BRIEF REPORT



# Prevalence of Auto-antibodies in Pulmonary Tuberculosis

# Matthew P. Cheng, <sup>12,3,©</sup> Guillame Butler-Laporte,<sup>4</sup> Leighanne O. Parkes,<sup>5</sup> Tyler D. Bold,<sup>6</sup> Marvin J. Fritzler,<sup>7</sup> and Marcel A. Behr<sup>4</sup>

<sup>1</sup>Division of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts; <sup>2</sup>Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts; <sup>3</sup>Harvard Medical School, Boston, Massachusetts; <sup>4</sup>Division of Infectious Diseases and Medical Microbiology, McGill University Health Center, Montreal, Canada; <sup>5</sup>Division of Infectious Diseases and Medical Microbiology, Jewish General Hospital, Montreal, OC, Canada; <sup>6</sup>Division of Infectious Diseases and International Medicine, Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota; <sup>7</sup>University of Calgary, Calgary, AB, Canada

The relationship between pulmonary tuberculosis and auto-antibodies remains undefined. In a study of 75 patients with pulmonary tuberculosis and 75 controls, the prevalence of auto-antibodies was assessed in a reference laboratory using a comprehensive panel with standardized methodology. No significant relationship was found between auto-antibody prevalence and pulmonary tuberculosis.

**Keywords.** tuberculosis; auto-immunity; rheumatological conditions.

Autoimmune disorders represent a broad spectrum of diseases characterized by a pathological immune response directed at self-antigens and are hypothesized to arise from a constellation of genetic, hormonal, immunological, and environmental factors [1]. Certain chronic infections are thought to trigger the production of auto-antibodies through molecular mimicry or exuberant and persistent host responses that result in auto-immune or inflammatory pathologies [2].

Tuberculosis (TB) is the most common chronic bacterial infection worldwide, with an estimated 10.2 million incident cases and 10.1 million prevalent cases per year [3]. Like other infections, it has been associated with autoimmune manifestations, including nodular vasculitis [4]. TB has reportedly been linked with autoimmune disorders such as Sjögren's syndrome, systemic lupus erythematosus, rheumatoid arthritis, dermatomyositis, and polymyositis [5]. However, the nature, directionality, and robustness of this association remain unknown.

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Serological studies have suggested that patients with TB have increased auto-antibody titers. Rates as high as 44%, 11%, and 6% have been reported for antineutrophil cytoplasmic autoantibody (ANCA), anti-cardiolipin antibody (ACA), and anti-Scl-70, respectively [6, 7].

Although it is biologically plausible for patients with TB to develop auto-antibodies, the extent and magnitude to which this phenomenon occurs are unknown. The relationship between pulmonary TB and auto-antibodies remains undefined due to conflicting reports in the literature, inconsistent test selection, and nonstandardized testing methodology. The objective of this study was to determine if active TB is associated with an increased prevalence of auto-antibodies using a comprehensive panel with standardized methodology performed in a reference laboratory.

# METHODS

We performed a cross-sectional study involving patients evaluated for active pulmonary tuberculosis from Bangladesh, South Africa, Peru, and Uganda. Patients 18 years of age or older who were treated at 1 of the study sites and provided written informed consent to participate were eligible. Patients were included in this study if they provided sputum samples for mycobacterial culture. Baseline characteristics were collected at the time of medical assessment. Covariates of interest included age, sex, and relevant medical comorbidities such as HIV co-infection status and chronic rheumatological diseases. Patients with a diagnosis of active pulmonary TB were compared with controls who were selected from a similar patient population and who sought medical attention due to a febrile respiratory illness. The subjects in the control group had multiple negative sputum cultures for *Mycobacterium tuberculosis*.

To test the hypothesis that patients with active TB have a higher prevalence of auto-antibodies, we performed comprehensive serological testing in our patient population. Patient samples were obtained at the time of presentation to medical care and before starting antimicrobial therapy. From a review of the literature, we identified several serological markers that could be produced in response to a chronic bacterial infection. Investigations were performed for ACA, ANCA (MPO-ANCA and PR-3 ANCA), antimitochondrial antibodies (AMAs), antinuclear antibodies (ANAs), B2GP1-Domain 1, dsDNA, and Rheumatoid Factor (RF). A comprehensive connective tissue panel was performed to assess for BIC-D2, Centromere, DFS70, Elastase, HCP1, HCP2, Jo-1, Ku, LAMP2, Nucleosome, p155, PCNA, Pm/Scl, Ribo-P, RNA Pol III, RNP, RNP A, RNP C, Ro52, Ro60, Rpp25, Rpp38, SS-B, Scl-70, Sm, Sm-Peptide, VCP1, and VCP2. Please see the Supplementary Data for a

Received 21 December 2018; editorial decision 26 February 2019; accepted 4 March 2019. Correspondence: M. A. Behr, MD, MSc, Division of Infectious Diseases, McGill University Health Centre, 1001 Decarie Boulevard, Montreal, QC H4A 3J1, Canada (marcel.behr@mcgill.ca).

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complete list of all antibodies tested, their methods of assessment, and cutoffs for positivity. These assays were performed in a blinded fashion at the Mitogen Diagnostic Laboratory in Calgary, Alberta, Canada.

The relationship between different serological markers and tuberculosis was first analyzed using direct graphical visualization, followed by a classical hypothesis testing framework using the Fisher exact and Mann-Whitney U tests. Subsequently, sensitivity analysis was performed using multiple machine learning algorithms. First, Lasso logistic regression was used. The Lasso method allows for automatic variable selection and shrinkage, bypassing multiple comparison and effect inflation problems inherent with methods like stepwise regression. Second, 2 highly nonparametric tree-based methods were implemented: random forests and hierarchical cluster analysis (HCA). Finally, principal component analysis (PCA) was performed, and the first 3 principal components were plotted against each other to determine if they could discriminate between TB patients and controls. A detailed explanation of each procedure can be found in the references [8, 9]. All analyses were performed using the base R statistical package (3.2.0) and the glmnet library (2.0-10). The study was approved by the FIND Office for Human Research Studies.

# RESULTS

One hundred fifty patients were selected to participate in the study and provided serum samples for this analysis. Patient characteristics are presented in Table 1. The median age of the cohort at the time of testing was 33 years; 17 patients (11.3%) had a previous history of active TB, and 65 (43.3%) had a history of Bacillus Calmette-Guérin vaccination. In total, 75 patients

# were diagnosed with active pulmonary tuberculosis, and 75 presented with an acute febrile respiratory illness and were found to have an alternative diagnosis (other than TB). The most common alternate diagnoses in the control group were viral and bacterial respiratory tract infections. No patient had a reported history of HIV infection or of a primary rheumatological condition, including granulomatosis with polyangitis.

A detailed summary of serum auto-antibody testing results is shown in Table 2. When comparing cases and controls, the prevalence of ANA was not statistically different regardless of staining pattern: 46.7% of cases and controls had a nuclear pattern, 14.7% of cases and 18.7% of controls had a cytoplasmic pattern, and 30.7% of cases and 24.0% of controls had a mitotic pattern.

Similar proportions were found among both groups for common rheumatological auto-antibodies, including ACA (1.3% in cases, 4.0% in controls),  $\beta$ 2GP1-Domain 1 (1.3% in cases, 1.4% in controls), centromere (8.0% in cases, 2.7% in controls), dsDNA (1.3% in cases, 0% in controls), Ro-52 (4.0% in cases, 5.3% in controls), Ro-60 (1.3% in cases, 0% in controls), Scl-70 (1.3% in cases, 0% in controls), Sm (1.3% in cases, 0% in controls), and SS-B (1.3% in cases, 1.4% in controls). The most commonly present auto-antibodies were RF (56.0% in cases, 53.3% in controls) and antimitochondrial antibodies (12.0% in cases, 8.0% in controls). The proportion of ANCA positivity was found to be 1.3% and 0% for MPO-ANCA and 1.3% and 1.3% for PR3-ANCA among cases and controls, respectively. No patient in either group tested positive for Jo-1.

Among less frequently tested auto-antibodies, both groups had a similar prevalence of positive results (see Table 2 for

# Table 1. Patient Characteristics

Patient Characteristics	Tuberculosis (n = 75)		Controls (n = 75)	
	No.	% <sup>a</sup>	No.	%ª
Median age (range), y	31 (18–70)		35 (18–76)	
Male sex	45	63.4	21	50.0
Country				
Peru	61	81.3	34	45.3
Bangladesh	4	5.3	33	44.0
South Africa	1	1.3	8	10.7
Uganda	9	12.0	0	0
Medical comorbidities				
Asthma	0	0	3	4.0
Bronchiectasis	0	0	1	1.3
HIV	0	0	0	0
Rheumatological conditions	0	0	0	0
BCG vaccination	51	92.7	14	43.8
History of tuberculosis	3	6.4	14	18.7

Abbreviation: BCG, Bacillus Calmette-Guérin.

<sup>a</sup>% refers to available data; no imputations were made for missing data.

