## 1 **ONLINE REPOSITORY**

2

# 3 MATERIALS AND METHODS

4

# 5 Human subjects

6	All studies were completed under protocol 11-AR-0223, which was approved by
7	the National Institute of Arthritis and Musculoskeletal and Skin Diseases/National
8	Institute of Diabetes and Digestive and Kidney Diseases Institutional Review Board.
9	Written informed consent and assent was obtained for conduct of research, use of
10	photographic images, and publication of findings.

11

# 12 Genetic analysis

13 Whole human exome sequencing was performed (Otogenetics Corporation) on 14 patient, parents, and unaffected sister peripheral leukocyte DNA using Agilent 51Mb 15 Human Exome V5 (Agilent Technologies) capture and PE100-125 Illumina HiSeq2500 16 (Illumina) sequencing with a 50x average read coverage. A computational pipeline was 17 developed to process the read data and perform tasks such as quality control (QC), 18 variant discovery, annotation, and filtering. Briefly, sequence reads were aligned to 19 human reference genome (GRC Build 37) with Burrows-Wheeler Aligner (BAM). BAM 20 files were then processed to remove duplicate reads, refine alignment indels and

21 recalibrate base quality scores, according to the best practice guideline by the Genome 22 Analysis Toolkit (GATK) from the Broad Institute. UnifiedGenotyper from GATK was 23 used to make joint variant calls across multiple samples, followed by a variant quality 24 score recalibration step by the GATK VQSR tool. Variants were annotated with 25 functional impact and allele frequency in public databases and local datasets. Sex and 26 sample kinship were analyzed to identify potential sample errors and false family 27 relationships (i.e. erroneous maternity or paternity) using KING software. Possible 28 disease-causing mutations were selected and prioritized based on quality score, allele 29 frequency, functional impact, inheritance, and review of literature. While no autosomal 30 recessive mutations were detected, de novo mutations in MYD88, GFPT2, and WFIKKN2 31 were identified. Considering the critical role of MYD88 in the immune response and its relevance to arthritis in animal models<sup>E6-E8</sup> and rheumatoid arthritis,<sup>E10</sup> further efforts 32 33 were focused on MYD88. Presence (or absence) of MYD88 S222R mutation was 34 confirmed by Sanger sequencing (ACGT, Inc.) peripheral leukocyte DNA from all family 35 members, as well as from isolated CD14+ monocyte, EBV-LCL, and cultured dermal 36 fibroblast DNA from patient and mother.

37

# 38 Cell Culture

Human primary dermal fibroblasts were isolated from outgrowth of Dispase
(StemCell Technologies) digested skin biopsies and maintained in DMEM supplemented
with 10% FBS and 100 U/mL Penicillin/Streptomycin (P/S, Gibco). EBV-LCLs were
generated from fresh whole blood and maintained in RPMI 1640 supplemented with 20%

43	FBS and 100 U/mL P/S. THP-1 cells were maintained in RPMI 1640 medium
44	supplemented 10% FBS and 100 U/mL P/S. Both U2932 and SUDHL2 cell lines were
45	maintained in RPMI 1640 RPMI 1640 supplemented with 20% Hyclone FBS (GE
46	Healthcare) and 100 U/mL P/S. All cells listed grown at $37^{\circ}$ C with 5% CO <sub>2</sub> .

