic cells [5].

Macrophages are classified as M1 macrophages and M2 macrophages depending on the activation stimuli, expression of surface antigens, secretome and their biological functions. Macrophages can also switch between polarization states during the course of disease progression in response to microenvironmental stimuli [6]. M1 macrophages are classically activated macrophages with pro-inflammatory responses and are typically induced by immune system as part of innate immunity and antitumor immunity [7]. M1 macrophages produce proinflammatory cytokines like TNF-α and IL1-β and contribute to microbial defense. While M1 macrophages are critical for host defense, excessive and prolonged M1 response can contribute to chronic inflammatory conditions and tissue damage [8].

M2 macrophages are alternatively activated and are divided into the following subgroups. M2a macrophages are fibrotic macrophages which secrete copious amounts of TGF-β, a key driver of fibrosis [9,10]. M2a macrophages also increase the local production of extracellular matrix (ECM) proteins and play critical roles in wound healing and tissue repair [10]. M2b macrophages are regulatory macrophages with anti-inflammatory function and are stimulated by immune complexes, apoptotic cells in conjunction with TLR ligands. M2b macrophages do not secrete ECM proteins and inhibit the effects of pro-inflammatory cytokines [4]. M2b macrophages signal disease remission in lupus nephritis mouse models [11]. M2c macrophages are anti-inflammatory macrophages which are efficient in clearing apoptotic cells and debris. These macrophages can also be therapeutic in treatment of chronic diseases where apoptotic cells trigger autoimmune responses [12,13]. Balance between M1 and M2 macrophages is critical for maintaining immune homeostasis and tissue health.

Polarization	Classification	Identification Markers	Function
M1	Pro-inflammatory	CD80, CD86, MHC II, TNF-α	Antimicrobial and antitumor immunity
M2a	Pro-fibrosis	CD163, CD206, Arginase 1, iNOS	Wound healing, matrix remodeling and tissue repair
M2b	Immune regulation	CD86, MHC-II, CCL1, IL6R	Antigen presentation and Th2 differentiation
M2c	Anti-inflammatory	B7-H4, CD150, CD206	Phagocytosis of apoptotic cells

Table 1: Macrophage phenotypes and identification markers.

Macrophages have garnered significant attention due to their involvement in disease progression from acute kidney injury (AKI) to chronic kidney disease (CKD). Studies have shown that the inability of macrophages to shift from pro-inflammatory M1 phenotype to reparative M2 phenotype triggers the ongoing renal inflammation and fibrosis [14]. Conversely, prolonged presence of M2 macrophages can lead to elevated levels of pro-fibrotic cytokines like TGF-β1 and excessive ECM deposition. Both M1 and M2 macrophages play critical roles in renal fibrosis [15]. Cytokines secreted by macrophages stimulate resident renal cells to deposit more ECM proteins, causes epithelial to mesenchymal transition in podocytes and proximal tubule cells and differentiates fibroblasts into myofibroblasts [16-18]. Treatment strategies targeting macrophages have shown to be effective in mouse models of renal disease highlighting the importance of macrophages in disease /progression [6]. While M1 macrophages have been detected in all stages of kidney disease, M2 macrophages are only present in AKI and not in CKD [7]. This makes phenotyping of macrophages particularly interesting while evaluating kidney biopsies.

Chronic kidney disease classification and evaluation of therapeutic efficiency is based on correlation of clinical parameters and traditional histopathological evaluation of biopsy tissue. Since immunohistochemistry was limited to 2-3 antibodies per tissue section, detailed profiling of tissue infiltrating macrophages was not feasible but newer proteomic platforms like imaging mass cytometry, facilitate the quantification of 35 different protein markers in the same tissue section. These allow for better understanding the composition, spatial distribution and molecular profile of the infiltrating immune cells in tissue biopsy [19]. These platforms will aid in better understanding the mechanisms of renal disease progression and changes in spatial distribution of M1 and M2 macrophages in the kidney during different stages of disease. Based on the prevalence of M1/M2 macrophages in kidney biopsies, therapeutics can be targeted to address the underlying inflammation or fibrosis. Alternatively, specific therapeutics can be developed to balance macrophage polarizations, which might offer better management of chronic kidney diseases.

