

Analysis and modulation of the TH1/TH2 cytokine balance

CD4+ helper cells form the key regulatory unit of our adaptive immune system. The total number of CD4+ helper cells can be measured in the cellular immune profile but this does not provide any information about the distribution of the functional subpopulations. Depending on the type of cytokines they secrete, CD4+ helper cells are classified into five subgroups, all of which have different and in some cases opposing functions (see Fig. 1). The five subgroups are analysed in the TH1/TH2/TH17 profile.

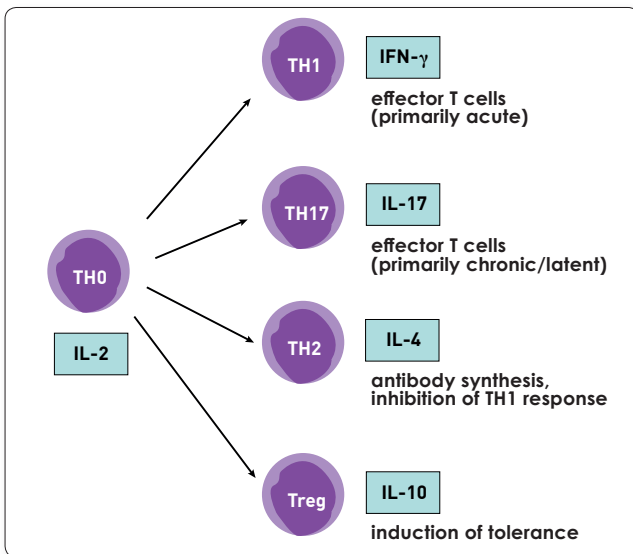


Fig. 1 TH1, TH17, TH2 and Treg cells can all develop from Th0 cells after the initial antigen contact. The interactions between these cells ensure a targeted, efficient and well-controlled immune response.

In light of the costs, often only the TH1 and TH2 immune system is examined, particularly for chronic inflammatory diseases, because these two subpopulations are pathognomonic independently of the Treg and TH17 cells. These two subpopulations are identified by their marker cytokines interferon-gamma (IFN-γ = TH1 marker) and interleukin-4 (IL-4 = TH2 marker) following stimulation of patient lymphocytes with T cell stimulants (ConA/SEB).

Interferon-γ

IFN-γ is the most important effector and marker cytokine of TH1 helper cells. It triggers proinflammatory immune responses. The processes induced by IFN-γ serve to efficiently eliminate an intracellular pathogen (viruses, intracellular bacteria) but may also damage tissues and be responsible

for chronic inflammatory diseases if their response is excessive or inadequate (type IV immune responses).

Interleukin-4

IL-4, like IL-5, IL-10 and IL-13, is secreted by TH2 helper cells. These interleukins facilitate the differentiation of B cells into plasma cells and stimulate them to synthesise antibodies. An increase in IL-4 synthesis indicates a dominant TH2 immune response and often occurs in atopic persons and some autoimmune diseases. In the advanced stages of various chronic infections and inflammatory diseases, there is often a TH2 shift that further encourages chronification.

Because TH1 and TH2 cells have antagonistic effects on one another, that is, they mutually inhibit the other's function, TH2 dominance is usually associated in the medium and long term with a weakening of the TH1 immune response and vice versa. This is one explanation for the immunodeficiency that is commonly associated with chronic inflammatory diseases.