# Table 2. Prevalence of Different Auto-antibodies Among Patients With Active Pulmonary TB and Controls<sup>a</sup>

Non-Week Hisp 2 Mok lat with DAPI     Non-Week Hisp 2 Mok lat with DAPI       Orap attern (proportion > 1.80)     1175 (14.7)     1475 (24.7)     462       Michice pattern (proportion > 1.80)     2075 (20.7)     1475 (24.6)     464       Michice pattern (proportion > 1.80)     20.0 (18.0-24.0)     19.0 (16.8-24.0)     66.874       Michice pattern (proportion > 1.80)     20.0 (18.0-24.0)     19.0 (16.8-24.0)     66.90       Michice pattern (proportion > 1.80)     20.0 (28.0-42.0)     60.0 (2245.0)     30.0 (25.8-40.5)     70.0       Michice pattern (proportion pattern)     17.5 (13.3)     0.716 (3.3)     711     56.00     70.5 (3.3)     711       Sin (Michic) in = 150.0     83.0 (61.5-0.65.1)     70.0 (8.0-27.0)     .180     55.8.4.600     70.5 (8.2-4.6.0)     .924       Sin (Michic) in = 150.0     83.0 (61.5-0.65.1)     70.0 (8.2-4.6.0)     .924     .925     .925     .926 </th <th>Test<sup>b</sup></th> <th>Tuberculosis</th> <th>Controls</th> <th><i>P</i> Value</th>	Test <sup>b</sup>	Tuberculosis	Controls	<i>P</i> Value
Nuclear partern (argonotion > 1.80)     1397 (94.67)     1477 (14.77)     1477 (18.7)     0.602       Mator pattern (proportion > 1.80)     2207 (50.7)     180.7 (19.7)     0.602       Mator pattern (proportion > 1.80)     220 (18.0-24.0)     10.0		NovaView HEp-2 ANA kit with DAPI		
Opcode/sinc partierry (proportion > 1:80)     11/75 (14.7)     14/75 (18.7)     662       Made pattern (proportion > 1:80)     MagPix (CTD	Nuclear pattern (proportion > 1:80)	35/75 (46.7)	35/75 (46.7)	1
Micros pattern (responsion > 1.80)     237 (30.7)     1975 (24.0)     4975 (20.0)       dDNA (http) n = 150)     20.0 (18.0-24.0)     10.0 (10.5-24.0)     3.0 (75.10)     1       Micros patterns     175 (13.3)     0.75 (0.0)     1     1       Micros patterns     175 (13.3)     0.75 (0.0)     1     1       Sim (PC) n = 150     3.0 (75.42.0)     3.0 (25.4-0.5)     1     1       Sim (PC) n = 150     13.00 (88.8-16.12)     11.00 (88.8-16.12)     10.10 (88.7-16.2)     4.15       Sim (PC) n = 150     35.0 (46.7-00.5)     70.0 (16.7-07.0)     1.18       SSA/R00 (MFL) n = 150     35.0 (46.7-00.5)     70.0 (16.7-07.0)     1.18       SSA/R00 (resports no patitive)     176 (13.3)     0.77 (10.0)     1       SSA/R00 (resports no patitive)     176 (17.7)     0.77 (10.0)     1       SSA/R00 (resports no patitive)     176 (17.7)     0.77 (10.0)     1       SSA/R00 (resports no patitive)     176 (17.7)     0.77 (10.0)     1       SSA/R00 (resports no patitive)     176 (17.7)     0.75 (10.0)     1       SSA/R00 (resports no patitive)     176 (17.5)<	Cytoplasmic pattern (proportion > 1:80)	11/75 (14.7)	14/75 (18.7)	.662
MagPax (CTD     MagPax (CTD       GENR MPEU, n = 150/     20.0 186-2-40/     30.0 (16.5-24.0)     0.878       dSDNA (procortion positive)     1775 11.33)     0.75 (0)     1       NPL PMEU, n = 150/     23.0 23.0 -24.20     35.0 (32.4 3.5)     .168       Sim (MPU, n = 150)     25.0 122.0 -25.0     30.0 (25.8 -0.5)     .012       Sim (MPU, n = 150)     150.0 188.8 -181.2)     116.0 (4.8 -166.2)     .418       SS-AR60 (progenotino positive)     1775 113.3)     0.75 (0)     .1       SS-AR60 (progenotino positive)     1775 113.3)     0.75 (0)     .1       SS-AR60 (progenotino positive)     1775 113.3)     0.77 (0)     .1       SS-AR60 (progenotino positive)     1775 113.3)     0.77 (0)     .1       SS-AR60 (progenotino positive)     1775 113.3)     1771 173.51     .1       SS-AR60 (progenotino positive)     1775 113.3     0.75 (0)     .1       SS-AR60 (progenotino positive)     1775 113.3     170 (0)     .6       SS-AR60 (progenotino positive)     1775 113.3     170 (0)     .6       SS-AR60 (progenotino positive)     0.75 (0)     .257 (0)	Mitotic pattern (proportion > 1:80)	23/75 (30.7)	18/75 (24.0)	.464
abn/A MPL n = 150     20 018 0-240     10 016 0-240     0       NP Incontron positivel     175 1133     075 103     1       NP Incontron positivel     175 1133     075 103     1       Sim Information positivel     175 1133     075 103     1       Sim Information positivel     175 1133     075 10     1       Sim Information positivel     175 1133     075 10     1       Sim Information positivel     175 1133     075 10     1     1       Sim Information positivel     175 1133     075 10     1     1       Sim Information positivel     175 1133     075 10     1     1       Sim Information positivel     175 1133     075 10     1     1       Sim Information positivel     175 1133     076 10     1		MagPiX CTD		
isDNA for point on positivel     1/75 (1.33)     0/75 (0)     1       NP MUC; n = 150     2.5 (22-35.6)     3.60 (02-47.5)     .55       NP for points positivel     1/75 (1.33)     0/75 (0)     1       Sm (MPL) n = 150     130 (08.8 - 161.2)     116 (0.8 5 - 165.2)     .415       Ro2/TIM/X1 (MPL) n = 150     130 (08.8 - 161.2)     116 (0.8 5 - 165.2)     .415       SS-AMB00 (proportion positive)     3/75 (10.00)     175 (15.3)     .791       SS-AMB00 (proportion positive)     1/75 (1.33)     0/75 (0)     1       SS-AMB00 (proportion positive)     1/75 (1.34)     1/70 (12.2 - 96.0)     .00557       SS-AMB00 (proportion positive)     1/75 (1.33)     1/70 (12.2 - 96.0)     .00557       SS-AMB00 (proportion positive)     1/75 (1.33)     1/70 (12.2 - 96.0)     .00557       SS-AMB00 (proportion positive)     1/75 (1.33)     1/70 (12.2 - 96.0)     .00557       SS-AMB00 (proportion positive)     1/75 (1.33)     1/70 (12.2 - 96.0)     .0056       SS-AMB00 (proportion positive)     0/75 (0     .075 (0     .075 (0       SS-AMB00 (proportion positive)     0/75 (0     .075 (0     .07	dsDNA (MFU; n = 150)	20.0 (18.0–24.0)	19.0 (16.5–24.0)	.0878
BPL PMPLy n= 150     32.0.28.0-42.0)     36.0.102.4-25.0)     158       BNP (proportion positive)     175 (1.33)     0.075 (0)     11       Sin (proportion positive)     175 (1.33)     0.075 (0)     11       Sin (proportion positive)     170 (0.08.4-16.5.2)     16.0 (0.45-16.5.2)     .415       Sin (proportion positive)     32.0 (0.40-4-0.5.5)     0.0 (1.0.0-97.0)     .018       SS-AM600 (MPL), n= 150)     32.0 (0.40-40.5.5)     .00 (1.0.0-97.0)     .018       SS-AM600 (MPL), n= 150)     32.0 (0.6-10.5.5)     .070 (0.40-97.0)     .018       SS-BLa (MPL), n= 150)     45.0 (3.80-5-151)     .077 (0.0227.0)     .11       SS-BLa (MPL), n= 150)     45.0 (3.80-5-151)     .077 (0.0027.5)     .016       SS-D1 (MPL), n= 150)     45.0 (3.80-5-151)     .077 (0.0027.5)     .016       SS-D1 (MPL), n= 150)     45.0 (3.80-5-151)     .075 (0.0027.5)     .027       SS-D1 (MPL), n= 150)     45.0 (3.80-5-151)     .075 (0.0027.5)     .027       SS-D1 (MPL), n= 150)     25.0 (0.65-178.0)     .776 (0.0027.5)     .027       SS-D1 (MPL), n= 150)     25.0 (0.773-5.5)     .190 (0.1622.5)	dsDNA (proportion positive)	1/75 (1.33)	0/75 (0)	1
BNP (arcportion positive)     175 (132)     075 (0)     1       Sm (MPL), n = 160     250 (22.0-66.0)     30.0 (25.6-40.5)     0.12       Sm (MPL), n = 160     130.0 (08.8-161.2)     116.0 (94.5-16.5.2)     4.15       B62/TIMM2 (uppertoine positive)     47.07 (4.0.0)     47.07 5 (0.0)     11       SS-AR-600 (proportion positive)     47.07 (4.0.0)     47.07 5 (0.0)     11       SS-AR-600 (proportion positive)     17.07 (13.0)     0.70 (14.0-97.00)     11       SS-AR-600 (proportion positive)     17.07 (13.0)     17.01 (13.0)     11       SS-PAR-600 (proportion positive)     17.07 (13.0)     17.01 (13.0)     11       SS-PAR-600 (proportion positive)     17.07 (12.7)     0.075 00     10       SS-PAR-600 (proportion positive)     0.75 00     4.05 (28.0-5.10)     2.27       SS-PAR-600 (proportion positive)     0.75 00     0.75 00     0.75 00     0.75 00       SS-PAR-600 (proportion positive)     0.75 00     0.75 00     0.75 00     0.75 00       SS-PAR-600 (proportion positive)     0.75 00     0.75 00     1     Nucleosome (proportion positive)     0.75 00     0.75 00	BNP (MEU: $n = 150$ )	32.0 (28.0–42.0)	36.0 (30.2–43.5)	.158