## 48 Flow cytometry

49 Peripheral blood from patient and controls were collected in sodium heparin BD 50 Vacutainer tubes and used within 1 hour of collection. For immunophenotyping, red 51 blood cells were lysed with BD Pharm Lyse lysing buffer and washed with PBS. 52 Remaining cells were fixed with 4% paraformaldehyde, then incubated with specific 53 antibodies for 1 hour at 4 °C, and then washed. After exclusion of dead cells using 54 LIVE/DEAD Fixable Red Dead Cell Stain Kit (ThermoFisher Scientific), leukocytes 55 were identified using the following antibodies (BD Biosciences unless otherwise 56 specified): anti-CD3 (SK7), anti-CD4 (SK3), anti-CD8 (SK1), anti-CCR6 (11A9), anti-57 CD19 (SJ25C1), anti-CD20 (2H7), anti-CD56 (B159), anti-HLA-DR (G46-6), anti-CD16 58 (B73.1), anti-CD123 (7G3), anti-CD11c (B-ly6), anti-CD14 (MγP9), anti-CD1c (L161; 59 Biolegend), anti-CD303 (201A; Biolegend), anti-CD203c (NP4D6; Biolegend), and anti-60 CD141 (AD5-14H12; Miltenyi). For phosphorylated-STAT3 analysis, peripheral blood 61 was stained with cell subset-specific antibodies and stimulated with IL-6 50 ng/mL 62 (PeproTech) for 20 minutes at 37°. Red blood cells were then lysed and remaining cells 63 fixed for 10 minutes with BD Phosflow Lyse/Fix Buffer, then permeabilized with BD 64 Phosflow Perm Buffer III. After washes, cells were stained with anti-pSTAT3 (4/P-

STAT3) overnight at 4° C. Cell surface markers and p-STAT3 intracellular staining were
measured via BD LSR-Fortessa flow cytometer and analyzed with FlowJo software
v10.1r5.

68

## 69 Whole blood and dermal fibroblast cytokine/chemokine secretion assays

70 For whole blood cytokine secretion, peripheral blood from patient and controls 71 were collected in sodium heparin BD Vacutainer tubes, diluted 1:2 with RPMI 1640 72 medium (Gibco), and incubated for 22 hours at 37° C within one hour of blood collection. Supernatants were then collected and stored at -80° C. To assess dermal 73 fibroblast cytokine secretion,  $1 \times 10^5$  cells/well of patient and mother fibroblasts were 74 75 seeded into 12-well plates. After resting overnight, cells were washed with PBS and 76 media replaced. Supernatants were then collected 24 hours later and stored at -80° C. 77 Concentrations of supernatant cytokines and chemokines from whole blood and 78 fibroblasts were subsequently measured via multiplex immunoassay using ProcartaPlex 79 Human Th1/Th2 & Chemokine Panel 1 20-plex (Affymetrix eBioscience) per 80 manufacturer's instructions.

81

#### 82 Neutrophil chemotaxis assay

Neutrophil chemotaxis was measured using CytoSelect 96-Well Cell Migration
 Assay 3 µm (Cell Biolabs, Inc.) per manufacturer's instructions. Briefly, patient and
 mother fibroblast conditioned supernatants were generated by seeding 2.5x10<sup>5</sup> cells/well

86	into 6 well plates and allowing them to rest at 37° C overnight. The next day, media was
87	removed and cells washed with PBS. 1 mL of FBS-free DMEM was then placed into
88	wells and incubated at $37^{\circ}$ for 24 hours. Resultant supernatants were then collected and
89	stored at -80° C. On day of assay, thawed supernatants were placed into feeder wells in
90	triplicate. Freshly elutriated healthy donor neutrophils were placed into upper chambers
91	at density of $5 \times 10^5$ /well after propidium iodide exclusion viability testing. After 4 hours,
92	migratory cells in feeder wells were lysed, CyQuant GR Fluorescent Dye added, and
93	quantified using a fluorescence plate reader at 480nm/520nm.

## 95 Molecular dynamics studies

96 Four replicate 1.5 microsecond molecular dynamic calculations of the wild type MyD88 TIR domain (PDB code: 4DOM, Ref. 79) or S222R mutant was performed using 97 98 Gromacs with the Charmm36 forcefield, explicit solvent and a 1fs time step. Using 99 Visual Molecular Dynamics (VMD), 500 snapshots of the last 500 ns of each simulation 100 were superposed based on the backbone atoms of the central beta sheet, and these 101 superposed structures were clustered in 5 groups based only on the position of the alpha 102 C-helix (residues 243-255) backbone atoms using an rmsd distance function with 1.5 Å 103 cutoff. For cluster analysis of the alpha C helix, all four replicates were analyzed 104 separately. In these analyses, the most populated clusters contain >60% of all clustered 105 structures.