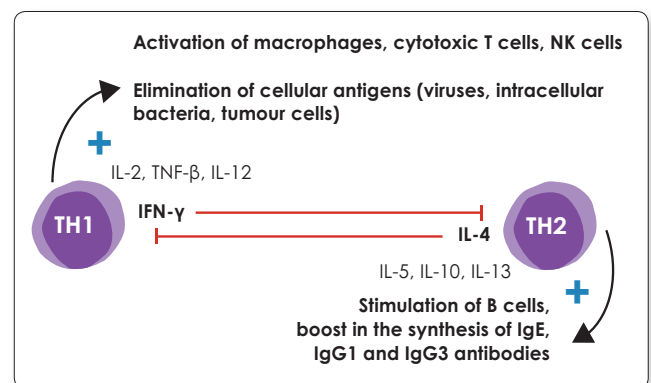


Fig. 2 Function and antagonism of TH1 and TH2 cells

Interpretation of the results

TH1 dominance (IFN-γ ↑, IL-4 ↓) is usually a consequence of an increased but otherwise intact immune response, e.g., during an ongoing infection but also as a result of therapeutic immunostimulation. TH2 dominance, on the other hand, is a pathognomonic factor indicating progression of many chronic inflammatory diseases. TH2 dominance (IFN-γ ↓, IL-4 ↑) is often seen in immediate-type allergic reactions such as hay fever, asthma, atopic dermatitis, psoriasis, a range of autoimmune diseases caused by auto-antibodies, chronic infections and inflammatory bowel diseases as well as often being detected secondary to cancer.

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IMD Labor Berlin		medical report	
Test	Result	Unit	Reference range
TH1/TH2 - balance			
IFN- γ (TH1)	234	pg/ml	374 - 1660
IL-4 (TH2)	544	pg/ml	28 - 141
TH1 / TH2 ratio	0.43		6.1 - 21
<p>The stimulated cytokine release from the T lymphocytes reveals an expanded TH2 cell fraction (increased IL-4) with a simultaneous reduction in the TH1 response (lowered IFN-γ). The lowered TH1/TH2 ratio indicates that there has been a TH2 shift.</p>			

Fig. 3 Sample results showing TH2 dominance

Determining the TH1/TH2 balance is indicated particularly before and during immunomodulatory therapy to verify the treatment outcomes.

Material

5 ml heparin blood

Sample receipt within 24 hrs has to be ensured. The sample should be stored and transported at room temperature. Within the Berlin city area, we offer a courier service (+49 (0)30 7701- 250). For collections beyond Berlin, please contact our complimentary courier service (+49 (0)30 77001-450).

Invoicing

For self-payers the costs are 64.11 €.

IL-4 inhibition test to evaluate the individual response to TH2-reducing preparations

Particularly for chronic inflammatory diseases and with a verified TH2 shift in the cellular immune response (IL-4 \uparrow , IFN- γ normal or \downarrow), an adjuvant immunomodulatory therapy can be administered that aims to lower the increased IL-4 values. In practice, a range of preparations are used, however, they show highly individual differences between patients in terms of their efficacy. Therefore, preliminary testing using the IL-4 inhibition test is useful for selecting the most efficacious preparation in vitro for a particular individual.

IMD Labor Berlin		medical report	
Test	Result	Unit	
Interleukin-4 inhibition test (PIA)			
IL4 response	533	pg/ml	
IL4 preparation 1 Curcumin	411	pg/ml	
IL4 preparation 2 Boswellia serrata	72.2	pg/ml	
IL4 preparation 3 Resveratrol	655	pg/ml	

Fig. 4 Sample results for IL-4 inhibition test. Preparation 2 had the greatest effect.

TH1 dominance (IFN- γ \uparrow , IL-4 \downarrow) usually occurs in acute or subacute T-cellular immune reactions. From a therapeutic point of view, the focus here is on causal diagnostics (infections?, autoimmune reactions?, others?), which is why we do not work on an IFN- γ inhibition test for laboratory diagnostics.

Material for the IL-4 inhibition test

5 ml heparin blood

The preparations to be tested must be indicated or sent to the laboratory along with the blood. Sample receipt within 24 hrs has to be ensured. The sample should be stored and transported at room temperature. Within the Berlin city area, we offer a courier service (+49 (0)30 7701- 250). For collections beyond Berlin, please contact our complimentary courier service (+49 (0)30 77001-450).

Invoicing for the IL-4 inhibition test

For self-payers the costs are 40.80 € for the first preparation and 20.40 € for each subsequent preparation.

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