IL-17F depletion accelerates chitosan conduit guided peripheral nerve regeneration

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Research

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Abstract

Nerve guidance conduit (NGC) serves as the most promising alternative to autografts for repairing long-range defects of peripheral nerves. In this study, we investigated whether modulating the immune microenvironment by Interleukin-17F (IL-17F) could promote NGC mediated peripheral nerve repair. Chitosan conduit were used to bridge sciatic nerve defect in IL-17F knockout mice with wild-type mice and autografts as controls. Our data revealed that IL-17F knockout mice had improved functional recovery and axonal regeneration of sciatic nerve bridged by chitosan conduits comparing to the wild-type mice. Notably, IL-17F knockout mice had enhanced pro-healing M2 macrophages in the NGC repairing microenvironment. In vitro data revealed that IL-17F knockout peritoneal macrophages had increased M2 markers after treatment with the extracts from chitosan conduits, while higher inflammatory M1 markers were detected in the Raw264.7 macrophage cell line and wild-type peritoneal macrophages after the same treatment. The biased M2 macrophage phenotype by IL-17F knockout probably contributed to the improved chitosan conduit guided sciatic nerve regeneration. These results not only revealed a role of IL-17F in macrophage function, but also provided a unique and promising target, IL-17F, to modulate the microenvironment and enhance the peripheral nerve regeneration.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures

