



TEST UPDATE

Quick Facts

Free Light Chain Assays

- ▶ For diagnosis, free light chain assays should be used in conjunction with high-resolution electrophoresis and immunofixation.
- ▶ Free light chain measurements can be used to monitor response to treatment of patients with all types of plasma cell dyscrasias.
- ▶ Free light chain testing can help stratify patients for the risk of progression.
- ▶ Upon request, PAML will offer rebaselining of Free Light Chains at no additional charge for three months.

For more information, please contact Client Services or see us on the web at

WWW.PAML.COM

Free Light Chain Assays

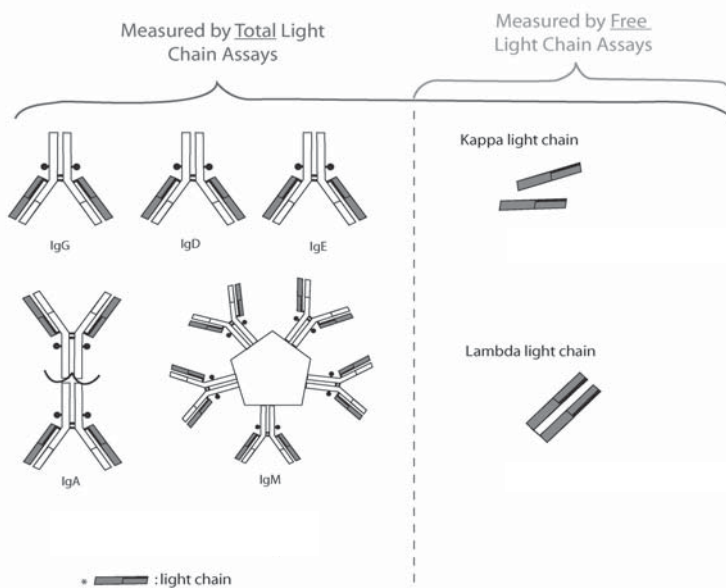
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Enhanced Tools for the Diagnosis and Monitoring of Monoclonal Gammopathies

CLINICAL BACKGROUND

Beginning on January 20, 2009, PAML will offer the quantitative measurement of free Kappa and free Lambda light chains in serum for diagnosis and monitoring of monoclonal gammopathies.

PAML currently offers testing for total Kappa and Lambda light chains in serum. The current tests include those light chains bound to IgA, IgG, IgM, IgD and IgE heavy chains to form intact immunoglobulin molecules as well as free light chains that are not bound to heavy chains. The new test measures only free light chains. Much has been published in recent years about how best to apply free light chain measurements in monoclonal gammopathies and applications continue to evolve as our knowledge advances.



CLINICAL MANAGEMENT

Diagnosis

Free light chain assays are most effective for diagnosis when used in conjunction with traditional high-resolution electrophoresis and immunofixation (IFE). Studies have shown that when the three techniques are used together on serum specimens, diagnostic sensitivity can be as high as 99% for multiple myeloma, 99% for light chain myeloma, 98% for AL amyloidosis, and 82% for non-secretory

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multiple myeloma. (Studies vary in percent detection rate.) These detection rates are an improvement over electrophoresis and IFE, particularly for AL amyloidosis, light chain myeloma and non-secretory multiple myeloma. We recommend the Serum Gammopathy Panel -- which includes serum electrophoresis, IFE and free light chains -- for initial diagnostic testing. Urine electrophoresis and immunofixation can also play a role in diagnosis, either in the initial workup or as secondary testing when serum tests are negative, but there is a clinical suspicion of gammopathy. Some studies have suggested that the diagnostic sensitivity of serum testing with free light chains is such that urine studies are not necessary, but we feel urine should remain a part of the diagnostic armamentarium.

Monitoring Response to Treatment

Evidence is growing for the use of free light chains in monitoring response to treatment of patients with all types of plasma cell dyscrasias. The main benefits derive from two factors:

- The shorter half-life of free light chains (< 6 hours with normal renal function) as compared with intact immunoglobulins (2 – 25 days). The levels of clonal free light chains decrease sooner than intact immunoglobulins in response to therapy, and they increase faster in relapse.
- Free light chains can often be detected in patients when other clonal markers cannot. In patients with what would appear to be non-secretory disease with conventional markers, free light chains can be detected in about 75% of cases and used to assess response to therapy. The same is true in patients with low-level or oligosecretory myeloma.

Prognosis

Studies have shown that free light chain testing to establish a baseline at diagnosis can help stratify patients for the risk of progression. In general, an abnormal Kappa/Lambda ratio or high levels of the clonal free light chain at diagnosis are associated with poor prognosis. Here are some examples with specific disorders:

- Patients with either monoclonal gammopathy of undetermined significance (MGUS), smoldering myeloma or solitary plasmacytoma with an abnormal Kappa/Lambda ratio at baseline show a higher risk of progression to plasma cell dyscrasia.
- In patients with AL amyloidosis, higher baseline free light chain levels are associated with a higher risk of death. Conversely, normalization of free light chain levels in AL amyloidosis patients predict longer survival.
- In multiple myeloma, high free light chain levels are associated with aggressive myeloma subtypes and poor prognosis.

Rebaselining Your Patients

As with most tumor markers, different analytical methodologies for free light chains can give different results. Therefore, it is important to know the methodology being used with your patients. PAML is using Binding Site reagents on a Beckman Immage 800® analyzer. We recommend you rebaseline any patients you have been following with free light chain assays. PAML will offer rebaselining at no charge for three months, beginning on January 20, 2009 and ending on April 20, 2009.

