

Researchers of BSRC “Al. Fleming” contribute to a EU consortium in order to propose strategies for balancing the pathogenic/beneficial effects of TNF in opportunistic infections appearing in anti-TNF treated patients.

Al. Fleming researchers participate in the TB REACT European consortium, constituted of 5 teams, expert in their fields. The aim of this high-quality consortium is to analyze alternative strategies to prevent tuberculosis (TB) reactivation after TNF neutralization therapy for inflammatory diseases.

Tumor necrosis factor-alpha (TNF) exerts both deleterious and beneficial effects: It is a main actor in the pathology of inflammatory diseases and therefore a target for clinical intervention. Conversely, the essential role of TNF in immune regulation and in host defence was demonstrated in mice. Indeed, anti TNF therapies appear to be indispensable in the management of many inflammatory diseases such as Rheumatoid Arthritis, Crohn’s disease and Psoriasis as no other effective treatment exists (>1 million patients already treated worldwide, indications expanding). Clinical trials are ongoing for evaluating anti-TNF therapy in several other diseases, including cancer. However, unexpected adverse effects put these novel therapies into question, limit their use, and introduce a new threat as anti-TNF therapies turned out to increase the risk of developing TB and other opportunistic infections. This TB recurrence is likely to be due to reactivation of a latent, previous TB infection. Primary TB infection concerns one third of the global population ([WHO Factsheet n°104, April 2005](#)). It is estimated that only 5-10 % finally develops clinical symptoms whereas the infection is clinically silent in 90% of the infected individuals, but the *Mycobacterium tuberculosis* is still present and viable, ready to flare-up when the immune surveillance fails. Second generation TNF blocking drugs with a reduced cost have the potential for widespread use in inflammatory diseases and TB reactivation is likely to increase under TNF blockade therapy therefore indicating a serious risk for European Society. This risk might hamper the development of widespread anti-TNF therapy, or conversely, the lack of understanding of the phenomenon might put a lot of patients with inflammatory diseases at risk of serious TB complications.

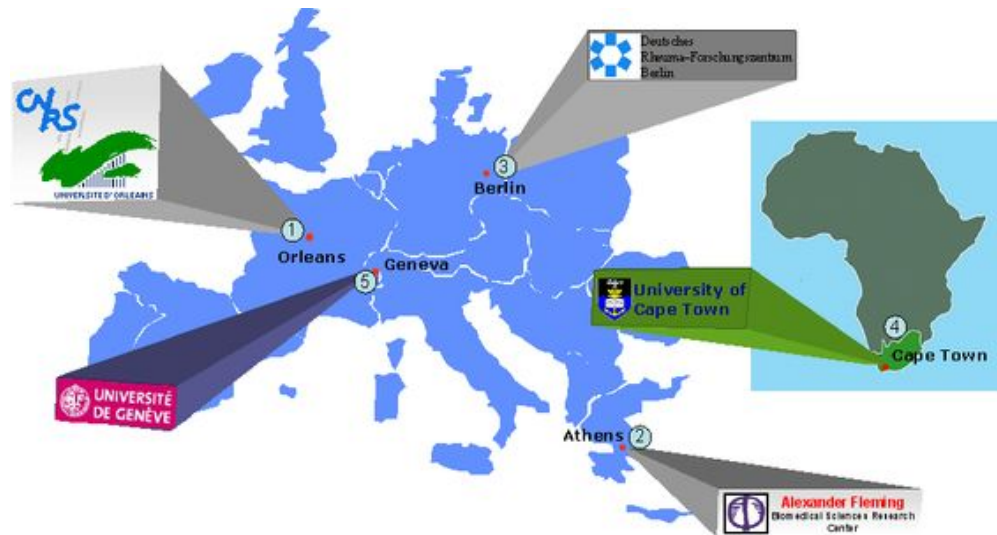
TB REACT addresses a lack of scientific understanding of TNF contribution in infection control and it is a “task-force” to systematically analyse the scientific roots of the new risk. The goal is:






- to develop in-depth scientific understanding of the role of the different molecular forms and origin of TNF and TNF receptors in controlling TB infection,
- to test the potential of cell type-restricted TNF ablation, or blockade of soluble TNF only on host resistance to mycobacterial infection and
- to propose candidate strategies for specific TNF neutralisation sparing the molecular forms essential for efficient control of tuberculosis.

Having gained a greater understanding of the problem, the partners will perform experiments to test and validate potentially improved therapeutic approaches. Success in this stage would leave the basic scientific insights from the project ripe for further preclinical and clinical development.

To this aim a set of unique genetic models will be used, newly created by the expert and the complementary partners of the project. This data is highly relevant for robust decision making in designing safer, second generation anti TNF therapies for expanding inflammatory diseases.

The EU strongly supports this coordination action over three-year period.
 (Total cost of the project: 2.321.500€, EU funding: 1.830.000 €).



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