

Tissue resident macrophages turn inflammatory in a mouse model of peritoneal dialysis induced fibrosis.

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Peritoneal dialysis (PD) has significant initial benefits to patient autonomy, survival rates and healthcare costs compared to haemodialysis. However, prolonged PD is associated with severe side-effects, including peritoneal sclerosis and bowel obstruction, negating these initial beneficial effects. Of note, the induction of pathological consequences in PD is closely correlated to repeated episodes of peritonitis and activation of the immune system. In particular macrophages have been shown to promote the pathology. However, in other fibrotic diseases macrophages can also inhibit and in some cases even revert disease progression. Recent advances in macrophage biology suggest this divergent function may be due to the prevalence of macrophage subpopulations with differing ontogeny. Monocyte-derived, inflammatory macrophages have been suggested to promote fibrosis, whereas tissue-resident macrophages are rather considered anti-fibrotic. Thus, we explored the role of tissue resident macrophages in a murine model of PD-fluid induced fibrosis. Here we show that during PD tissue resident peritoneal macrophages gradually lose their homeostatic phenotype, correlating with the length of treatment. Moreover, tissue resident macrophages from PD-fluid injected animals gradually became pro-inflammatory responding more quickly and strongly to external stimulation both in vitro as well as in vivo. Consequently, animals subjected to repeated PD-fluid injection showed enhanced inflammation during bacterial inoculation. These data indicate that tissue resident macrophage during PD may promote disease progression through enhancing inflammatory responses and increase the risk of peritonitis.

These data highlight the ongoing adaptation of the immune system to an altering environment and identifies a novel therapeutic avenue in the treatment of PD associated pathologies by limiting tissue resident macrophage promoted inflammation.