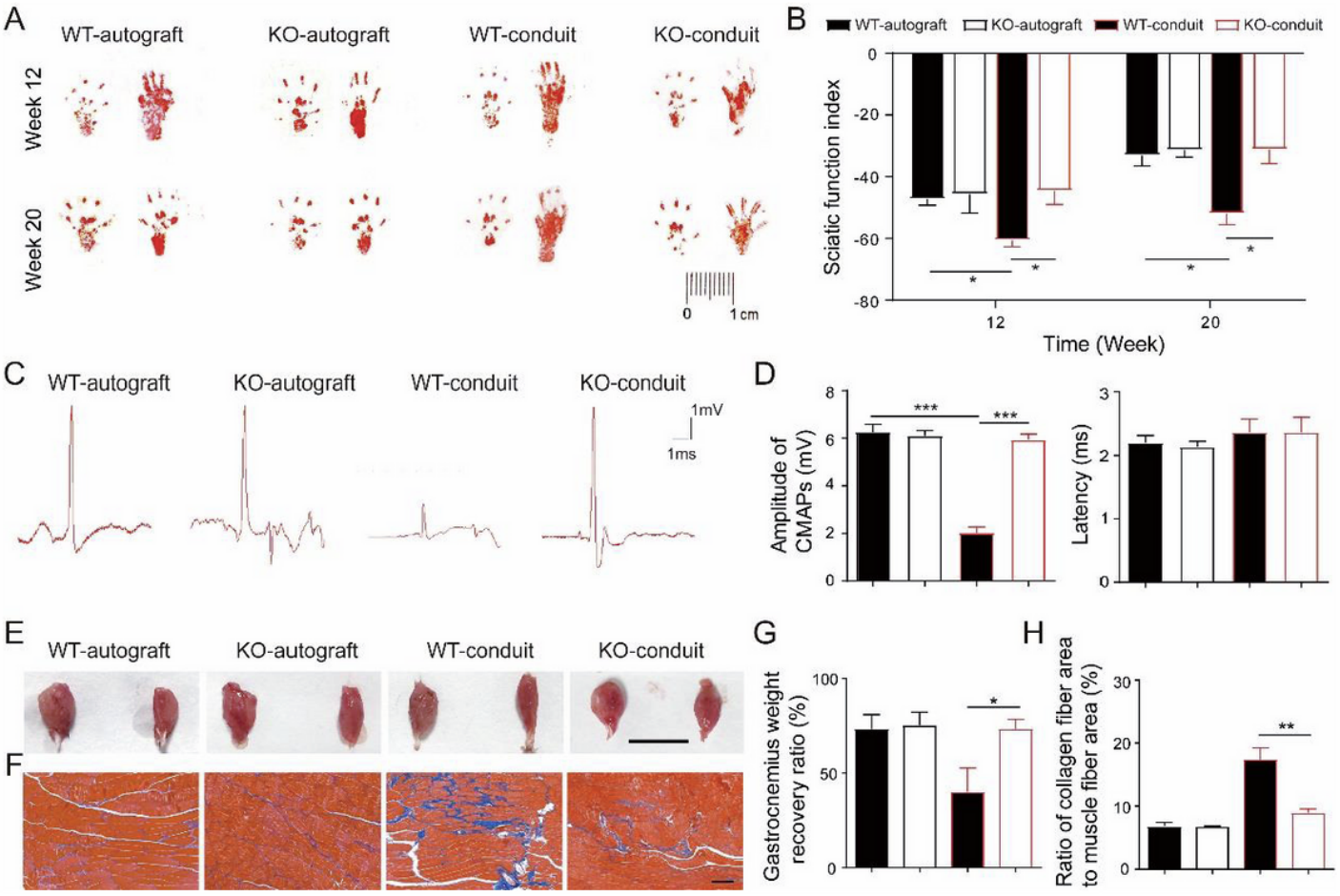

Figure 1

KO mice had improved functional recovery of sciatic nerve comparing to WT mice. (A) Representative image of walking track. (B) SFI analysis. (C) Representative CMAPs recorded on the regenerated nerve. (D) Analysis of peak amplitude and latency of CMAPs. (E) Images of gastrocnemius muscle from both normal (left) and operative (right) sides. Bar = 1 cm. (F) Masson's trichrome staining of gastrocnemius muscle sections. Bar = 100 □m. (G) The gastrocnemius weight recovery ratio. (H) The ratio of collagen fiber area to muscle fiber area. 12 *, P < 0.05; **, P < 0.01; ***, P < 0.001.