Dm MFU, n = 150     25.0 (220–36.0)     30.0 (25.8–40.5)     .012       Sm (proportion pashiel     10.75 (1.33)     .075 (0.0)     .1       Rolz/TIMUZI (broportion positive)     30.75 (4.00)     .475 (5.33)     .471       SS-MR00 (MFU), = 150)     82.0 (420–376.0)     .0014 -9700     .018       SS-MR00 (MFU), = 150)     82.0 (460–310.65)     .70.0 (4.0–9700)     .018       SS-MR00 (MFU), = 150)     85.0 (660–32.5)     .70.0 (4.0–9700)     .018       SS-MR1 (MFU), = 150)     86.0 (660–32.5)     .70.0 (7.82–48.0)     .00557       SS-R01 (proportion positive)     .70.7 (1.61)     .75.0 (.000     .75.7 (.000)     .012       Log most monopative)     .70.7 (0.0)     .75.0 (.000     .75.0 (.000     .75.0 (.000     .75.7 (.000)     .75.0 (.000) <td>RNP (proportion positive)</td> <td>1/75 (1.33)</td> <td>0/75 (0)</td> <td>1</td>	RNP (proportion positive)	1/75 (1.33)	0/75 (0)	1
Sm (preparation positive)     1/75 (133)     0.075 (0)     1       Res2/T1M21 (MPU, n = 150)     1300 (98.8–1612)     1160 (94.6–1652)     .4.15       SS-AR600 (MPU; n = 150)     83.0 (84.5–106.5)     70.0 (84.0–707)     .0183       SS-AR600 (MPU; n = 150)     83.0 (84.5–106.5)     70.0 (84.0–707)     .0183       SS-AR600 (MPU; n = 160)     35.5 (28.5–11)     370 (28.2–48.0)     .964       SS-AR600 (more positive)     175 (133)     174 (125)     .1       SS-AR600 (preportion positive)     175 (132)     70.6 (82.0–80.0)     .00537       SS-AR600 (preportion positive)     145 (0.33)     .076 (0.0–106.5)     .0126       Contramere (NPU; n = 150)     95.0 (66.6–128.5)     .70.6 (60.0–106.5)     .0126       Contramere (NPU; n = 150)     90.0 (96.0–197.5)     .95.6 (20.0)     .0126       Contramere (NPU; n = 150)     90.0 (96.0–197.5)     .95.6 (20.0)     .1       Nucleosome (NPU; n = 150)     90.0 (96.0–197.5)     .95.6 (20.0)     .1       Nucleosome (NPU; n = 150)     20.0 (17.5–25.0)     .0.126     .0.127       Star (MPU; n = 150)     20.0 (17.5–15.0)     .0.175 (10.0)	Sm (MEU: n = 150)	25.0 (22.0–35.0)	30.0 (25.8–40.5)	012
Backgr/TRM2/1 (are positive)     100 (1863–1612)     116 0 (14.5–165.2)     415       Res2/TRM2 (are positive)     37/5 (400)     47/5 (533)     .741       SSA/Re60 (MPL) (n = 150)     83 0 (46.5–106.5)     70.0 (16.0–97.0)     .0189       SSA/Re60 (MPL) (n = 160)     83.0 (46.5–105.5)     70.0 (16.0–97.0)     .0189       SS-Mark (MPL) (n = 160)     85.0 (46.5–102.5)     77.0 (17.2–96.0)     .0083       SS-Mark (MPL) (n = 160)     45.0 (38.8–50.5)     45.0 (36.0–102.5)     .1       Jo-1 (MPL) (n = 150)     45.0 (39.8–56.0)     45.0 (36.0–102.5)     .075 (0)     .0       Lop (100 (100 (107.50))     95.0 (66.5–180.0)     77.0 (10.0–105.6)     .0226       Centromare (MPL) (n = 150)     95.0 (66.5–180.0)     77.0 (10.0–105.6)     .0226       Centromare (MPC) (n = 150)     90.0 (60.0–187.5)     .65.5 (2.0–13.8)     .0766       DPS7.0 (107.1) (n = 150)     90.0 (60.0–187.5)     .65.5 (2.0–13.8)     .0768       DPS7.0 (107.1) (n = 150)     20.0 (10.0–24.5)     .12     Nucleoseme (MPC) (n = 150)     .026 (10.0–25.5)     .12       Nucleoseme (MPC) (n = 150)     27.6 (2.53)     .075 (10.0)     .42	Sm (proportion positive)	1/75 (1.33)	0/75 (0)	1
BAD2/TRIM21 interportion positive)     3/75 (14.00)     4/75 (15.33)	$B_052/TBIM21$ (MEU: $n = 150$ )	130.0 (88.8–161.2)	116 0 (84 5–165 2)	415
Integration protocols     10.0 (10.0)     10.0 (10.0)     10.0 (10.0)     10.0 (10.0)     10.0 (10.0)       SSA-M600 (MPU) n = 150)     10.0 (10.0 (10.0)     11.0 (10.0)     10.0	$B_{0}52/TRIM21$ (proportion positive)	3/75 (4 00)	4/75 (5 33)	.413
SAVR.000 (module of module of mod	SS A/Baco (MELL: p = 150)	92 0 (64 5 106 5)	70.0 (54.0, 970)	.741
BACHROOM (proportion positive)     177 (1.33)     070 (0.7)     178       SSR/a (MCP), n = 150)     55 (76.5-51.5)     370 (128.2-48.0)     .964       SSR/a (MCP), n = 150)     66 (66.0-125.5)     770 (157.2-96.0)     .0537       Sol-70 (MCP), n = 150)     45 (129.4-56.0)     45.0 (29.4-56.0)     .267       Jo 1 (MCP), n = 150)     95.0 (66.5-188.0)     770 (60.0-106.5)     .0126       Centromere (MCP), n = 150)     95.0 (66.5-188.0)     770 (60.0-106.5)     .0126       Centromere (MCP), n = 150)     90.0 (60.0-187.5)     66.5 (52.0-133.8)     .0766       DFS70 (MCP), n = 150)     20.0 (18.0-22.5)     .12     Nucleosome (MCP), n = 150     .020 (18.0-25.6)     .0127       Nucleosome (MCP), n = 150)     20.2 (17.0-35.5)     .90.0 (4.5-26.5)     .0127       Nucleosome (MCP), n = 150)     22.0 (17.0-35.5)     .90.7 (10.0)     .497       Ku (MCP), n = 150)     27.5 (2.3)     .075 (0)     .0712       Nucleosome (MCP), n = 150)     78.6 (4.0-129.2)     .93.0 (62.8-126.0)     .162       Nucleosome (MCP), n = 150)     78.6 (4.0-129.2)     .93.0 (62.8-126.0)     .162       Nucleosome (MCP), n	SS-A(Robot (million, n = 150)	1/75 (1 22)	0/75 (0)	.0105
SSE/LG (appropriate     375 (LG.3)     17/4 (13.5)     1       SSE/LG (appropriate positive)     175 (LG.3)     17/4 (13.5)     1       SSI-70 (appropriate positive)     175 (LG.2)     770 (SG.2)     1       Jo-1 (MFU; n = 150)     450 (39.8-55.0)     450 (38.0-51.0)     257       Jo-1 (MFU; n = 150)     95.0 (66.5-188.0)     778 (60.0-106.5)     0.126       Centromere (MFU; n = 150)     95.0 (66.2-185.0)     278 (60.0-106.5)     0.126       DFS70 (MFU; n = 150)     90.0 (60.0-187.5)     68.5 (52.0-13.3)     0.766       DFS70 (MFU; n = 150)     0.75 (0)     0.775 (0)     1     Nucleosome (MFU; n = 150)     0.75 (0)     0.775 (0)     0.78 (0)     .74       Nucleosome (MFU; n = 150)     2.20 (170-35.5)     1.9 (114.5-6.5.5)     0.127       Ku (MFU; n = 150)     42.0 (275-51.5)     40.5 (34.0-50.5)     0.791       Ku (MFU; n = 150)     7.75 (LO.00)     9.73 (10.4.6.5)     3.10 (24.2-4.5.0)     .492       NEA P (MFU; n = 150)     3.70 (21.0-4.6.5)     3.10 (24.2-4.5.0)     .0493       PCNA (MFU; n = 150)     3.70 (21.0-4.6.5)     3.0 (24.2-4.5.0)     .0494	SS-A(1000 (proportion positive)	1775 (1.33) 25 5 (26 5 51 5)	270 (28.2, 48.0)	064
32-BL Alpha Dapha D	SS-D/La (IVII 0, II = 143)	1/75 (1 22)	1/74 (1 25)	.304
3ch / 0 (mp) (in = 150)     3ch / 0 (mp) (	Sol-30 (MELLing 150)	1/75 (1.33) 96 0 (66 0, 122 E)	770 (572,00,0)	00527
Sar JV (proportion positive)     1/76 (1.27)     0.76 (0)     1/7       Jon Largopertion positive)     0/75 (0)     0/75 (0)     7/8       Centromere (WFU; n = 150)     950 (68.5-188.0)     7/8 (80.0-106.5)     0.126       Dertromere (WFU; n = 150)     900 (60.0-187.5)     69.5 (2.0-133.8)     0.766       DFS70 (wportion positive)     10/75 (0)     1     2.75       DFS70 (wportion positive)     0.75 (0     0.18.0-22.5)     .12       Nucleosome (MFU; n = 150)     2.20 (19.0-24.0)     2.00 (18.0-22.5)     .12       Nucleosome (proportion positive)     0.75 (0)     0.75 (0)     .48       Rioo-P (MFU; n = 150)     2.20 (17.5 (2.5)     0.72 (0)     .43       Ku (proportion positive)     2.75 (2.5)     .00 (2.8 - 126.0)     .073 (1)       Ku (proportion positive)     1.75 (1.43)     .175 (1.33     .1       RNP A (proportion positive)     1.75 (1.40)     .330 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)     .040 (2.4 - 245.0)	Sci-70 (MPO; $H = 150$ )	80.0 (00.0-123.5)	77.0 (57.2–90.0)	.00537