106

# 107 THP-1 Cell lines, retroviral transduction, and NF-κB reporter system

108	THP1-Dual KO-MyD Cells (Invivogen), where MyD88 gene expression is
109	knocked-out via nuclease technology, was retroviral transduced sequentially with N-
110	terminal MyD88-AU1, then C-terminal MyD88-GFP constructs. <sup>4</sup> Vectors were packaged
111	into vesicular stomatitis virus envelope (VSV-G) containing retroviral particles (Alstem)
112	and THP-1 cells transduced overnight at MOI=5. Successfully transduced cells were
113	isolated via Ly-2 magnetic bead selection (Miltenyi) and purity of both MyD88-AU1 and
114	MyD88-GFP cells were verified via flow cytometry (Ly-2) and immunoblot for MyD88.
115	THP-1 clones produced for this study were MyD88 KO clones re-expressing equal
116	amounts of WT MyD88 with two different tags (WT-MyD88-AU1 and WT-MyD88-
117	GFP), WT MyD88 and S222R MyD88 with AU1 and GFP tags, respectively (WT-
118	MyD88-AU1 and S222R-MyD88-GFP), WT MyD88 and S222R MyD88 with the
119	alternative tags (S222R-MyD88-AU1 and WT-MyD88-GFP), and S222R MyD88 with
120	two different tags (S222R-MyD88-AU1 and S222R-MyD88-GFP). THP1-Dual KO-MyD
121	Cells used contain stable integration of secreted embryonic alkaline phosphatase (SEAP)
122	reporter gene containing IFN- $\beta$ minimal promoter fused to five copies of the NF- $\kappa B$
123	consensus response element and three copies of the c-Rel binding site. Baseline
124	(unstimulated) SEAP over a 24-hour period was detected via enzyme-substrate driven
125	colorimetry per manufacturer's instructions (Invivogen).

# **Proximity ligation assay (PLA)**

128 THP-1 cells were attached to coverslips with phorbol 12-myristate 13-acetate
129 (PMA, 10 ng/mL) for 24 hours and then allowed to rest in fresh complete RPMI media
130 for at least 72 hours. PLA was performed on THP-1 double transduced clones (above)

131	using Duolink In Situ Orange Mouse/Rabbit kit (Sigma) per manufacturer's instructions.
132	Briefly, cells were washed with HBSS, fixed with 4% paraformaldehyde (Electron
133	Microscopy Sciences) in PBS for 15 minutes, and subsequently permeabilized/washed
134	with 0.04% saponin (Calbiochem). After 1 hour blocking in 1% BSA (Sigma), 2% horse
135	serum (Abcam), 3% donkey goat serum (Abcam), 0.04% saponin, and 0.01% sodium
136	azide (Sigma), cells were incubated for 16 hours at 4° C with rabbit anti-GFP antibody
137	(Abcam, ab290) and mouse anti-AU1 (Biolegend) both at 1:1000 in blocking solution.
138	Next, cells were washed with 0.04% saponin in PBS and incubated with anti-rabbit PLUS
139	and anti-mouse MINUS for 1 hour. Then, cells were subject to ligation for 30 minutes
140	and then amplification for 100 minutes. Cells were mounted with the kit's DAPI-
141	containing medium. Per cell clone, confocal images were taken from 4 randomly selected
142	fields using 63x objective, then maximum projection images were produced from 14 z-
143	slices. Identical imaging settings were used for all images. PLA events were quantitated
144	using CellProfiler v2.2 Spot Detection pipeline (https://github.com/tischi/cellprofiler-
145	practical-NeuBIAS-Lisbon-2017/blob/master/practical-handout.md) from maximum
146	projection images collected. For each experiment of each clone, at least 65 cells were
147	counted in each of 4 field-of-views, or at least 260 cells for all 4 fields-of-view total.
148	

# 149 Cell lysis, antibodies, and immunoblotting

Cells were lysed in buffer containing 20 mM Tris-Cl pH 7.5, 100 mM NaCl, 10
mM EDTA, 1% triton x-100, protease inhibitor cocktail (Roche), 0.04% NaN<sub>3</sub>, 0.5 mM
PMSF, 1 mM Na<sub>3</sub>VO<sub>4</sub>, 10 mM NaF, and 10 mM sodium pyrophosphate dibasic. After
Bradford protein concentration measurement and normalization of protein amounts,