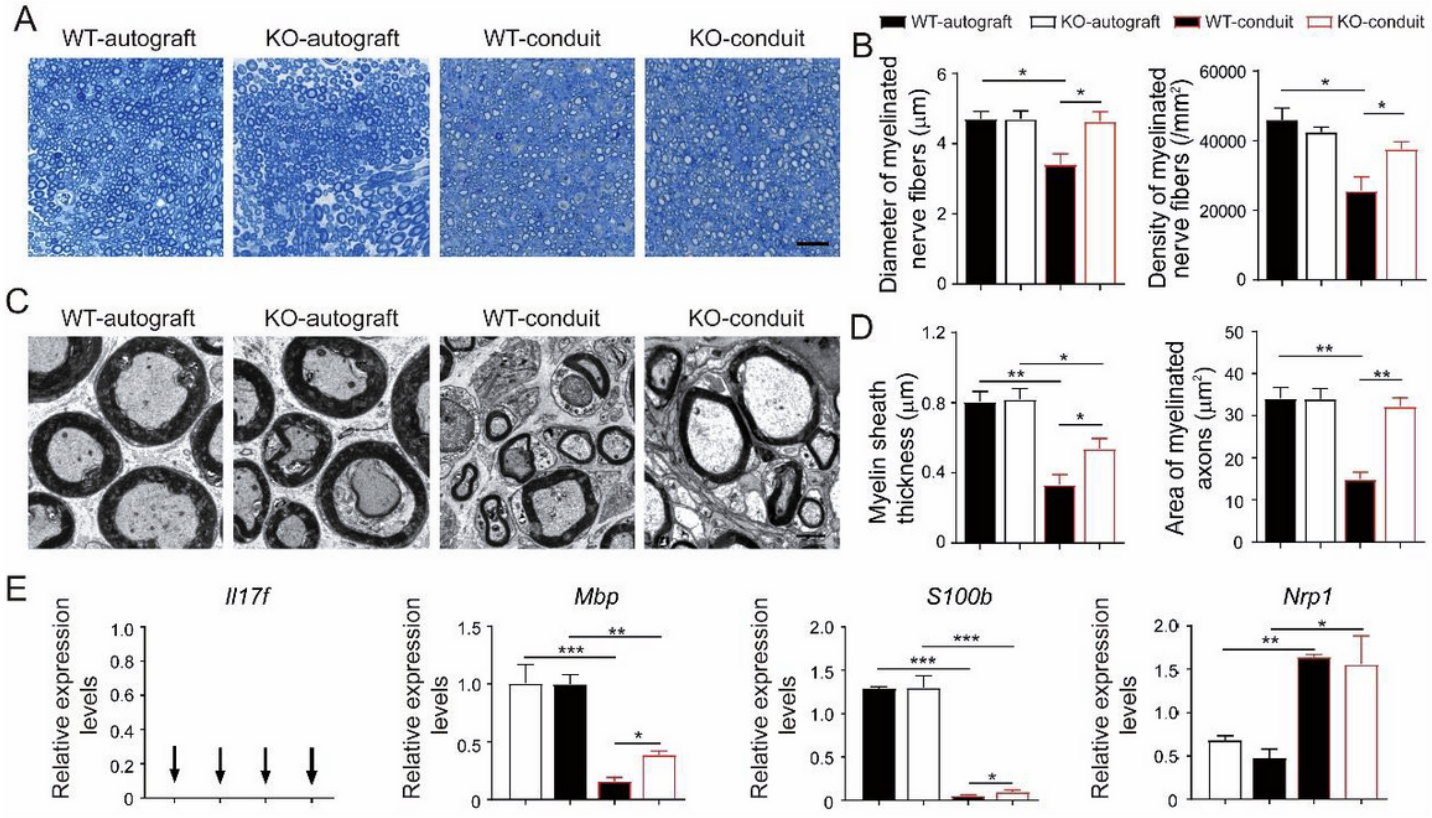

Figure 2

KO mice had improved axonal regeneration of sciatic nerve comparing to WT mice. (A) Toluidine blue staining of regenerated nerves. Bar = 20 μm. (B) Analysis of the myelinated nerve fibers based on toluidine blue staining. (C) TEM images of regenerated nerves. Bar = 2 μm. (D) Analysis of the myelinated nerve fibers based on TEM images. (E) Quantitative PCR analysis of regenerated nerves. *, P < 0.05; **, P < 0.01; ***, P < 0.001.

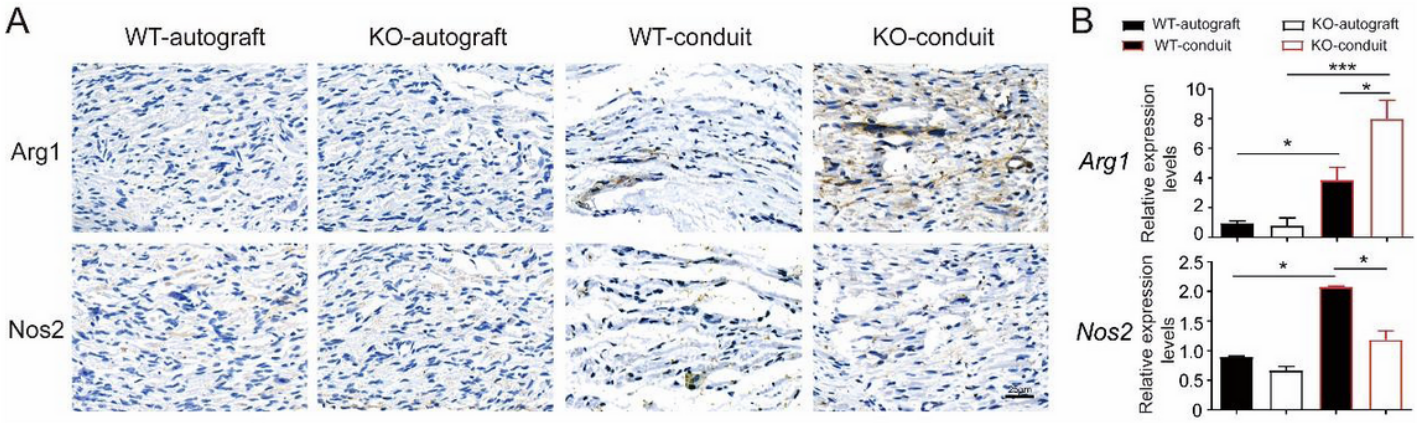

Figure 3

KO mice had enhanced M2 macrophages in sciatic nerve repairing microenvironment comparing to WT mice. (A) Immunohistochemical staining of Arg1 and Nos2 in the regenerated nerves. Bar = 25 μm. (B)

Quantitative PCR analysis of the regenerated nerves. *, P < 0.05; ***, P < 0.001.