John 1 (MPU), In = 150)     42.0 (3.9.4-96.0)     97.0 (00)     m/a       Centromere (MPU), n = 150)     95.0 (66.5-188.0)     73.0 (60.0-106.5)     0.125       DFS70 (MPU), n = 150)     90.0 (60.0-187.5)     69.5 (52.0-133.8)     0.766       DFS70 (MPU), n = 150)     20.0 (19.0-187.5)     69.5 (52.0-133.8)     0.766       DFS70 (MPU), n = 150)     20.0 (19.0-24.0)     20.0 (18.0-22.5)     1.2       Nucleosome (MFU), n = 150)     23.0 (17.0-35.5)     19.0 (14.5-26.5)     0.0127       Ribb-P (WPU), n = 150)     23.0 (17.0-35.5)     19.0 (14.5-26.5)     0.0127       Ribb-P (wopportion positive)     17/5 (1.33)     17     1.33     1.6       RIP A (MPU), n = 150)     73.6 (54.0-129.2)     93.0 (62.8-126.0)     1.62       RIP A (MPU), n = 150)     37.0 (21.2-45.5)     3.10 (24.2-45.0)     0.403       RIN A (MPU), n = 150)     37.0 (21.2-45.5)     3.10 (24.2-45.0)     0.403       RIN A (MPU), n = 150)     37.0 (21.2-45.6)     3.00 (24.0-33.0)     1.72       RIN A (MPU), n = 150)     37.0 (21.2-45.6)     3.00 (24.0-33.0)     1.72       RIN A (MUU), n = 150)     28.0 (24.0-36.8)	Sci-70 (proportion positive)	1/75 (1.27) 45.0 (20.0, 55.0)	0/75 (0)	1
Jac I groportion positive)     U/s (U)     U/s (U)     U/s (U)     Na       Centromere (MPU): n = 150)     95.0 (66.5-188.0)     73.0 (60.0-167.5)     0.25       Centromere (MPU): n = 150)     95.0 (60.6-178.0)     1757 (2.67)     2.76       DFS70 (moportion positive)     167/5 (21.3)     157/5 (20.0)     1       Nucleosome (MFU): n = 150)     2.0 (19.0-24.0)     2.0 (18.0-25.5)     1.9 (14.5-26.5)     0.127       Ribo-P (MFU): n = 150)     2.3 (170-35.5)     1.9 (14.5-26.5)     0.127       Ribo-P (MFU): n = 150)     2.0 (275-51.5)     4.05 (34.0-50.5)     0.791       Ku (proportion positive)     1.775 (1.33)     1.76     1.33     1       RNP A (MFU): n = 150)     7.8 (64.0-122.2)     9.3 0 (62.8-126.0)     1.62       RNP A (proportion positive)     0.775 (0)     9.75 (1.0)     .043       PCNA (MFU): n = 150)     3.70 (29.2-46.5)     3.10 (24.2-45.0)     .0403       PCNA (forportion positive)     0.775 (0)     1.75     1.72       RNA POI III (MFU): n = 150)     2.80 (24.0-36.8)     2.60 (22.0-33.0)     1.27       RNA POI III (MFU): n = 150)     2.80 (24.0-36	JO-1 (IVIFU; n = 150)	45.0 (39.8–55.0)	45.0 (38.0-51.0)	.257
Centromere (WHU) h = 150/     95.0 (eb.5-188.0)     27.0 (e0.0-10.5)     0.02.0       Centromere (proportion positive)     6/75 (6.00)     27.75 (2.67)     2.76       DFS70 (proportion positive)     16/75 (21.3)     15.75 (20.0)     1       Nucleosome (WHU) n = 150)     20.0 (19.0-24.0)     20.0 (18.0-22.5)     .12       Nucleosome (wroportion positive)     075 (6)     075 (0)     n/4       Ribo-P (proportion positive)     27.75 (2.53)     07.75 (0)     .49       Ku (proportion positive)     17.75 (1.33)     1.17     1.33)     1       RIP A IMFU; n = 150)     42.0 (37.5-51.5)     40.5 (34.0-50.5)     0.791     1.62       RIP A IMFU; n = 150)     7.8 (64.0-129.2)     93.0 (62.8-126.0)     .162       RIP A IMFU; n = 150)     37.0 (29.2-46.5)     30.0 (24.2-45.0)     .0403       PCNA (proportion positive)     07.5 (4.00)     17.5 (1.33)     1       RIN A FOILI (INC-yr = 150)     37.0 (29.2-46.5)     58.0 (44.2-45.0)     .0403       PCNA (proportion positive)     07.5 (0)     17.5 (1.33)     1       RIN A FOILI (INC-yr = 150)     28.0 (24.0-36.8)     26.0 (22.0-	Jo-1 (proportion positive)	0/75 (0)	0/75 (0)	n/a
Centomere (proportion positive)     67/5 (8.00)     27/5 (2.67)     27.6       DFS70 (MFL): n = 150)     90.0 (60.0-187.5)     96.5 (62.0-133.8)     0.7060       DFS70 (MFL): n = 150)     20.0 (19.0-24.0)     20.0 (18.0-22.5)     .12       Nucleosome (MFL): n = 150)     23.0 (170-35.5)     19.0 (14.5-26.5)     .0127       Ribo-P (MFU): n = 150)     23.0 (170-35.5)     40.5 (54.0-50.5)     .0771       Ku (MFU): n = 150)     22.0 (375-51.5)     40.5 (54.0-50.5)     .0791       Ku (MFU): n = 150)     77.8 (64.0-129.2)     33.0 (62.8-126.0)     .162       RNP A (proportion positive)     3775 (4.00)     .0775 (10.0)     .162       RNP A (proportion positive)     3775 (4.00)     .075 (10.0)     .130       PCNA (MFU): n = 150)     37.0 (29.2-46.5)     31.0 (24.2-45.0)     .04033       PCNA (MFU): n = 150)     37.0 (29.2-46.5)     31.0 (24.2-45.0)     .04033       PCNA (MFU): n = 150)     37.0 (24.2-45.5)     .31.0 (24.2-45.0)     .04033       PCNA (MFU): n = 150)     28.0 (24.0-36.8)     .26.0 (22.0-33.0)     .127       RDA POI IIII (WPU): n = 150)     28.0 (24.0-35.5)     .88.01	Centromere (MFU; n = 150)	95.0 (66.5–188.0)	/8.0 (60.0–106.5)	.0126
DFS70 (intPoting positive)     90.0 (60.0-18/5)     99.6 (52.0-133.8)     .0768       DFS70 (intPoting positive)     167/5 (213)     157/5 (20.0)     1       Nucleosome (intPut; n = 150)     20.0 (19.0-24.0)     20.0 (18.0-22.5)     .12       Nucleosome (intPut; n = 150)     23.0 (170-95.5)     19.0 (14.5-26.5)     .0127       Ribo-P (introportion positive)     27.75 (2.53)     07.75 (0)     .497       Ku (NFU; n = 150)     42.0 (37.5-51.5)     40.5 (34.0-50.5)     .0791       Ku (proportion positive)     17.75 (133)     11.75 (133)     .11       RNP A (MFU; n = 150)     78.6 (54.0-129.2)     93.0 (62.8-126.0)     .162       RNP A (MFU; n = 150)     37.0 (29.2-46.5)     31.0 (24.2-45.0)     .0403       PCNA (intPU; n = 150)     37.0 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (Inteportion positive)     075 (0)     17.75 (1.33)     .1       RNA Fol IIII (proportion positive)     37.0 (31.0-46.5)     36.0 (22.0-43.0)     .127       Rpp25 (MFU; n = 150)     65.0 (53.2-86.5)     58.0 (48.5-772.)     .0844       RNA Continue positive)     17.75 (1.33)     07.75 (0)	Centromere (proportion positive)	6/75 (8.00)	2/75 (2.67)	.276
DFS70 (proportion positive)     16/75 (21.3)     15/75 (20.0)     1       Nucleosome (NFU; n = 150)     20.0 (19.0–22.6)     .0.2     .0.12       Nucleosome (NFU; n = 150)     23.0 (170–35.5)     19.0 (14.5–26.5)     .0.127       BibD-P (proportion positive)     275 (2.53)     .0.75 (0)     .4.97       Ku (MFU; n = 150)     42.0 (375–51.5)     40.5 (34.0–50.5)     .0.791       Ku (MFU; n = 150)     75.6 (54.0–129.2)     93.0 (62.8–126.0)     .162       RNP A (MFU; n = 150)     37.0 (29.2–46.5)     31.0 (24.2–45.0)     .0403       PCNA (MFU; n = 150)     37.0 (29.2–46.5)     31.0 (24.2–45.0)     .0403       PCNA (Proportion positive)     .075 (0)     .076     .0     .078       RNA Pol III (MFU; n = 150)     37.0 (29.2–46.5)     33.0 (24.2–45.0)     .0644       RNA Pol III (MFU; n = 150)     28.0 (24.0–36.8)     26.0 (22.0–33.0)     .127       Rpp25 (moportion positive)     .075 (0)     .075 (0)     .0     .0       RNA POL III (MFU; n = 150)     63.0 (24.0–33.5)     28.0 (23.0–35.5)     .841       Rpp36 (IMFU; n = 150)     40.0 (31.0–82.0)     42.0 (32.0–60.2)	DFS70 (MFU; n = 150)	90.0 (60.0–187.5)	69.5 (52.0–133.8)	.0766
Nuclessome (MFU; n = 150)     20,0 (19,0–24,0)     20,0 (18,0–22,5)     1,12       Nuclessome (MFU; n = 150)     23,0 (170–35,5)     19,0 (14,5–26,5)     ,0127       Ribo-P (MFU; n = 150)     23,0 (170–35,5)     19,0 (14,5–26,5)     ,0127       Ribo-P (MFU; n = 150)     42,0 (375–515)     40,5 (34,0–50,5)     ,0791       Ku (proportion positive)     1775 (1,33)     175 (1,33)     1       RNP A (proportion positive)     375 (4,00)     9775 (12,0)     ,130       PCNA (MFU; n = 150)     370 (23,2–46,5)     31,0 (24,2–45,0)     ,0603       PCNA (MFU; n = 150)     370 (23,2–46,5)     34,0 (24,8–45,0)     ,0603       RNA Pol III (MFU; n = 150)     370 (31,0–46,5)     34,0 (24,8–45,0)     ,0604       RNA Pol III (moportion positive)     0/75 (0)     1/75 (1,33)     1       RNA Pol III (moportion positive)     370 (31,0–46,5)     34,0 (24,8–45,5)     ,0694       RNA Pol III (moportion positive)     0/75 (0)     1/75 (1,33)     1       RNP C (moportion positive)     1775 (1,33)     0/75 (0)     1       RNA POL III (moportion positive)     3/75 (4,00)     3/75 (4,00)     1	DFS70 (proportion positive)	16/75 (21.3)	15/75 (20.0)	1