154 samples were added to SDS loading buffer and heated to 95° C for 3 minutes. After 155 PAGE (4-20% Criterion TGX, Bio-Rad), proteins were transferred to PVDF membranes 156 (Bio-Rad), blocked with 5% BSA, and incubated overnight with primary antibodies at  $4^{\circ}$ 157 C. Horseradish peroxidase (HRP) conjugated anti-rabbit IgG or anti-mouse IgG (R & D Systems) secondary antibodies were used with Pierce ECL or West Pico (Thermo 158 159 Scientific) to detect protein expression and visualized with Amersham Hyperfilm (GE) or 160 Bio-Rad ChemiDoc Imaging System. Primary antibodies used: mouse anti-vinculin 161 (V284, Millipore), mouse anti-GAPDH (Santa Cruz Biotech, clone 6C5, sc-32233), 162 mouse anti-beta actin (Abcam, ab8226), rabbit, anti-beta tubulin (Abcam, ab6046), rabbit 163 anti-MYD88 (D80F5), rabbit anti-A20/TNFAIP3 (D13H3), rabbit anti-TIRAP (Abcam, ab17218), and rabbit anti-NF-KB p65 (D14E12) (all from Cell Signaling Technology 164 165 unless otherwise noted). Quantification of immunoblots are densitometric values performed using ImageJ. 166

167

# 168 SUDHL2, U2932, and EBV B lymphoblastoid (EBV-LCL) p-STAT3 studies

169 SUDHL2, U2932, and EBV-LCLs used in this study were maintained at cell 170 density of 0.8-1x10<sup>6</sup> cells/mL. Media changes for EBV B lymphoblastoids was performed 171 by removing 50% of media and replacing it with an equal amount of fresh media every 3 172 days. Supernatant testing for cytokines in all cases was performed immediately before 173 media changes. IRAK4 inhibition of EBV-LCLs was accomplished using 200 nM IRAK4 174 inhibitor AS2444697 (Sigma) for 16 hours, which had no effect on viability as 175 determined by propidium iodide exclusion.

176	For conditioned-media P-STAT3-induction experiments, U2932 were pre-treated
177	with their own growth media containing either nothing, human serum IgG (Sigma) 200
178	ng/mL, or tocilizumab 200 ng/mL (TCZ; Actemra, Genentech) for 2 hours. Next, cells
179	were centrifuged and resuspended in their own warmed media (U2932-conditoned) or
180	SUDHL2-conditioned media also containing nothing, human IgG, or TCZ. After 2 hours,
181	cells were lysed for protein and probed for loading control GAPDH, STAT3 (Cell
182	Signaling Technology, clone 124H6, #9139), and P-STAT3 (Y705) (Cell Signaling
183	Technology, clone D3A7, #9145). Similarly, unrelated healthy control EBV-LCLs were
184	pre-treated with their own growth media containing either nothing, human serum IgG 200
185	ng/mL, or TCZ 200 ng/mL for 2 hours. Next, cells were centrifuged and resuspended in
186	either its own warmed media, mother's EBV-LCL conditioned media, or patient's EBV-
187	LCL conditioned media also containing nothing, human IgG 200 ng/mL, or TCZ 200
188	ng/mL. After 2 hours, cells were lysed for protein and probed for loading control
189	GAPDH, STAT3, and P-STAT3. For all STAT3 immunoblots, quantification of p-
190	STAT3/STAT3 was calculated by dividing GAPDH-normalized p-STAT3 from one gel
191	by GAPDH-normalized STAT3 from another gel. Protein levels were determined by
192	densitometry using ImageJ.
193	

# 194 **RNA isolation, cDNA synthesis, and gene expression analysis**

- 195 In all cases, total RNA was isolated via phenol-chloroform extraction (Life
- 196 Technologies), and purity and quantity was assessed by NanoDrop 8000
- 197 Spectrophotometer (ThermoFisher Scientific). cDNA was produced via reverse
- 198 transcription of 1000 ng of RNA using iScript cDNA Synthesis Kit (Bio-Rad). qPCR was

