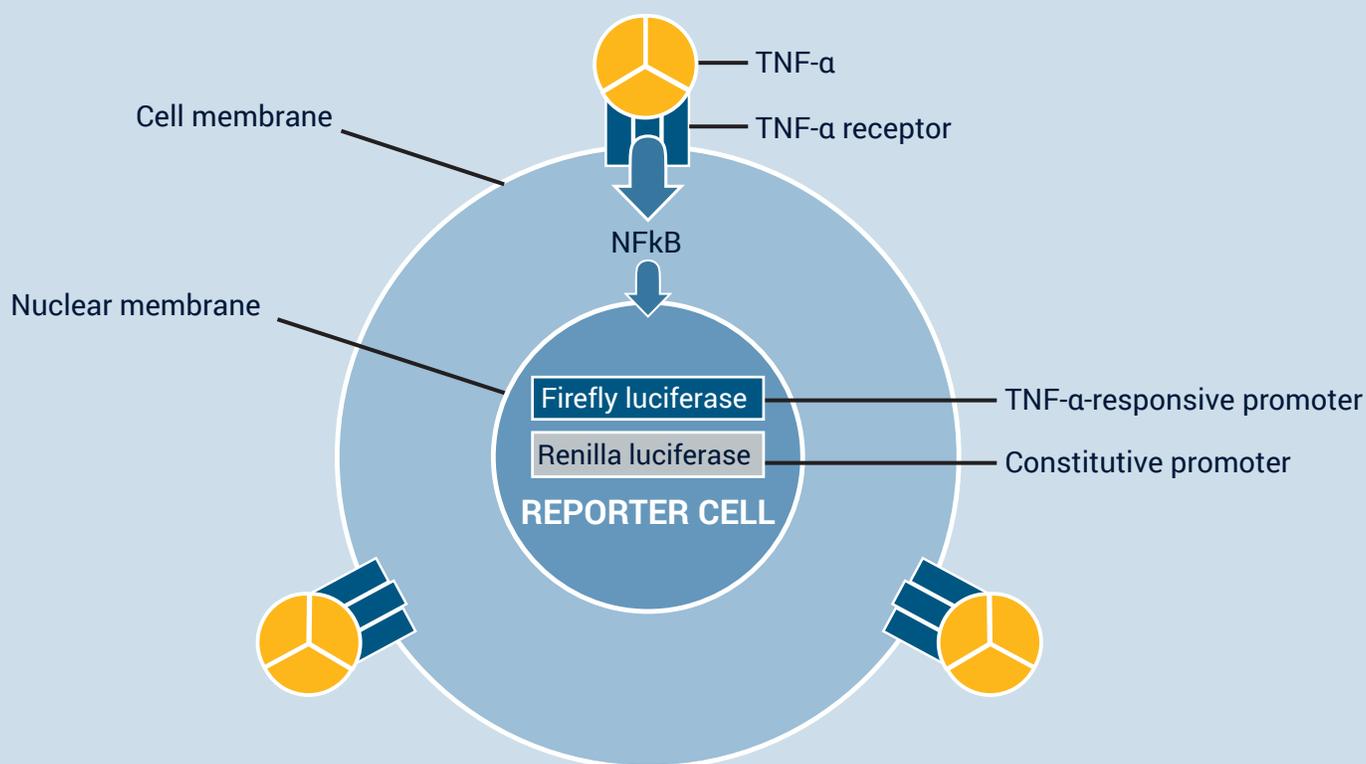


# Infliximab

Activity and Neutralizing Antibody

# INTRODUCTION

Reporter cells carry a TNF-alpha-inducible, NFkB-regulated, firefly luciferase reporter-gene construct. When TNF-alpha is added to the reporter cells, the reporter gene turns on and generates firefly luciferase. Firefly luciferase expression is normalized relative to the expression of the renilla luciferase gene, which is under the control of a constitutive promoter also carried by the same reporter cell.



