

Phospho-signaling Defect Assays: IL12/IFN γ axis

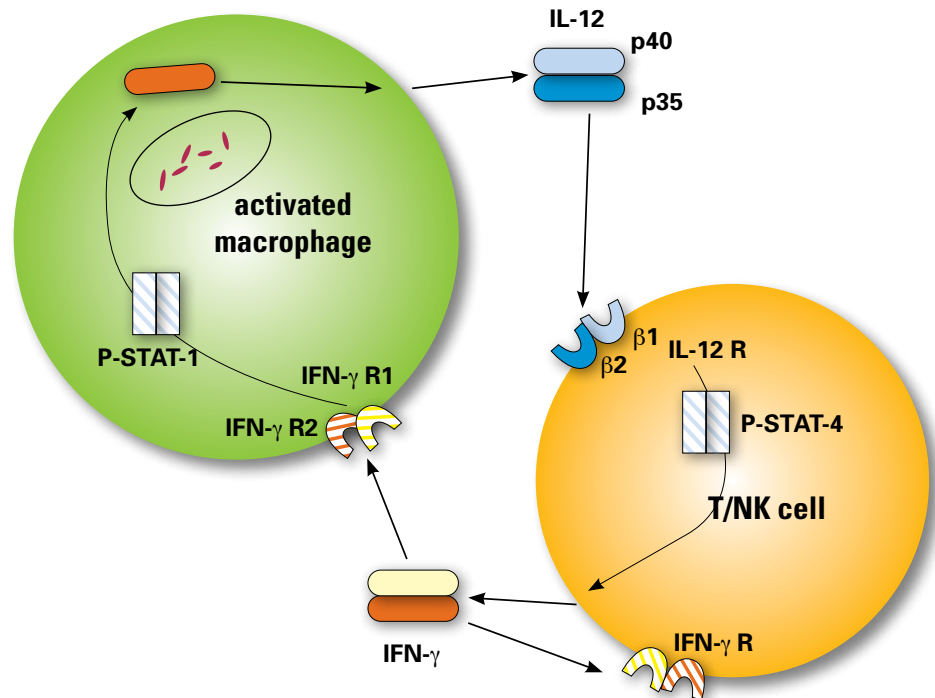
Assessing proper function of the IL12/IFN γ axis is important in the diagnosis of Primary Immunodeficiency Disease. The IL12/IFN γ pathway is central to the control of intracellular infections by organisms such as mycobacteria and salmonella. In addition, the pathway is a pivotal player in generation of both adaptive and innate immune responses and has a role in the pathogenesis of autoimmune diseases as well as control of tumorigenesis.

Mutations have been described in the IFN γ receptor 1 (IFN γ R1) (1), IFN γ R2 (2), IL12p40 subunit (3), IL-12R β 1(4, 5) and STAT-1 (6), all of which increase susceptibility to mycobacterial and salmonella infections in otherwise healthy individuals. Mutations in receptors lead to a downstream signaling defect and may or may not manifest as loss of receptor expression on immune cells. Therefore, analysis of the IFN γ /IL-12 axis should include functional analysis of downstream signaling by: (1) stimulation of the IFN γ and IL-12 receptors with their cognate cytokines (IFN γ and IL-12); and (2) measurement of phosphorylation of their respective signaling molecules, STAT1 and STAT4.

What is the assay?

- Lymphocytes are analyzed for the expression of IFN γ and IL-12 receptors by flow cytometry.
- Lymphocytes are stimulated with IFN γ and IL-12. Phosphorylated STAT1 and STAT4 are then identified by intracellular staining for the phosphorylated epitopes (flow cytometry).

IFN- γ /IL - 12 axis



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Test Information

Test code:	IFN γ /STAT1 IL12/STAT4	GRSTAT1 12RSTAT4
Method:	Lymphocyte stimulation followed by flow cytometry for phosphorylation status	
Reference range:	By report	
Specimen requirements:	10 ml heparinized whole blood (green top tube), room temperature	
Transport requirements:	Within 24 hrs of draw	
Turn around time:	7 days	
CPT code:	86353 Lymphocyte blastogenesis 88184 Flow cytometry	

References

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6. Dupuis, S., et al. 2001. Impairment of mycobacterial but not viral immunity by a germline human STAT1 mutation. *Science* 293:300-303.