

TNF α Inhibitor



testing at ARUP Laboratories



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keyword: TNF


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Monitoring the concentration of TNF- α inhibitor drugs and the development of anti-drug antibodies (ADA) enables physicians to optimize patient treatment over time. The test results help physicians understand underlying causes of suboptimal outcomes, make informed therapy choices, and provide more effective treatment to their patients. The use of TNF- α inhibitors has revolutionized the treatment of patients with several non-infectious inflammatory disorders, including Crohn disease and ulcerative colitis.

50% 

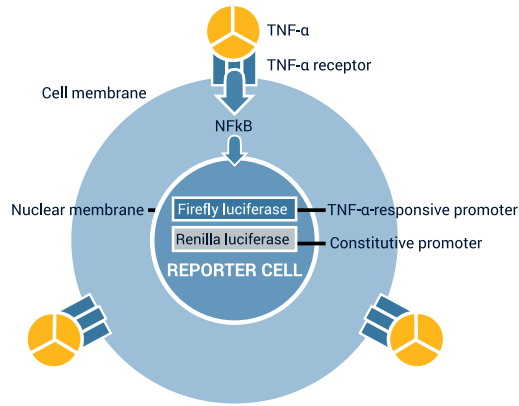
of patients suffering from non-infectious inflammatory disorders experience treatment failure.

There is currently no established standard for handling patients with treatment failure to TNF- α inhibitors. One approach is to monitor drug levels and anti-drug antibodies. Current methods for ADA detection are complicated by the fact that most TNF- α inhibitors are antibodies and by the complexity of measuring antibodies against antibodies in non-functional binding assays. More importantly, all non-ARUP methods fail to differentiate binding from neutralizing ADA.

ARUP's TNF- α activity and neutralizing antibody assays are cell-based bioassays that measure the ability of a drug to inhibit TNF- α . The assays also detect the presence of antibodies that neutralize drug activity. Emergence of these neutralizing antibodies in a patient leads to treatment failure. Other methods measure drug and drug antibodies that bind to infliximab. Unlike ARUP's assays, these methods cannot distinguish whether the antibodies neutralize drug activity or not.

How ARUP's Test Works

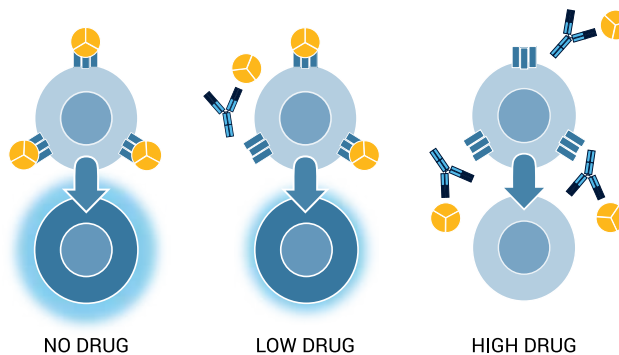
This cell function assay uses the principles of iLite technology.



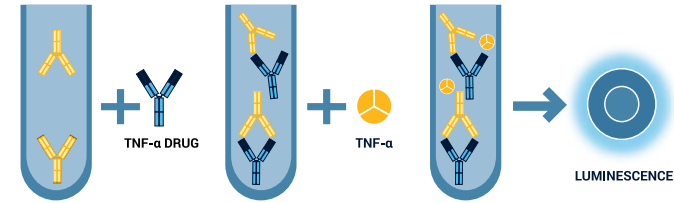
Reporter cells carry a TNF- α -inducible, NF κ B-regulated firefly luciferase reporter-gene construct. When TNF- α is added to the cells, the reporter gene turns on and generates firefly luciferase, which is measured by a luminometer. Results of firefly luciferase expression are normalized relative to the expression of the renilla luciferase gene, which is carried by the same reporter cell and under the control of a constitutive promoter.

Drug Measurement

Serum of a patient taking a TNF- α drug is mixed with TNF- α and added to the cells. The drug blocks the activity of TNF- α . The amount of drug inversely correlates to the amount of luminescence. Drug amount in serum can be calculated from the amount inhibiting TNF- α compared to calibrators of known drug concentrations.



Antibody Development



Some patients develop antibodies to the drug. In the presence of neutralizing antibodies, the reporter gene is turned on despite the presence of exogenous drug in the assay. The antibody titer is obtained by identifying the dilution point of a patient's serum where blocking of the drug activity is no longer observed.

Laboratory Testing

ARUP test code and name

2008320	Infliximab Activity and Neutralizing Antibody
2011248	Adalimumab Activity and Neutralizing Antibody

The two ARUP cell-function assays were clinically validated for diagnosing and monitoring infliximab or adalimumab treatment failure.

Currently, the ARUP assays are the only clinical assays available for the detection of biological TNF- α neutralization (infliximab or adalimumab activity) and ADA with drug-neutralizing function, as recommended by the FDA.

The assays resemble in vivo conditions in tissue and circulations under which TNF- α antagonists are believed to function, and can easily be adapted for all known anti-TNF- α drugs.