Reporter cell



TNF-α receptor



TNF-α



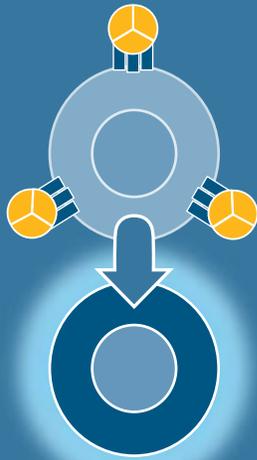
Infliximab



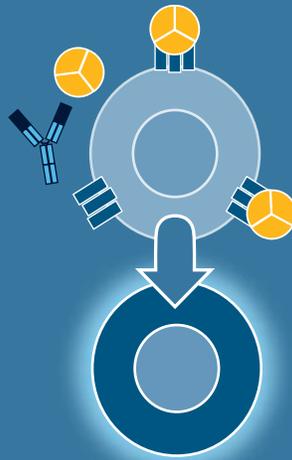
Neutralizing antibodies

# ACTIVITY LEVEL

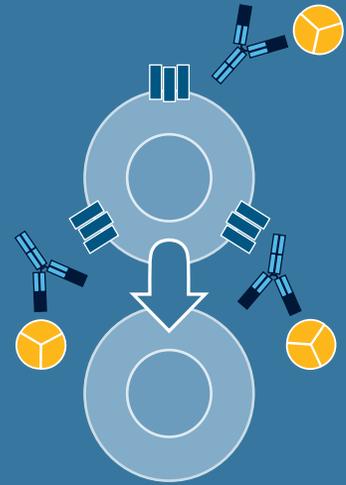
Serum from a patient taking infliximab is mixed with TNF- $\alpha$  and added to the reporter cells. Infliximab blocks the activity of TNF- $\alpha$ . The amount of infliximab present inversely correlates to the amount of luminescence.