Nucleasome (proportion positive)     0/75 (0)     0/75 (0)     n/a       Ribo-P (MFU; n = 150)     23.0 (170-35.5)     19.0 (14.5-26.5)     0.0127       Ribo-P (MFU; n = 150)     42.0 (37.5-51.5)     40.5 (44.0-50.5)     0.0731       Ku (MFU; n = 150)     17.5 (1.33)     17.5 (1.33)     1       RNP A (MFU; n = 150)     37.5 (4.00)     97.5 (12.0)     .162       RNP A (MFU; n = 150)     37.0 (29.2-46.5)     31.0 (24.2-45.0)     .0403       PCNA (MFU; n = 150)     37.0 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (MFU; n = 150)     37.0 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (MFU; n = 150)     28.0 (24.0-36.8)     26.0 (22.0-33.0)     .127       Rpp25 (INFU; n = 150)     28.0 (24.0-36.5)     58.0 (48.5-77.2)     .0844       RNP C (MFU; n = 150)     65.0 (53.2-86.5)     58.0 (48.5-77.2)     .0844       RNP C (MFU; n = 150)     29.0 (24.0-33.5)     28.0 (23.0-35.5)     .841       RNP C (MFU; n = 150)     46.0 (31.0-82.0)     42.0 (32.0-60.2)     .31       Rpp38 (Incoportion positive)     77.5 (10.     n/a     .844	Nucleosome (MFU; n = 150)	20.0 (19.0–24.0)	20.0 (18.0–22.5)	.12
Rbo-P (MFU; n = 150) 23.0 (170-35.5) 19.0 (14.5-26.5) .0172   Ribo-P (proportion positive) 27.5 (2.53) .075 (0) .497   Ku (MFU; n = 150) 42.0 (37.5-51.5) 40.5 (34.0-50.5) .0791   Ku (proportion positive) 17.5 (1.33) 175 (1.33) 1   RNP A (proportion positive) 37.5 (54.0-129.2) 93.0 (62.8-126.0) .162   RNP A (proportion positive) 37.7 (29.2-46.5) 31.0 (24.2-45.0) .0403   PCNA (MFU; n = 150) 37.0 (29.2-46.5) 31.0 (24.2-45.0) .0403   PCNA (MFU; n = 150) 37.0 (29.2-46.5) 31.0 (24.2-45.0) .0403   PCNA (Infru); n = 150) 37.0 (21.0-46.5) 34.0 (24.8-44.5) .0694   RNA Pol III (foroportion positive) 07.5 (0) 17.7 1.33 1   Rp25 (proportion positive) 07.5 (0) 17.7 1.33 1   Rp25 (proportion positive) 17.7 (1.33) 07.75 (0) 1 1   Rp25 (proportion positive) 17.7 (1.33) 07.75 (0) 1 1   Rp26 (MFU; n = 150) 65.0 (53.2-86.5) 58.0 (48.5-72.2) .0844   RNP C (proportion positive) 37.75 (4.00) 37.5 (4.00) 1   Rp38 (WFU; n = 150) 46.0 (31.0-82.0) 42.0 (32.0-60.2) .31	Nucleosome (proportion positive)	0/75 (0)	0/75 (0)	n/a
Ribo P (proportion positive)     2/75 (2.53)     0/75 (0)     4497       Ku (MFU; n = 150)     42.0 (37.5-51.5)     40.5 (34.0-50.5)     .0791       Ku (MFU; n = 150)     78.5 (54.0-129.2)     93.0 (62.8-126.0)     .162       RNP A (MFU; n = 150)     78.5 (54.0-129.2)     93.0 (62.8-126.0)     .162       RNP A (proportion positive)     3/75 (4.00)     9/75 (12.0)     .100       PCNA (MFU; n = 150)     37.0 (29.2-46.5)     31.0 (24.2-45.0)     .0403       PCNA (proportion positive)     0/75 (0)     0/75 (0)     .0403       PCNA (MFU; n = 150)     37.0 (21.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (MFU; n = 150)     28.0 (24.0-36.8)     26.0 (22.0-33.0)     .127       Rpp25 (proportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (MFU; n = 150)     28.0 (24.0-33.5)     28.0 (23.0-35.5)     .841       Rpp38 (MFU; n = 150)     29.0 (24.0-33.5)     .209     .311       Rpp38 (MFU; n = 150)     40.0 (31.0-82.0)     47.0 (32.0-60.2)     .31       Rpp38 (MFU; n = 150)     54.0 (41.0-84.0)     49.0 (38.5-73.5)     .184 <td< td=""><td>Ribo-P (MFU; n = 150)</td><td>23.0 (17.0–35.5)</td><td>19.0 (14.5–26.5)</td><td>.0127</td></td<>	Ribo-P (MFU; n = 150)	23.0 (17.0–35.5)	19.0 (14.5–26.5)	.0127
Ku (MFU; n = 150)     42.0 (37.5-51.5)     40.5 (34.0-50.5)     .0791       Ku (proportion positive)     1/75 (1.33)     1/75 (1.33)     1       RNP A (MFU; n = 150)     75.6 (4.0-12.2.2)     33.0 (62.8-126.0)     .1622       RNP A (MFU; n = 150)     370 (29.2-46.5)     31.0 (24.2-45.0)     .04033       PCNA (proportion positive)     0/75 (0)     0/75 (0)     .0763       RNA Pol III (MFU; n = 150)     370 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (proportion positive)     0/75 (0)     1/75 (1.33)     1       RNA Pol III (proportion positive)     0/75 (0)     1/75 (1.33)     1       RNA Pol III (proportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (MFU; n = 150)     65.0 (53.2-86.5)     58.0 (48.5-772)     .0844       RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     .074       Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     .184       Bp38 (proportion positive)     57.0 (6.67)     1/75 (1.33)     .209       BIC-D2 (prop	Ribo-P (proportion positive)	2/75 (2.53)	0/75 (0)	.497
Ku (proportion positive)     1/75 (1.33)     1/76 (1.33)     1       RNP A (MFU; n = 150)     78.5 (54.0-129.2)     93.0 (62.8-126.0)     .162       RNP A (proportion positive)     370 (29.2-46.5)     31.0 (24.2-45.0)     .0403       PCNA (MFU; n = 150)     370 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol IIII (MFU; n = 150)     370 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol IIII (proportion positive)     0/75 (0)     176 (1.33)     1       RNA Pol IIII (proportion positive)     0/75 (0)     176 (1.33)     1       RNA Pol IIII (proportion positive)     0/75 (0)     176 (1.33)     1       RNP C (incroportion positive)     0/75 (4.00)     176 (1.30)     1       RNP C (incroportion positive)     3/75 (4.00)     3/76 (4.00)     1       Rpp38 (incrportion positive)     0/75 (6.0)     0/75 (0)     n/a       Rpp38 (incrportion positive)     0/75 (6.7)     176 (1.33)     209       BiC-D2 (MFU; n = 150)     64.0 (31.0-82.0)     42.0 (32.0-60.2)     .31       Rpp38 (incroportion positive)     0/75 (6.67)     176 (1.33)     209	Ku (MFU; n = 150)	42.0 (37.5–51.5)	40.5 (34.0–50.5)	.0791
RNP A (MFU; n = 150)   78.5 (54.0-129.2)   93.0 (62.8-126.0)   .162     RNP A (proportion positive)   3/75 (4.00)   9/75 (12.0)   .130     PCNA (MFU; n = 150)   370 (29.2-46.5)   31.0 (24.2-45.0)   .0403     PCNA (proportion positive)   0/75 (0)   0/75 (0)   .74     RNA Pol III (proportion positive)   0/75 (0)   1/75 (1.33)   1     Rpp25 (MFU; n = 150)   28.0 (24.0-36.8)   26.0 (22.0-33.0)   .127     Rpp25 (proportion positive)   1/75 (1.33)   0/75 (0)   1     RNP C (MFU; n = 150)   65.0 (53.2-86.5)   58.0 (48.5-77.2)   .0844     RNP C (proportion positive)   3/75 (4.00)   3/75 (4.00)   1     Rpp38 (MFU; n = 150)   29.0 (24.0-33.5)   28.0 (23.0-60.2)   .31     Rpp38 (MFU; n = 150)   46.0 (31.0-82.0)   42.0 (32.0-60.2)   .31     Rpp38-1 (proportion positive)   5/75 (6.67)   1/75 (1.33)   .209     BIC-D2 (MFU; n = 150)   63.0 (47.8-88.0)   570 (47.8-96.8)   .664     Pm/Scl (MFU; n = 150)   63.0 (47.8-88.0)   570 (47.8-96.8)   .664     Pm/Scl (proportion positive)   3/75 (4.00)   4/75 (5.33)   1 <td>Ku (proportion positive)</td> <td>1/75 (1.33)</td> <td>1/75 (1.33)</td> <td>1</td>	Ku (proportion positive)	1/75 (1.33)	1/75 (1.33)	1
RNP A (proportion positive)     3/75 (4.00)     9/75 (12.0)     .130       PCNA (MFU; n = 150)     370 (29.2-46.5)     31.0 (24.2-45.0)     .0403       PCNA (proportion positive)     0/75 (0)     0/75 (0)     .0694       RNA Pol III (MFU; n = 150)     370 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (proportion positive)     0/75 (0)     1/75 (1.33)     1       Rp25 (MFU; n = 150)     28.0 (24.0-36.8)     26.0 (22.0-33.0)     .127       Rp25 (groportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (INFU; n = 150)     28.0 (24.0-36.5)     58.0 (48.5-77.2)     .0844       RNP C (INFU; n = 150)     370 (29.2 (24.0-33.5)     28.0 (23.0-35.5)     .841       Rp28 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rp38 (proportion positive)     1/75 (1.33)     0/75 (0)     .1       Rp38 (proportion positive)     5/75 (6.07)     1/75 (1.33)     .209       BIC-D2 (proportion positive)     5/75 (6.07)     1/75 (1.33)     .209       BIC-D2 (proport	RNP A (MFU; n = 150)	78.5 (54.0–129.2)	93.0 (62.8–126.0)	.162
PCNA (MFU; n = 150)     370 (29.2–46.5)     31.0 (24.2–45.0)     .0403       PCNA (proportion positive)     0/75 (0)     0/75 (0)     n/a       RNA Pol III (MFU; n = 150)     37.0 (31.0–46.5)     34.0 (24.8–44.5)     .0694       RNA Pol III (proportion positive)     0/75 (0)     17     f(1.3)     1       Rpp25 (MFU; n = 150)     28.0 (24.0–36.8)     26.0 (22.0–33.0)     .127       Rpp25 (proportion positive)     1/75 (1.3)     0/75 (0)     1       RNP C (INFU; n = 150)     65.0 (53.2–86.5)     58.0 (48.5–77.2)     .0844       RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rpp38 (proportion positive)     0/75 (6.7)     1/76 (1.3)     .209       BIC-D2 (MFU; n = 150)     46.0 (31.0–82.0)     42.0 (32.0–60.2)     .31       Rpp38 1 (proportion positive)     5/75 (6.67)     1/76 (1.33)     .209       BIC-D2 (roportion positive)     1/75 (1.33)     0/75 (0)     1       Pm/Scl (MFU; n = 150)     63.0 (47.8–88.0)     570 (47.8–96.8)     .664       <	RNP A (proportion positive)	3/75 (4.00)	9/75 (12.0)	.130
