

# FOUNDATION FOR BLOOD RESEARCH ANNOUNCES THE AVAILABILITY OF SERUM FREE LIGHT CHAIN MEASUREMENT

## Background

Monoclonal immunoglobulin production occurs in several plasma cell proliferative disorders, including multiple myeloma (MM), amyloidosis (AL), light chain multiple myeloma (LCMM), nonsecretory multiple myeloma (NSMM), Waldenstrom's macroglobulinemia, solitary plasmacytoma of bone, and plasma cell leukemia. In the laboratory, a monoclonal immunoglobulin is typically detected by serum protein electrophoresis (SPE) and immunofixation electrophoresis (IFE); population-wide, up to 61% of these findings are not associated with clinical symptoms and are termed monogammopathy of undetermined significance (MGUS). SPE and IFE do not, however, detect all monoclonal immunoglobulins, particularly when only light chains are secreted.

Plasma cells secrete free light chains (FLC, kappa or lambda) in addition to intact immunoglobulin molecules, and serum light chain levels are determined by the relative rates of synthesis ( $\kappa > \lambda$ ) and renal excretion ( $\kappa > \lambda$ ). In the presence of a monoclonal immunoglobulin,  $\kappa:\lambda$  ratios may be either higher or lower than the normal range, depending on the class of the involved FLC. In combination with SPE and IFE testing, serum FLC measurement contributes significantly to the detection and management of plasma cell dyscrasias, as shown in the Table.<sup>1,2</sup>

Paraprotein detected by serum testing (%)				
LABORATORY TEST	MM	AL	LCMM	NSMM
SPE/IFE	95	70	75	0
FLC (abnormal $\kappa:\lambda$ ratio)	96	98	100	68
FLC/SPE/IFE	99	98	100	68

## Clinical Applications of Serum FLC Measurement

- Increase detection of LCMM, NSMM and AL.** The serum FLC assay is more sensitive than SPE/IFE alone for conditions associated with low serum levels of monoclonal immunoglobulins.<sup>1,2</sup>
- Monitor treatment response in MM, LCMM, NSMM and AL.** The serum half-life of FLCs is 2-6 hours, compared with 5 days for IgA, 6 days for IgM and 21 days for IgG. Thus, measurement of serum FLC levels allows a far more rapid evaluation of tumor response to therapy than measurement of intact immunoglobulin. Likewise, serum FLC measurements allow earlier detection of relapse.<sup>3</sup>
- Assess progression risk in MGUS.** Patients with MGUS progress to MM at an overall rate of 1% per year.<sup>4</sup> An abnormal  $\kappa:\lambda$  ratio (~33% of MGUS patients) helps to identify those at increased risk for progression.<sup>5</sup>

## References

- Dispenzieri A, Kyle R, Merlini G et al. International Myeloma Working Group guidelines for serum free light chain analysis in multiple myeloma and related disorders. *Leukemia* advance online publication, 20 Nov 2008, doi:10.1038/leu.2008.307.
- Katzmann JA, Abraham RS, Dispenzieri A et al. Diagnostic performance of quantitative  $\kappa$  and  $\lambda$  free light chain assays in clinical practice. *Clin Chem* 2005;51(5): 878-81.
- Durie BG, Harousseau JL, Miguel JS et al. International uniform response criteria for multiple myeloma. *Leukemia* 2006;20:1467-1473
- Kyle RA, Therneau TM, Rajkumar SV et al. A long-term study of prognosis in monoclonal gammopathy of unknown significance. *NEJM* 2002;346:564-69.
- Rajkumar SV, Kyle RA, Therneau TM et al. Serum FLC ratio is an independent risk factor for progression in monogammopathy of unknown significance. *Blood* 2005;106:812-17.

**SEE REVERSE FOR ORDERING INFORMATION**

## ORDERING INFORMATION

### SERUM FREE LIGHT CHAIN MEASUREMENT

sFLC measurement is available as a single test or as a component of FBR's revised Block VI (Monogammopathy profile: IgG, IgA, IgM, SPE, IFE, sFLC). sFLC testing will be performed reflexively with IFE on samples received for Block 3 or IA testing when: a monoclonal band (or questionable band) is observed on SPE; when protein precipitates are seen at the origin on SPE; and, when hypogammaglobulinemia suggests the presence of light chain disease. Exceptions will be based on clinical laboratory judgment. We will perform only IFE (and not serum FLC) testing reflexively when SPE shows possible immune complexes.

- To order FLC as a single test check the appropriate box under Individual Studies on the FBR General Requisition form (version 02/09).
- To order the Block VI, Monogammopathy Profile, check the appropriate box under the profile section of the General Requisition form. If you are using an earlier version of the Requisition, check the Block VI panel and write "FLC" in the "other" box.
- If you do not want IFE or FLC testing to be performed reflexively as part of the Block 3 or Immunoassay profile, check "Omit confirmatory IFE and FLC". On earlier versions of the Requisition, check "Omit confirmatory IFE" and reflexive FLC will not be performed either.

*Specimen:* 2mL of nonhemolyzed, nonlipemic serum

*Storage and shipping:* Room temperature (3 days) or 4 weeks at 2-8°C

*Days test set up:* Testing is performed 2x per week.

*Price:* Contact Dave Groft for further information

*CPT code:* 83883 x 2

## CLIENT SUPPORT

**Clinical information:** contact Walter C. Allan, MD, Medical Director.

**Technical information:** contact Thomas B. Ledue, BA, RDL Technical Supervisor, or Wendy Y. Craig, Ph.D., Senior Research Scientist.

**General information or to schedule an inservice appointment:**

contact Dave Groft, MS, Director of Client Services.

**To provide input to FBR:** please call Dave Groft or complete our on-line survey at [www.fbr.org](http://www.fbr.org). If you use this survey to request further information or to schedule an informational meeting, it is VERY IMPORTANT to include your contact information.

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