Promises and challenges of selectively targeting TNF receptors in multiple sclerosis

Pegoretti, Valentina

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Propositions

1. Lack of understanding of MS etiology poses pivotal challenges for drug discovery

2. An effective treatment strategy for MS must not only prioritize immunomodulation but also, crucially, tissue regeneration

3. The development and evaluation of an agonistic molecule present greater challenges compared to an antagonist since it requires identifying the precise degree of receptor activation while mitigating the risks of receptor desensitization or overstimulation

4. TNF signaling balances life and death states of a cell, requiring stress signals to trigger its pro-survival or apoptotic properties

5. Rebalancing TNF signaling by targeting both TNFR1 and TNFR2 selectively is more beneficial than single treatments to reveal protective and regenerative effects (*Chapter 4*)

6. Cuprizone-induced demyelination is quickly restored, while glia activation persists long-term (*Chapter 5*)

7. Beyond myelin thickness and axon diameter, myelin compaction and composition are critical factors affecting the de- and remyelination processes (*Chapter 6*)

8. Animal models capture specific aspects of human disease, but the lack of accurate models for some key pathological mechanisms hinders understanding and contributes to drug development failures

9. Rapid, accurate and cheap antimicrobial susceptibility tests are necessary to improve treatment strategies and surveillance of antibiotic resistance in health, agriculture and the environment

10. Commercial scientific publishing profits in four different ways by exploiting the unhealthy culture of ‘publish or perish’ and researchers’ free labor in providing content and peer-reviewing, topped off by page charges and astronomic library fees

11. Times and plans change