PCNA (proportion positive)     0/75 (0)     0/75 (0)     0/74 (0)       RNA Pol III (MFU; n = 150)     37.0 (31.0-46.5)     34.0 (24.8-44.5)     .0694       RNA Pol III (proportion positive)     0/75 (0)     1/75 (1.33)     1       Rpp25 (MFU; n = 150)     28.0 (24.0-36.8)     26.0 (22.0-33.0)     .127       Rpp25 (proportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (MFU; n = 150)     65.0 (53.2-86.5)     58.0 (48.5-772)     .08444       RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rpp38 (proportion positive)     29.0 (24.0-33.5)     28.0 (23.0-35.5)     .841       Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rpp38 (proportion positive)     0/75 (0)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     46.0 (31.0-82.0)     42.0 (32.0-60.2)     .31       Rpp38.1 (proportion positive)     1/75 (1.33)     .209     .201       BIC-D2 (MFU; n = 150)     63.0 (47.8-88.0)     57.0 (47.8-86.8)     .664       Pm/Scl (MFU; n = 150)     1.75 (1.33)     .209     .410       Sm-Peptide (M	PCNA (MFU; n = 150)	37.0 (29.2–46.5)	31.0 (24.2–45.0)	.0403
RNA Pol III (MFU; n = 150)     37.0 (31.0–46.5)     34.0 (24.8–44.5)     .0694       RNA Pol III (proportion positive)     0/75 (0)     1/75 (1.33)     1       Rpp25 (MFU; n = 150)     28.0 (24.0–36.8)     26.0 (22.0–33.0)     .127       Rpp25 (proportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (MFU; n = 150)     65.0 (53.2–66.5)     58.0 (48.5–77.2)     .0844       RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rpp38 (MFU; n = 150)     29.0 (24.0–33.5)     28.0 (23.0–35.5)     .841       Rpp38 (proportion positive)     0/75 (0)     0/76 (0)     n/a       Rpp38 (proportion positive)     0/75 (6.67)     1/75 (1.33)     .00       RDC-D2 (proportion positive)     5/75 (6.67)     1/75 (1.33)     .01       BIC-D2 (MFU; n = 150)     63.0 (47.8–88.0)     570 (47.8–96.8)     .664       Pm/Scl (MFU; n = 150)     163.0 (47.8–88.0)     570 (47.8–96.8)     .664       Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     160.0 (15.0–18.5)     16.0 (14.0–18.0)     .176	PCNA (proportion positive)	0/75 (0)	0/75 (0)	n/a
RNA Pol III (proportion positive)     0/75 (0)     1/75 (1.33)     1       Rpp25 (MFU; n = 150)     28.0 (24.0-36.8)     26.0 (22.0-33.0)     .127       Rpp25 (proportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (MFU; n = 150)     65.0 (53.2-86.5)     58.0 (48.5-772)     .0844       RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rpp38 (MFU; n = 150)     29.0 (24.0-33.5)     28.0 (23.0-35.5)     .841       Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rpp38 (proportion positive)     0/75 (0.67)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     46.0 (31.0-82.0)     42.0 (32.0-60.2)     .31       Rpp38-1 (proportion positive)     5/75 (6.67)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     63.0 (47.8-88.0)     90.0 (38.5-73.5)     .184       BIC-D2 (IMFU; n = 150)     63.0 (47.8-88.0)     57.0 (47.8-96.8)     .664       Pm/Scl (proportion positive)     1/75 (1.33)     .1     .1       Sm-Peptide (MFU; n = 150)     16.0 (15.0-18.5)     16.0 (14.0-18.0)     .1       Sm-P	RNA Pol III (MFU; n = 150)	37.0 (31.0–46.5)	34.0 (24.8–44.5)	.0694
Rpp25 (MFU; n = 150)   28.0 (24.0-36.8)   26.0 (22.0-33.0)   .127     Rpp25 (proportion positive)   1/75 (1.33)   0/75 (0)   1     RNP C (MFU; n = 150)   65.0 (53.2-86.5)   58.0 (48.5-772)   .0844     RNP C (proportion positive)   3/75 (4.00)   3/75 (4.00)   1     Rpp38 (MFU; n = 150)   29.0 (24.0-33.5)   28.0 (23.0-35.5)   .841     Rpp38 (proportion positive)   0/75 (0)   0/75 (0)   n/a     Rpp38 (proportion positive)   0/75 (0)   1/75 (1.33)   .209     BIC-D2 (MFU; n = 150)   46.0 (31.0-82.0)   42.0 (32.0-60.2)   .31     Rpp38 (proportion positive)   5/75 (6.67)   1/75 (1.33)   .209     BIC-D2 (MFU; n = 150)   54.0 (41.0-84.0)   49.0 (38.5-73.5)   .184     BIC-D2 (proportion positive)   1/75 (1.33)   0/75 (0)   1     Pm/Scl (MFU; n = 150)   63.0 (47.8-88.0)   57.0 (47.8-96.8)   .664     Pm/Scl (proportion positive)   3/75 (4.00)   4/75 (5.33)   1   .176     Sm-Peptide (MFU; n = 150)   16.0 (15.0-18.5)   16.0 (14.0-18.0)   .176	RNA Pol III (proportion positive)	0/75 (0)	1/75 (1.33)	1
Rpp25 (proportion positive)     1/75 (1.33)     0/75 (0)     1       RNP C (MFU; n = 150)     65.0 (53.2–86.5)     58.0 (48.5–77.2)     .0844       RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rpp38 (MFU; n = 150)     29.0 (24.0–33.5)     28.0 (23.0–35.5)     .841       Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rpp38 (proportion positive)     0/75 (6.7)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     54.0 (41.0–84.0)     49.0 (38.5–73.5)     .841       BIC-D2 (proportion positive)     1/75 (1.33)     .209     .200	Rpp25 (MFU; n = 150)	28.0 (24.0–36.8)	26.0 (22.0–33.0)	.127
RNP C (MFU; n = 150)   65.0 (53.2–86.5)   58.0 (48.5–77.2)   .0844     RNP C (proportion positive)   3/75 (4.00)   3/75 (4.00)   1     Rpp38 (MFU; n = 150)   29.0 (24.0–33.5)   28.0 (23.0–35.5)   .841     Rpp38 (proportion positive)   0/75 (0)   0/75 (0)   n/a     Rpp38.1 (MFU; n = 150)   46.0 (31.0–82.0)   42.0 (32.0–60.2)   .31     Rpp38.1 (proportion positive)   5/75 (6.67)   1/75 (1.33)   .209     BIC-D2 (MFU; n = 150)   54.0 (41.0–84.0)   49.0 (38.5–73.5)   .184     BIC-D2 (proportion positive)   1/75 (1.33)   0/75 (0)   1     Pm/Scl (MFU; n = 150)   63.0 (47.8–88.0)   57.0 (47.8–96.8)   .664     Pm/Scl (MFU; n = 150)   63.0 (47.8–88.0)   57.0 (47.8–96.8)   .664     Pm/Scl (MFU; n = 150)   16.0 (15.0–18.5)   16.0 (14.0–18.0)   .176     Sm-Peptide (MFU; n = 150)   16.0 (15.0–18.5)   16.0 (14.0–18.0)   .176     Sm-Peptide (proportion positive)   0/75 (0)   0/75 (0)   .999     Anti-IgG (MFU; n = 150)   2105.5 (1873.0–2364.0)   2097.0 (1841.0–2422.8)   .999     Anti-IgG (proportion positive)   75/75 (100-1 <t< td=""><td>Rpp25 (proportion positive)</td><td>1/75 (1.33)</td><td>0/75 (0)</td><td>1</td></t<>	Rpp25 (proportion positive)	1/75 (1.33)	0/75 (0)	1
RNP C (proportion positive)     3/75 (4.00)     3/75 (4.00)     1       Rp38 (MFU; n = 150)     29.0 (24.0–33.5)     28.0 (23.0–35.5)     .841       Rp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rp38.1 (MFU; n = 150)     46.0 (31.0–82.0)     42.0 (32.0–60.2)     .31       Rp38.1 (proportion positive)     5/75 (6.67)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     54.0 (41.0–84.0)     49.0 (38.5–73.5)     .184       BIC-D2 (mFU; n = 150)     54.0 (41.0–84.0)     49.0 (38.5–73.5)     .184       BIC-D2 (mFU; n = 150)     63.0 (47.8–88.0)     57.0 (47.8–96.8)     .664       Pm/Scl (MFU; n = 150)     63.0 (47.8–88.0)     57.0 (47.8–96.8)     .664       Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     16.0 (15.0–18.5)     16.0 (14.0–18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0–2364.0)     2097.0 (1841.0–2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     .76/75 (100)	RNP C (MFU; n = 150)	65.0 (53.2–86.5)	58.0 (48.5–77.2)	.0844