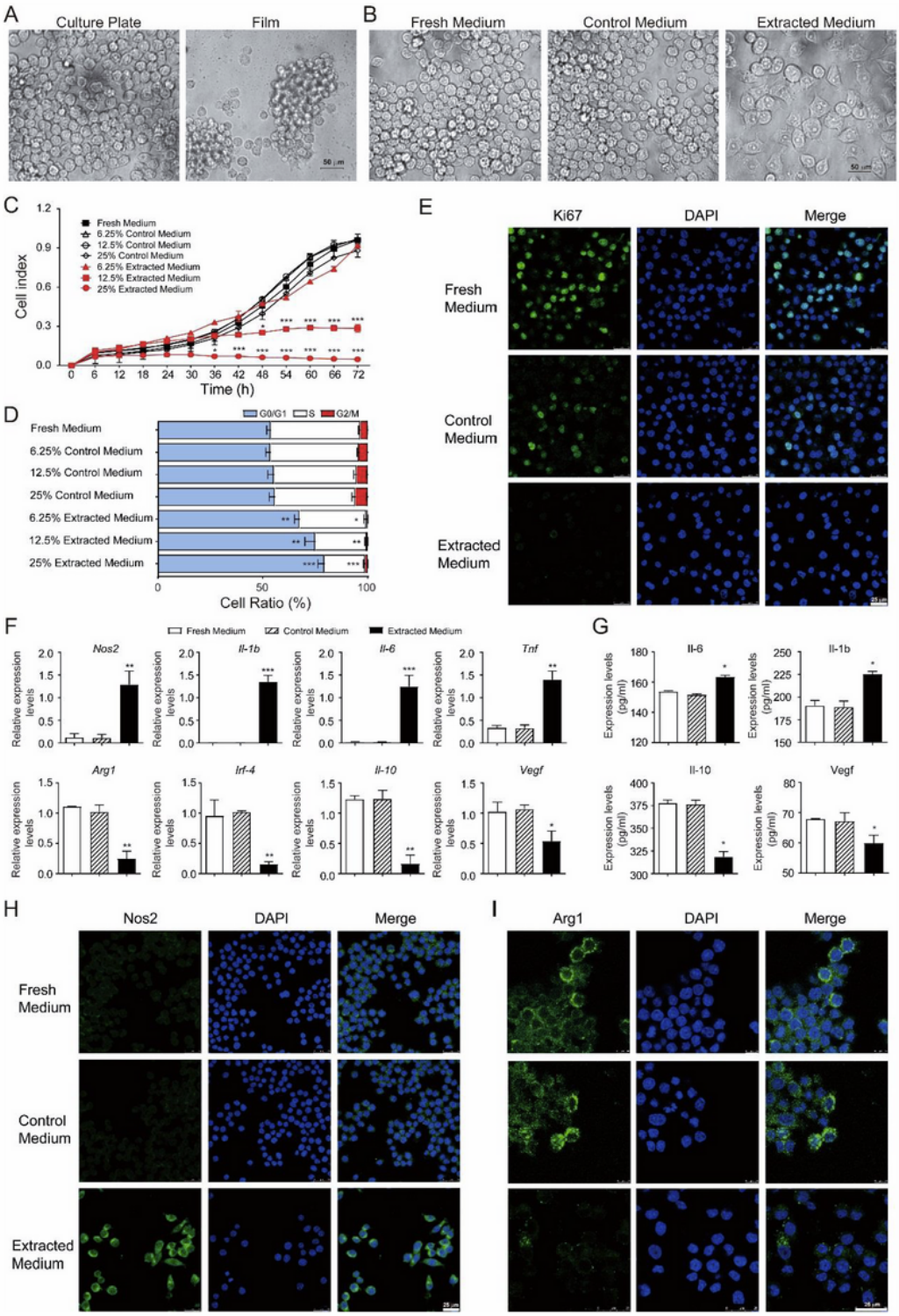

Figure 4

Chitosan conduits affected the growth and polarization of Raw264.7 macrophage cells. (A) Light microscope images of cells cultured on the plate and chitosan film. (B) Light microscope images of cells cultured in 25% different mediums for 24 h. (C) RTCA analysis of cells cultured in different mediums. (D) Cell cycle analysis by flow cytometry of cells cultured in different mediums for 24 h. (E)

Immunofluorescence images of cells cultured in 25% different mediums for 24 h. (F) Quantitative PCR analysis of cells cultured in 25% different mediums for 24 h. (G) Elisa analysis of the supernatants from cells cultured in 25% different mediums for 24 h. (H, I) Immunofluorescence images of cells cultured in 25% different mediums for 24 h. *, P < 0.05; **, P < 0.01; ***, P < 0.001; comparing to control medium with the same concentration.