References

1. Anders HJ, Ryu M (2011) Renal microenvironments and macrophage phenotypes determine progression or resolution of renal inflammation and fibrosis. Kidney Int 80(9): 915-925.

2. Rao J, Wang H, Ni M, Wang Z, Wang Z, et al. (2022) FSTL1 promotes liver fibrosis by reprogramming macrophage function through modulating the intracellular function of PKM2. Gut 71(12): 2539-2550.

3. Kishore A, Petrek M (2021) Roles of Macrophage Polarization and Macrophage-Derived miRNAs in Pulmonary Fibrosis. Front Immunol 12: 678457.

4. Mosser DM, Edwards JP (2008) Exploring the full spectrum of macrophage activation. Nature reviews Immunology 8(12): 958-969.

5. Pollard JW (2009) Trophic macrophages in development and disease. Nature reviews Immunology 9(4): 259-270.

6. Wang Y, Harris DCH (2011) Macrophages in renal disease. J Am Soc Nephrol 22(1): 21-27.

7. Cao Q, Wang Y, Harris DCH (2013) Pathogenic and protective role of macrophages in kidney disease. American journal of physiology Renal physiology 305(1): F3-11.

8. Martinez FO, Sica A, Mantovani A, Locati M (2008) Macrophage activation and polarization. Frontiers in bioscience: a journal and virtual library 13: 453-461.

9. Meng XM, Nikolic-Paterson DJ, Lan HY (2016) TGF-β: the master regulator of fibrosis. Nature reviews Nephrology 12(6): 325-338.

10. Wang X, Chen J, Xu J, Xie J, Harris DCH, et al. (2021) The Role of Macrophages in Kidney Fibrosis. Frontiers in physiology 12: 705838.

11. Schiffer L, Bethunaickan R, Ramanujam M, Huang W, Schiffer M, et al. (2008) Activated renal macrophages are markers of disease onset and disease remission in lupus nephritis. J Immunol 180(3): 1938-1947.

12. Yao Y, Xu XH, Jin L (2019) Macrophage Polarization in Physiological and Pathological Pregnancy. Front Immunol 10: 792.

13. Zizzo G, Hilliard BA, Monestier M, Cohen PL (2012) Efficient clearance of early apoptotic cells by human macrophages requires M2c polarization and MerTK induction. J Immunol 189(7): 3508-3520.

14. Ricardo SD, Goor HV, Eddy AA (2008) Macrophage diversity in renal injury and repair. The Journal of clinical investigation 118(11): 3522-3530.

15. Vernon MA, Mylonas KJ, Hughes J (2010) Macrophages and renal fibrosis. Seminars in nephrology 30(3): 302-317.

16. Wu F, Sun C, Lu J (2020) The Role of Chemokine Receptors in Renal Fibrosis. Reviews of physiology, biochemistry and pharmacology 177: 1-24.

17. Ma Y, Chen Y, Xu H, Du N (2023) The influence of angiopoietin-like protein 3 on macrophages polarization and its effect on the podocyte EMT in diabetic nephropathy. Front Immunol 14: 1228399.

18. Tan TK, Zheng G, Hsu TT, Wang Y, Lee VW, et al. (2010) Macrophage matrix metalloproteinase-9 mediates epithelial-mesenchymal transition in vitro in murine renal tubular cells. The American journal of pathology 176(3): 1256-1270.

19. Louis Sam Titus ASC, Tan Y, Tran P, Lindblom J, Ivbievbiokun M, et al. (2023) Molecular architecture of proliferative lupus nephritis as elucidated using 50-plex imaging mass cytometry proteomics. Clinical Immunology 254: 109713.