To request rebaselining:

- a. For electronic orders, "Rebaseline Free Light Chains" must be entered into the comments field when ordering FLCR or GAMPAN.
- b. For paper laboratory requisitions, write "Rebaseline Free Light Chains" when ordering FLCR or GAMPAN.

Interpretation of Results for Free Light Chains			
Condition	Kappa	Lambda	Kappa/Lambda Ratio
Normal	0.33 – 1.94 mg/dL	0.57 – 2.63 mg/dL	0.26 – 1.65
Monoclonal Kappa	Increased	Normal or Decreased	Increased
Monoclonal Lambda	Normal or decreased	Increased	Decreased
Biclonal or Multiclonal Disease	Increased	Increased	Variable
Renal Impairment	Increased	Increased	Normal or slightly increased
Polyclonal Hypergammaglobulinemia	Increased	Increased	Normal
Bone Marrow Suppression	Decreased	Decreased	Normal

TEST INFORMATION

DESCRIPTION Kappa/Lambda Free Light Chain with ratios

METHOD Nephelometry

ORDER CODE FLCR

CPT CODE 83883x2

SPECIMEN REQUIREMENTS 2 mLs serum (gold top tube). Separate serum from cells and put in separate plastic tube. Store and transport refrigerated.

COMMENTS 1) Min Amt: 0.5 mL.

2) Unacceptable conditions: plasma; repeated freeze/thaw cycles should be avoided. Contaminated samples, samples containing particulate matter and lipemic or hemolyzed serum samples.

3) Stability: Refrigerated-1 month.

RANGES Kappa FLC 0.33-1.94 mg/dL
 Lambda FLC 0.57-2.63 mg/dL
 (Kappa/Lambda FLC Ratio) 0.26-1.65

TEST INFORMATION

DESCRIPTION Free Light Chain Gammopathy Dx Panel

METHOD Nephelometry/Agarose Gel ELP, IFE

ORDER CODE GAMPAN

CPT CODE 83883x2, 84165, 86334

SPECIMEN REQUIREMENTS 3 mLs serum (gold top tube). Separate serum from cells and put in two separate plastic tubes. Store and transport refrigerated.

COMMENTS

- 1) Min Amt: 2 mLs.
- 2) Unacceptable conditions: plasma. Repeated freeze/thaw cycles should be avoided; contaminated samples, samples containing particulate matter and lipemic or hemolyzed serum samples should not be used.
- 3) Stability: Refrigerated-5 days, Frozen-1 month.

RANGES	Kappa FLC	0.33-1.94	mg/dL	
	Lambda FLC	0.57-2.63	mg/dL	
	(Kappa/Lambda FLC Ratio)	0.26-1.65		
	Protein, Total	0-12 mo 1-3 yrs 3-6 yrs 6-10 yrs 10-18 yrs 18-60 yrs 60 yrs+	4.3-6.9 5.2-7.4 5.6-7.7 6.5-8.3 6.1-8.0 6.3-8.0 6.1-7.8	g/dL
	Albumin	0-4 days 4 days-14 yrs 14-18 yrs 18-60 yrs 60-90 yrs 90 yrs+	2.9-4.6 3.9-5.6 3.3-4.7 3.5-5.0 3.3-4.8 3.0-4.7	g/dL
	Alpha-1		0.1-0.4	g/dL
	Alpha-2		0.5-1.1	g/dL
	Beta-1		0.4-0.8	g/dL
	Beta-2		0.2-0.5	g/dL
	Gamma		0.6-1.5	g/dL
	Albumin		45.0-80.0	%
	Alpha-1		1.0-6.0	%
	Alpha-2		6.0-17.0	%
	Beta-1		5.0-13.0	%
	Beta-2		2.0-8.0	%
	Gamma		7.5-24.0	%
	Interpretation			
	Monoclonal Peak Immunofixation			
	Interp			

Selected References

1. 5th International Symposium on Clinical Applications of Serum Free Light Chain Analysis. Bradwell, AR, Ed., Hematology Meeting Reports 2008;2:1-44.
2. Katzmann, JA and Dispenzieri, A. Editorial: Screening algorithms for monoclonal gammopathies. Clin Chem.2008;1753-1755
3. Pratt, G. Review: The evolving use of serum free light chain assays in haematology. British J. Haematol. 2008;141:413-422.
4. Dispenzieri, A., et al. Appraisal of immunoglobulin free light chain as a marker in response. Blood. 2008;111:4908-4915
5. Jagannah, S. Value of serum free light chain testing for the diagnosis and monitoring of monoclonal gammopathies in hematology. Clinical Lymphoma & Myeloma. 2007;7:518-523
6. Kyrtonis, M.C. Prognostic value of serum free light chain ratio at diagnosis in multiple myeloma. British J. Haematol. 2007;137:240-243.
7. Mead, et al. Serum free light chains for monitoring multiple myeloma. British J. Haematol. 2004;126:348-354.
8. Graham Mead et al. Response to: Serum free light chains for monitoring multiple myeloma. British J. Haematol. 2004;128:405-409.
9. Bradwell, et al. Serum test for assessment of patients with Bence-Jones myeloma. Lancet 2003;361:489-491.
10. Lachmann, et al. Outcome in systemic AL amyloidosis in relation to changes in concentration of circulating free immunoglobulin light chains following chemotherapy. British J. Haematol. 2003;122:78-84
11. Drayson, et al. Serum free light chain measurements for identifying and monitoring patients with non-secretory multiple myeloma. Blood. 2001;97:2900-2902