Intranasal Delivery of TGFα – A Novel Therapeutic Approach for Lesion Resolution in Multiple Sclerosis

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INTRODUCTION

After acute CNS lesions like Multiple Sclerosis (MS), the interplay among microglia, astrocytes, and immune cells influences the CNS microenvironment, impacting tissue damage resolution. However, understanding their specific roles in tissue recovery remains limited. Our research highlights microglia-produced TGFα as a key regulator in MS and its animal model EAE, suggesting its potential as a therapeutic target for recovery.

AIM

Evaluate the therapeutic potential of TGFα for the resolution of CNS inflammation.

RESULTS

TGFα is important during recovery phase of EAE

Microglial TGFα is essential for recovery from EAE by
- reducing the number of infiltrating T cells and pro-inflammatory myeloid cells
- reducing OLC loss, axonal damage, and demyelination.

TGFα promotes tissue-protective effects

Intranasal delivery of TGFα
- reduces lesion volume
- limits pro-inflammatory profile of CNS infiltrating immune cells

CONCLUSIONS

(A) Microglia as predominant producer of TGFα during CNS inflammation, illustrating its pleiotropic effects (B) on various CNS resident and infiltrating populations through EGFR signaling (demonstrated in blue circle). (C) Intranasal application of TGFα as therapeutic approach reduces neuroinflammation, neurodegeneration, cell death, demyelination, and cellular dysfunction, ultimately contributing to lesion resolution in the inflamed CNS context (D).

TAKE-HOME MESSAGE

TGFα acts on glial and infiltrating cells to promote the resolution of CNS inflammation.