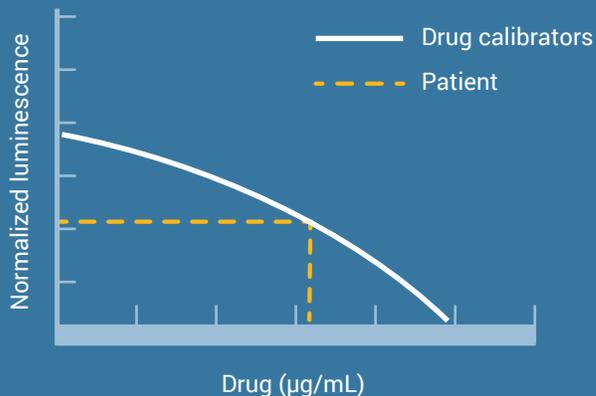
**NO DRUG**  
**HIGH LUMINESCENCE**



**LOW DRUG**  
**MODERATE LUMINESCENCE**



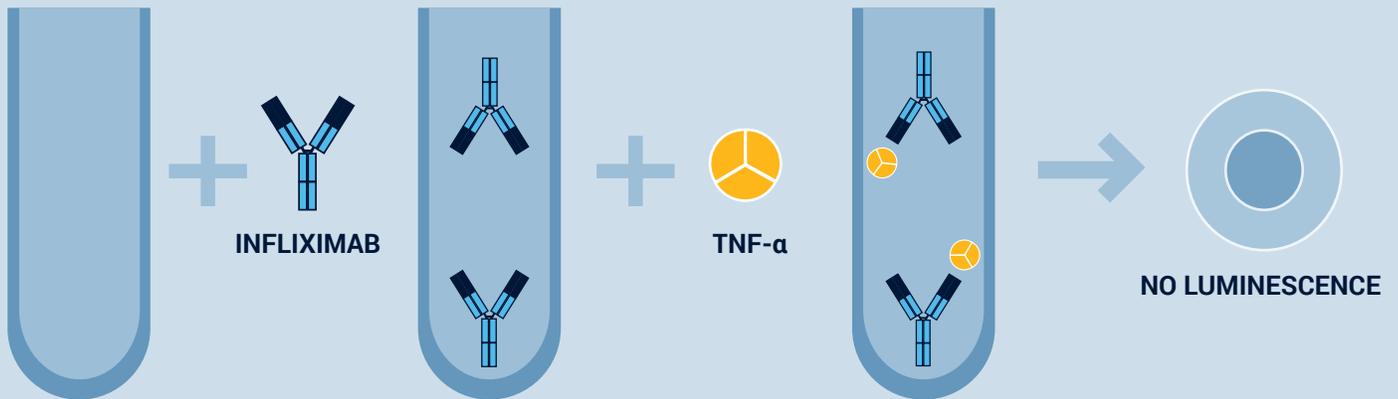
**HIGH DRUG**  
**NO LUMINESCENCE**



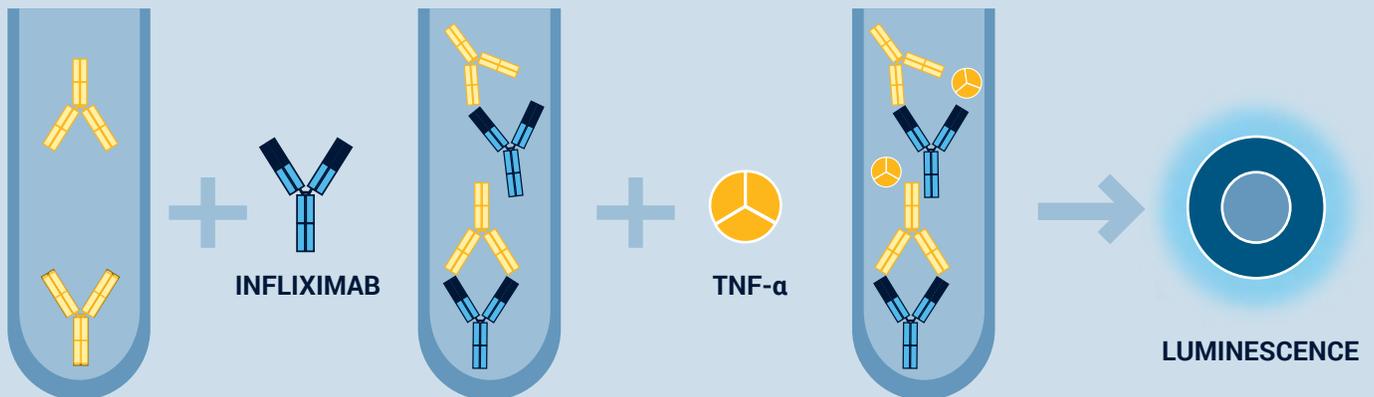
The amount of infliximab in serum can be calculated by comparing the level of TNF- $\alpha$  with calibrators of known infliximab concentrations.

# NEUTRALIZING ANTIBODIES

## PATIENT SERUM WITH NO NEUTRALIZING ANTIBODIES



## PATIENT SERUM WITH NEUTRALIZING ANTIBODIES

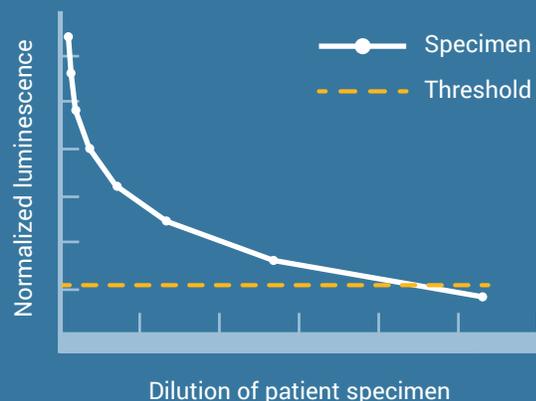


Some patients develop antibodies to infliximab.

It is important to detect detrimental antibodies that neutralize the drug and not those that bind to the drug but do not block drug activity.

In the presence of neutralizing antibodies, the reporter gene is turned on despite the presence of exogenous drug in the assay.

Antibody titer is obtained by identifying the dilution point of patient's serum where blocking of infliximab activity is no longer observed.



# REFERENCES

Bendtzen K. Personalized medicine: theranostics (therapeutics diagnostics) essential for rational use of tumor necrosis factor-alpha antagonists. *Discov Med* 2013;15(83):201–11.

Lallemand C, et al. Reporter gene assay for the quantification of the activity and neutralizing antibody response to TNF $\alpha$  antagonists. *J Immunol Meth* 2011;373(1–2):229–39.

Bendtzen K. Is there a need for immunopharmacologic guidance of anti-tumor necrosis factor therapies? *Arthritis Rheum* 2011;63:867–70.

Radstake TR, et al. Formation of antibodies against infliximab and adalimumab strongly correlates with functional drug levels and clinical responses in rheumatoid arthritis. *Ann Rheum Dis* 2009;68(11):1739–45.



A NONPROFIT ENTERPRISE OF THE UNIVERSITY OF UTAH  
AND ITS DEPARTMENT OF PATHOLOGY

[aruplab.com/IFX](http://aruplab.com/IFX)



**ARUP LABORATORIES**  
500 Chipeta Way  
Salt Lake City, Utah 84108-1221  
Phone: (800) 522-2787  
Fax: (801) 584-5209

© 2014 ARUP Laboratories