OSF
SYSTEM LABORATORY

MEMORANDUM

To: OSF System Laboratory Clients

From: James Siebert, M.D. – Laboratory Medical Director

Subject: **Connective Tissue Disease (CTD) screening / ANA Serology**

Date: October 21, 2016

Effective November 28, 2016, the OSF System Laboratory will move from enzyme immunoassay (EIA) for the detection and semi-quantitation of human antinuclear autoantibodies (ANA) to the ANA screen on the BioPlex® 2200 multiplex flow cytometry platform (Bio-Rad Laboratories, Hercules, CA, USA) as the initial screening test for autoimmune disorders such as systemic lupus erythematosus (SLE). The BioPlex® 2200 is a fully automated Luminex-based system developed for high-throughput simultaneous analysis of 13 autoimmune analytes in a single tube, reacting with SS-A (52 and 60 kDa), SS-B, Sm, SmRNP, RNP-A and RNP-68, Scl-70, Anti-centromere B, dsDNA, chromatin, Jo-1, and ribosomal P proteins. The advantages of the BioPlex include a shorter turnaround time, detection of multiple antibodies simultaneously, less inter-observer variability, and less phlebotomy for patients.

The test code for the ANA screen + reflex on the BioPlex® 2200 is **LAB 695.** Positive ANA screens will reflex to the following antibodies (dsDNA, chromatin, ribosomal protein, SSA-52, SSA-60, SS-B, Sm, SmRNP, RNP-A and RNP-68, Scl-70, Anti-centromere B and Jo-1).

Patients with a history of CTD may continue to be followed with serial ANA tests, as in the past, with the current IFA (LAB696 – ANA, anti-nuclear antibody screen, titer if positive) for ordering providers who prefer IFA to monitor response to treatment (patients undergoing successful therapy for autoimmune disorders may be negative for ANA). Note: LAB 697, ANA titer (IFA method) will be discontinued.

ANTIBODY	Associated CTD / Autoimmune Condition	**
Anti-Centromere B	Scleroderma; SLE	LAB4616
Chromatin	Mixed CTD, Polymyositis; Scleroderma; Sjogren's; SLE	LAB4614
dsDNA	Mixed CTD; Scleroderma; SLE	LAB713
Jo-1	Polymyositis	LAB1233
Ribosomal Protein	Scleroderma; SLE	LAB4615
RNP-68	Mixed CTD; SLE	LAB4617
RNP-A	Mixed CTD; SLE	LAB4617
Scl-70	Mixed CTD; Scleroderma	LAB1432
Sjogren's Panel	Mixed CTD, Sjogren's; SLE	LAB1498
Sm (Smith)	Mixed CTD; SLE	LAB1506
SmRNP	Mixed CTD; SLE	LAB1790
SS-A (52 & 60)	Mixed CTD, Polymyositis; Scleroderma; Sjogren's; SLE	LAB1496
SS-B	Scleroderma; Sjogren's; SLE	LAB1497

Table 1. Autoimmune analytes and corresponding CTD and LAB test order code. ****These codes would be applicable if single selected markers are desired vs. ordering ANA screen and reflex (LAB 695).**

Diagnosis of autoimmune disorders requires recognition of clinical findings with the appropriate accompanying laboratory results. The ANA on the BioPlex® 2200 is an excellent screening test for autoimmune disorders: more than 90% of patients with systemic lupus erythematosus (SLE) will have a positive ANA test using either BioPlex or IFA with human HEp-2 cells.[1,2] In addition, 95 – 100% of patients with mixed connective tissue will also have a positive BioPlex ANA screen. [1,2] However, a positive ANA result is not specific for autoimmune disease, since patients with viral infections, chronic inflammatory processes, cancer, rheumatoid arthritis, drug-induced lupus, and older persons with no clinical symptoms or evidence of autoimmune disease can have a positive ANA. A multicenter, prospective clinical study demonstrated that agreement between multiplex autoimmune testing and EIA testing ranged from 99% (95% CI: 98–100%) for Jo-1 to 70% (95% CI: 76–82%) for ANA.[2]

Because the ANA testing by IFA with human HEp-2 cells is highly labor-intensive test, over the past 5 years most reference laboratories have adopted multiplex systems, such as the BioPlex, for ANA testing. The 13 antibodies on the BioPlex ANA with reflex panel are calibrated according to World Health Organization (WHO) standards. The anti-dsDNA antibody results are quantitative and expressed in terms of IU/mL (values ≥10 IU/mL are reported as positive). All other antibody results are semi-quantitative, expressed in terms of Antibody Index (AI), and values ≥1.0 AI are reported as positive. The ANA screen will be reported as negative if the results for all 13 autoantibodies are negative, but if any of the 13 autoantibodies are positive, the ANA screen will be reported as positive along with the AI of accompanying positive antibodies as recommended by the WHO.[3,4]

Any questions or concerns may be addressed to your designated clinical client representative or to:

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1. Op De Beéck K, Vermeersch P, Verschueren P, et al. Antinuclear antibody detection by automated multiplex immunoassay in untreated patients at the time of diagnosis. Autoimmune Rev. 2012;12:137-43.
2. Sohn K-Y, Collin D, Keith PK, et al. Comparison between multiplex immunoassay and immunofluorescence methods in detection of anti-nuclear antibodies. Clin Biochem 2010;43:783–4.
3. Moder KG, Wener MH, Weisman MH, et al. Measurement of antinuclear antibodies by multiplex immunoassay: A prospective, multicenter clinical evaluation. J Rheumatol 2007;34:978–86.
4. Tozzoli R, Bonaguri C, Melegari A, et al. Current state of diagnostic technologies in the autoimmunology laboratory. Clin Chem Lab Med 2013;51:129–38.