



# **Introduction to Biological and Small Molecule Drug Research and Development: Chapter 14. The case of anti-TNF agents**

*Denis Mulleman, Marc Ohresser, Hervé Watier*

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Parallel studies in septic shock and cancer led to the discovery of the endogenous factors named cachectin and tumour necrosis factor (TNF), respectively, that were shown to be structurally and functionally similar. Further studies identified two forms of TNF, TNF- $\alpha$  and TNF- $\beta$ . The anticipation that specific anti-TNF antibody might have therapeutic potential in the resolution of sepsis was not realized; however, anti-TNF- $\alpha$  agents have been shown to have dramatic therapeutic efficacy in a number of inflammatory diseases. Currently, there are five anti-TNF agents approved that are equally effective in the treatment of rheumatoid arthritis but exhibit differing efficacy in other inflammatory conditions. Three are full-length immunoglobulin G (IgG) anti-TNF- $\alpha$  antibodies, one is an anti-TNF- $\alpha$  Fab fragment and another, a TNF receptor–Fc fusion protein. Their different structures reflect recent advances in our ability to apply genetic engineering for patient benefit.

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