Rp38 (MFU; n = 150)   29.0 (24.0-33.5)   28.0 (23.0-35.5)   .841     Rp38 (proportion positive)   0/75 (0)   0/75 (0)   n/a     Rp38.1 (MFU; n = 150)   46.0 (31.0-82.0)   42.0 (32.0-60.2)   .31     Rp38.1 (proportion positive)   5/75 (6.67)   1/75 (1.33)   .209     BIC-D2 (MFU; n = 150)   54.0 (41.0-84.0)   49.0 (38.5-73.5)   .184     BIC-D2 (proportion positive)   1/75 (1.33)   0/75 (0)   1     Pm/Scl (MFU; n = 150)   63.0 (47.8-88.0)   57.0 (47.8-96.8)   .664     Pm/Scl (proportion positive)   3/75 (4.00)   4/75 (5.33)   1     Sm-Peptide (MFU; n = 150)   16.0 (15.0-18.5)   16.0 (14.0-18.0)   .176     Sm-Peptide (proportion positive)   0/75 (0)   0/75 (0)   n/a     Anti-IgG (MFU; n = 150)   2105.5 (1873.0-2364.0)   20970 (1841.0-2422.8)   .999     Anti-IgG (proportion positive)   75/75 (100)   75/75 (100)   n/a     Bio-Flash CIA   Bio-Flash CIA   .716   .716     dsDNA (CU; n = 150)   0.0 (0.0-010.2)   0.0 (0.0-9.85)   .716     dsDNA (proportion positive)   2/75 (2.67)   3/75 (4.00)   1	RNP C (proportion positive)	3/75 (4.00)	3/75 (4.00)	1
Rpp38 (proportion positive)     0/75 (0)     0/75 (0)     n/a       Rpp38-1 (MFU; n = 150)     46.0 (31.0-82.0)     42.0 (32.0-60.2)     .31       Rpp38-1 (proportion positive)     5/75 (6.67)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     54.0 (41.0-84.0)     49.0 (38.5-73.5)     .184       BIC-D2 (proportion positive)     1/75 (1.33)     0/75 (0)     1       Pm/Scl (MFU; n = 150)     63.0 (47.8-88.0)     57.0 (47.8-96.8)     .664       Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     16.0 (15.0-18.5)     16.0 (14.0-18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0-2364.0)     2097.0 (1841.0-2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA	Rpp38 (MFU; n = 150)	29.0 (24.0–33.5)	28.0 (23.0–35.5)	.841
Rp38-1 (MFU; n = 150)   46.0 (31.0–82.0)   42.0 (32.0–60.2)   .31     Rp38-1 (proportion positive)   5/75 (6.67)   1/75 (1.33)   .209     BIC-D2 (MFU; n = 150)   54.0 (41.0–84.0)   49.0 (38.5–73.5)   .184     BIC-D2 (proportion positive)   1/75 (1.33)   0/75 (0)   1     Pm/Scl (MFU; n = 150)   63.0 (47.8–88.0)   57.0 (47.8–96.8)   .664     Pm/Scl (proportion positive)   3/75 (4.00)   4/75 (5.33)   1     Sm-Peptide (MFU; n = 150)   16.0 (15.0–18.5)   16.0 (14.0–18.0)   .176     Sm-Peptide (proportion positive)   0/75 (0)   0/75 (0)   n/a     Anti-IgG (MFU; n = 150)   2105.5 (1873.0–2364.0)   2097.0 (1841.0–2422.8)   .999     Anti-IgG (proportion positive)   75/75 (100)   75/75 (100)   n/a     Bio-Flash CIA   Bio-Flash CIA   .176   .176     MSDNA (proportion positive)   2/75 (2.67)   3/75 (4.00)   .176     MSDNA (proportion positive)   0.0 (0.0–10.2)   0.0 (0.0–9.85)   .716     MSDNA (proportion positive)   2/75 (2.67)   3/75 (4.00)   1	Rpp38 (proportion positive)	0/75 (0)	0/75 (0)	n/a
Rpp38-1 (proportion positive)     5/75 (6.67)     1/75 (1.33)     .209       BIC-D2 (MFU; n = 150)     54.0 (41.0–84.0)     49.0 (38.5–73.5)     .184       BIC-D2 (proportion positive)     1/75 (1.33)     0/75 (0)     1       Pm/Scl (MFU; n = 150)     63.0 (47.8–88.0)     57.0 (47.8–96.8)     .664       Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     16.0 (15.0–18.5)     16.0 (14.0–18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0–2364.0)     2097.0 (1841.0–2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     Bio-Flash CIA	Rpp38-1 (MFU; n = 150)	46.0 (31.0-82.0)	42.0 (32.0-60.2)	.31
BIC-D2 (MFU; n = 150)   54.0 (41.0–84.0)   49.0 (38.5–73.5)   .184     BIC-D2 (proportion positive)   1/75 (1.33)   0/75 (0)   1     Pm/Scl (MFU; n = 150)   63.0 (47.8–88.0)   57.0 (47.8–96.8)   .664     Pm/Scl (proportion positive)   3/75 (4.00)   4/75 (5.33)   1     Sm-Peptide (MFU; n = 150)   16.0 (15.0–18.5)   16.0 (14.0–18.0)   .176     Sm-Peptide (proportion positive)   0/75 (0)   0/75 (0)   n/a     Anti-IgG (MFU; n = 150)   2105.5 (1873.0–2364.0)   2097.0 (1841.0–2422.8)   .999     Anti-IgG (proportion positive)   75/75 (100)   75/75 (100)   n/a     Bio-Flash CIA   Bio-Flash CIA   .176   .176     MSDNA (CU; n = 150)   0.0 (0.0–10.2)   0.0 (0.0–9.85)   .716     MSDNA (proportion positive)   2/75 (2.67)   3/75 (4.00)   1     MPO-ANCA (CIU: n = 150)   0.0 (0.0–0.0)   0.0 (0.0–0.0)   0.0656	Rpp38-1 (proportion positive)	5/75 (6.67)	1/75 (1.33)	.209
BIC-D2 (proportion positive)     1/75 (1.33)     0/75 (0)     1       Pm/Scl (MFU; n = 150)     63.0 (47.8–88.0)     57.0 (47.8–96.8)     .664       Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     16.0 (15.0–18.5)     16.0 (14.0–18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0–2364.0)     2097.0 (1841.0–2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     Bio-Flash CIA	BIC-D2 (MFU; n = 150)	54.0 (41.0-84.0)	49.0 (38.5–73.5)	.184
Pm/Scl (MFU; n = 150)     63.0 (47.8–88.0)     57.0 (47.8–96.8)     .664       Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     16.0 (15.0–18.5)     16.0 (14.0–18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0–2364.0)     2097.0 (1841.0–2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     Bio-Flash CIA     .176       dsDNA (CU; n = 150)     0.0 (0.0–10.2)     0.0 (0.0–9.85)     .716       dsDNA (proportion positive)     2/75 (2.67)     3/75 (4.00)     1       MPO-ANCA (CIU: n = 150)     0.0 (0.0–0.0)     0.0 (0.0–0.0)     0.0656	BIC-D2 (proportion positive)	1/75 (1.33)	0/75 (0)	1
Pm/Scl (proportion positive)     3/75 (4.00)     4/75 (5.33)     1       Sm-Peptide (MFU; n = 150)     16.0 (15.0–18.5)     16.0 (14.0–18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0–2364.0)     2097.0 (1841.0–2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     Bio-Flash CIA	Pm/Scl (MFU; n = 150)	63.0 (47.8–88.0)	57.0 (47.8–96.8)	.664
Sm-Peptide (MFU; n = 150)     16.0 (15.0-18.5)     16.0 (14.0-18.0)     .176       Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0-2364.0)     2097.0 (1841.0-2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     Bio-Flash CIA     .176       dsDNA (CU; n = 150)     0.0 (0.0-10.2)     0.0 (0.0-9.85)     .716       dsDNA (proportion positive)     2/75 (2.67)     3/75 (4.00)     1       MPO-ANCA (CIU: n = 150)     0.0 (0.0-0.0)     0.0 (0.0-0.0)     0.0656	Pm/Scl (proportion positive)	3/75 (4.00)	4/75 (5.33)	1
Sm-Peptide (proportion positive)     0/75 (0)     0/75 (0)     n/a       Anti-IgG (MFU; n = 150)     2105.5 (1873.0–2364.0)     2097.0 (1841.0–2422.8)     .999       Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     800.0 (0.0–10.2)     0.0 (0.0–9.85)     .716       dsDNA (CU; n = 150)     0.0 (0.0–10.2)     3/75 (4.00)     1       MPO-ANCA (CIU: n = 150)     0.0 (0.0–0.0)     0.0 (0.0–0.0)     0.0656	Sm-Peptide (MFU; n = 150)	16.0 (15.0–18.5)	16.0 (14.0–18.0)	.176
Anti-IgG (MFU; n = 150) 2105.5 (1873.0–2364.0) 2097.0 (1841.0–2422.8) .999   Anti-IgG (proportion positive) 75/75 (100) 75/75 (100) n/a   Bio-Flash CIA   dsDNA (CU; n = 150) 0.0 (0.0–10.2) 0.0 (0.0–9.85) .716   dsDNA (proportion positive)   2/75 (2.67) 3/75 (4.00) 1   MPO-ANCA (CIU: n = 150) 0.0 (0.0–0.0) 0.0 (0.0–0.0) 0.0656	Sm-Peptide (proportion positive)	0/75 (0)	0/75 (0)	n/a
Anti-IgG (proportion positive)     75/75 (100)     75/75 (100)     n/a       Bio-Flash CIA     Bio-Flash CIA     0.0 (0.0–9.85)     .716       dsDNA (CU; n = 150)     0.0 (0.0–10.2)     0.0 (0.0–9.85)     .716       dsDNA (proportion positive)     2/75 (2.67)     3/75 (4.00)     1       MPO-ANCA (CIU: n = 150)     0.0 (0.0–0.0)     0.0 (0.0–0.0)     00656	Anti-IgG (MFU; n = 150)	2105.5 (1873.0–2364.0)	2097.0 (1841.0–2422.8)	.999
Bio-Flash CIA     0.0 (0.0–9.85)     .716       dsDNA (CU; n = 150)     2/75 (2.67)     3/75 (4.00)     1       MPO-ANCA (CIU: n = 150)     0.0 (0.0–0.0)     0.0 (0.0–0.0)     0.0656	Anti-IgG (proportion positive)	75/75 (100)	75/75 (100)	n/a
dsDNA (CU; n = 150)   0.0 (0.0–10.2)   0.0 (0.0–9.85)   .716     dsDNA (proportion positive)   2/75 (2.67)   3/75 (4.00)   1     MPO-ANCA (CIU: n = 150)   0.0 (0.0–0.0)   0.0 (0.0–0.0)   0.0656	Under the second s	Bio-Flash CIA	.,	
dsDNA (proportion positive)     2/75 (2.67)     3/75 (4.00)     1       MPO-ANCA (CIU: n = 150)     0.0 (0.0–0.0)     0.0 (0.0–0.0)     0.0656	dsDNA (CU: n = 150)	0.0 (0.0–10.2)	0.0 (0.0–9.85)	716
MPO-ANCA (CIU: n = 150) 0.0 (0.0–0.0) 0.0 (0.0–0.0) 0.0 (0.0–0.0)	dsDNA (proportion positive)	2/75 (2.67)	3/75 (4.00)	1
	MPO-ANCA (CIU; $n = 150$ )	0.0 (0.0–0.0)	0.0 (0.0–0.0)	.00656