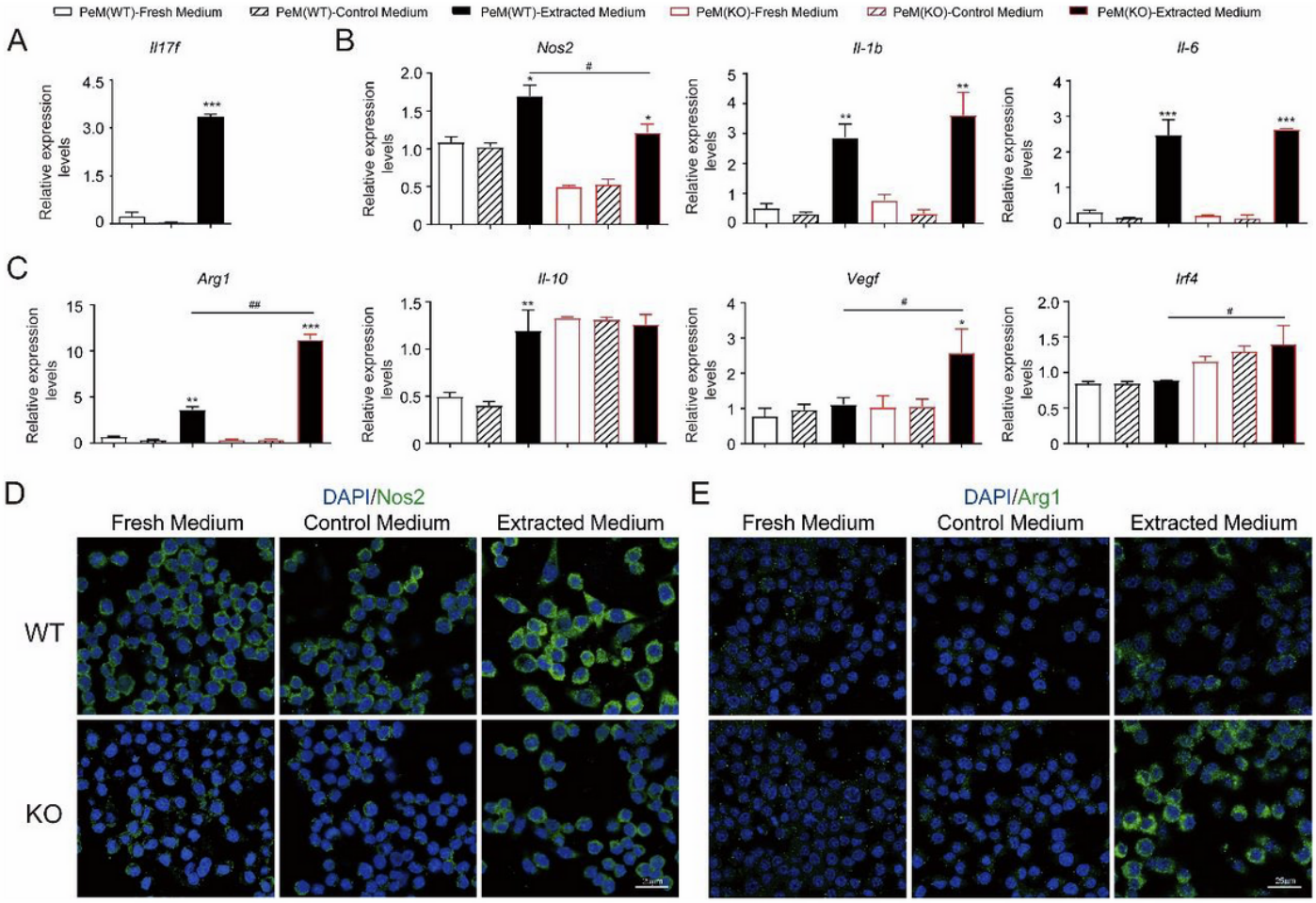

Figure 5

Peritoneal macrophages (PeM) from KO and WT mice polarized differently after chitosan conduits extracts treatment. (A-C) Quantitative PCR analysis of cells treated with 25% different mediums for 24 h. (D-E) Immunofluorescence images of cells treated with 25% different mediums for 24 h. *, P < 0.05; **, P < 0.01; ***, P < 0.001; comparing to control medium. #, P < 0.05; ##, P < 0.01.