# Table 2. Continued

Test <sup>b</sup>	Tuberculosis	Controls	<i>P</i> Value
MPO-ANCA (proportion positive)	1/75 (1.33)	0/75 (0)	1
PR3-ANCA (CIU; n = 150)	3.2 (0.0-4.55)	2.4 (0.0–3.35)	.0759
PR3-ANCA (proportion positive)	1/75 (1.33)	1/75 (1.33)	1
β2GP1-Domain 1 (CIU; n = 149)	4.0 (0.0–5.65)	3.8 (0.0–4.97)	.332
β2GP1-Domain 1 (proportion positive)	1/75 (1.33)	1/74 (1.35)	1
	QUANTA Lie ELISA (AU)		
β2GP1-GP1 lgG (AU; n = 149)	0 (0.0–0.0)	0 (0.0–0.0)	.195
β2GP1-GP1 lgG (proportion positive)	2/75 (2.67)	5/75 (6.67)	.442
ACA IgG (AU; n = 150)	4.56 (2.62-8.0)	3.52 (1.72–5.85)	.0879
ACA IgG (proportion positive)	1/75 (1.33)	3/75 (4.00)	.620
	ALBIA-FIDIS arthritis profile		
RF (MFU; n = 150)	39.1 (16.6–114.0)	43.6 (17.4–138.2)	.457
RF (proportion positive)	42/75 (56.0)	40/75 (53.3)	.870
HCP1 (MFU; n = 148)	10.5 (4.35–21.8)	6.78 (3.38–13.5)	.215
HCP1 (proportion positive)	0/74 (0)	1/74 (1.35)	1
HCP2 (MFU; n = 147)	4.37 (1.56–8.9)	4.37 (2.84–7.64)	.697
HCP2 (proportion positive)	0/74 (0)	0/73 (0)	n/a
VCP1 (MFU; n = 145)	2.76 (1.36–5.73)	3.78 (1.61–7.76)	.124
VCP1 (proportion positive)	1/73 (1.37)	2/72 (2.78)	.620
VCP2 (MFU; n = 142)	6.78 (2.6–14.2)	8.45 (3.51–13.7)	.269
VCP2 (proportion positive)	0/72 (0)	0/70 (0)	n/a
	ALBIA athipical-ANCA		
LAMP2 (MFU; n = 148)	342.5 (173.0–902.0)	653.5 (279.0–1437.0)	.0211
LAMP2 (proportion positive)	18/75 (24.0)	29/73 (39.7)	.520
Elastase (MFU; n = 148)	28.0 (23.0–38.0)	29.0 (23.0–38.0)	.855
Elastase (proportion positive)	0/75 (0)	2/71 (2.74)	.242
p155 (MFU; n = 149)	44.0 (33.5–76.5)	41.0 (32.0–55.8)	.091
p155 (proportion positive)	2/75 (2.67)	1/74 (1.35)	1
	QUANTA Lite M2 EP (MIT3)		
Mitochondria antibodies (AU; n = 150)	7.58 (4.57–12.7)	6.89 (4.86–12.7)	.952
Mitochondria antibodies (proportion positive)	9/75 (12.0)	6/75 (8.00)	.588

Data are presented as No. (%) or median (interquartile range).

Abbreviations: β2GP1, beta 2 glycoprotein 1; ACA, anticardiolipin antibody; ANCA, antineutrophil cytoplasmic antibodies; AU, absorbance unit; BICD2, bicaudal D2; CIU, chemi-iluminescence unit; DFS, dense fine speckled; dsDNA, double-stranded DNA; ELISA, enzyme-linked ummunosorbent assay; HCP, human citrullinated protein; IU, international unit; LAMP, lysosome-associated membrane protein; MFU, mean fluorescence unit; MIT, mitochondrial; MPO, myeloperoxidase; PCNA, proliferating cell nuclear antigen; PR3, proteinase 3; Ribo-P, ribosomal P protein (C22 peptide); RNP, ribonucleoprotein; RF, rheumatoid factor; TRIM, tripartite motif; ScI-70, 70 kDa sclerderma antigen/topisomerase I; SSA/SSB, Sjögren's syndrome antigen A/B; VCP, viral citrullinated protein.

<sup>a</sup>Some patients provided insufficient plasma for all testing requirements. No assumptions or imputations were made in these cases.

<sup>b</sup>Please see the Supplementary Data for a complete list of all antibodies tested, their methods of assessment, and cutoffs for positivity

details). The highest prevalence of auto-antibodies was found for LAMP2 (24.0% in cases, 39.7% in controls), followed by DFS70 (21.3% in cases, 20.0% in controls) and RNP-A (4.0% in cases, 12.0% in controls). No patient tested positive for the following antibodies: HCP2, nucleosome, PCNA, Rpp38, Sm-Peptide, and VCP2.

After Bonferroni correction, no single test was found to be statistically different between groups. Primary analysis using hypothesis testing and visual inspection did not reveal any statistically significant relationship between the diagnosis of tuberculosis and immune profiles. Variable selection using lasso regression also could not identify variables with significant discriminatory power. Random forests and HCA were used as nonparametric methods but failed to identify clusters of patients based on immune profile and tuberculosis diagnosis. PCA found no relationship between the covariates and the outcome of interest. Please see the Supplementary Data for additional details.

#### DISCUSSION

Despite effective antimicrobial therapy, TB remains a significant cause of morbidity and mortality and mortality worldwide. Although TB has been associated with autoimmune manifestations and rheumatological conditions, our data reveal that it is not associated with conventional or novel serological markers of autoimmunity. Our results contradict previous reports [6, 7] and suggest that active TB is not associated with the presence of ANCA, ACA, and Scl-70 positivity. Several studies have linked TB with the development of auto-antibodies. Several mechanisms have been proposed to explain this association, including molecular mimicry. In vitro data suggest homology between species in cell wall glycolipids and DNA [10], bystander activation of CD8+ lymphocytes [11], and TLR agonism [12]. However, conflicting data exist regarding the association between TB and clinical autoimmune disease; our patient population did not have any reported rheumatological conditions. It is of note that our population was tested before the onset of treatment, which could theoretically affect auto-antibody production. It is possible that antimycobacterial treatment increases auto-antibody production by exposing novel antigens, which could explain a higher prevalence of certain markers of auto-immunity in other studies [13].

Our results must be interpreted in the context of the study characteristics. We were unable to follow patients longitudinally to assess for the development of auto-antibodies or auto-immune manifestations. Furthermore, all samples in our study were obtained from passive case finding. As such, it was not possible to determine the duration of disease before seeking medical attention. From epidemiologic studies, those diagnosed passively tend to have more severe disease and a longer duration of symptoms than those detected through active case finding, such as immigrant screening [14]. We also evaluated auto-antibodies in a relatively small patient population with imbalances in baseline characteristics between groups. However, there is no reason a priori to suggest that these imbalances would explain the negative results of our study.

We selected patients with active TB from 4 geographically diverse areas and patients with febrile respiratory conditions as opposed to healthy volunteers. Due to the limited diagnostic capacity in many of the study centers, we were unable to diagnose a microbial pathogen in the control population. We performed the most thorough auto-immune workup in patients with active TB to date with a complete panel of novel serological assays and assessed them in a blinded fashion in a reference laboratory. In conclusion, we did not observe an association between serological markers of auto-immunity and active TB when compared with patients with acute febrile respiratory illnesses.

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**Potential conflicts of interest.** This manuscript was prepared as part of routine work. M.P.C., G.B.L., L.O.P., D.T.B., M.J.F., and M.A.B. have no disclosures to report. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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