199 performed on QuantStudio 6 Plex (Applied Biosystems) using 40 ng cDNA template, 200 oligonucleotide primers, and SsoFast EvaGreen Supermix (Bio-Rad). For qPCR, gene 201 expression relative to the housekeeping genes PPIA and HPRT1 was calculated using 202 comparative Ct method. Oligonucleotide primer sequences are available upon request. 203 NanoString gene expression analysis was performed on total RNA from isolated 204 peripheral monocytes via both CD14 positive and negative selection, and cultured dermal 205 fibroblasts, using nCounter Human Inflammation v2 pre-built CodeSet (NanoString 206 Technologies) per manufacturer's instructions. Briefly, 200 ng total RNA was hybridized 207 with Capture and Reporter probes in thermocycler at 65° C for 24 hours. Samples were 208 then loaded onto nCounter Cartridge using nCounter Prep Station and RNA counted by 209 the Digital Analyzer. After quality control checks, normalized RNA counts were 210 generated by negative control subtraction and geometric mean of housekeeping genes 211 TUBB, PGK1, GUSB, HPRT1, CLTC, and GAPDH using nSolver Analysis Software 212 v2.5. Genes were considered not expressed if normalized RNA counts were less than 213 twice the standard deviation of the negative control counts in both patient and controls.

214

# 215 siRNA-mediated protein knockdown

Protein knockdown was performed using Amaxa Nucleofector II with Human Dermal Fibroblast Nucleofector Kit (Lonza) per manufacturer's protocol. Briefly, after cell dissociation using Accutase (Life Technologies),  $6-7x10^5$  patient or mother dermal fibroblasts were resuspended in 100 µL Human Dermal Fibroblast Nucleofector Solution, siRNA added, nucleofected using program U-023, and then divided into 3 wells of a 6-

221	well plate containing pre	-warmed DMEM	supplemented	with	10%	FBS.	After	80 hou
	wen place containing pre	marinea Disillini	Supprementeu	** 1011	10/0	I DD.	1 11001	00 110 41

- 222 cells were lysed for protein and RNA analysis. siRNA (Ambion) and final concentrations
- 223 used are as follows: MYD88 (s9138), 30 nM; TNFAIP3 (s14260), 1000 nM; RELA
- 224 (s11914), 1000 nM; TIRAP (s195607), 1000 nM; and Negative Control (4390843), 1000
- 225 nM. Percent knockdown compared to negative control siRNA was calculated by
- 226 densitometry of patient fibroblast protein expression using ImageJ (NIH).

## 228 Statistical analysis

229	GraphPad Prism 6 software was used for all statistical calculations. Statistical
230	significance was determined using unpaired Student's t test. Differences with p-values <
231	0.05 (*), < 0.01 (**), <0.001 (***), and <0.0001 (****) were considered significant.

232

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265	<b>TABLE E1.</b> Summary of patient clinical laboratory values and peripheral leukocyte
266	immunophenotyping. Subject laboratory values over span of 3 years given as a range.
267	Reference range defined as range of normal values according to National Institutes of
268	Health Clinical Center Department of Laboratory Medicine. Immunophenotyping data
269	presented as mean (range of 3 values over span of 27 months).
270	
271	FIG E1. Genotype of pedigree and patient CD14+ monocytes, dermal fibroblasts, and
272	EBV-LCLs. A, Sanger sequencing chromatograms of peripheral leukocyte DNA. P,
273	patient; M, mother; F, father; S, sister. B, Sanger sequencing chromatograms
274	demonstrating the presence of c.666T>G mutation in patient CD14+ monocytes, dermal
275	fibroblasts, and EBV B lymphoblastoids.
276	
277	FIG E2. Immunophenotyping of peripheral blood dendritic cells. CD1c (BDCA-1),
278	CD303 (BDCA-2), CD141 (BDCA-3), and CD203c surface expression for
279	CD123+CD11c- (Q1), CD123+CD11c+ (Q2), and CD123-CD11c+ (Q3) dendritic cells.
280	Positive control CD203c+ cells were gated from HLA-DR+ myeloid fraction of
281	peripheral leukocytes.
282	
283	FIG E3. Molecular dynamics modeling and effect of S222R on MyD88 self-association.
284	A, Molecular dynamics cluster analysis of wild type (left) and S222R (right) MyD88 TIR
285	domains. Images show superposition of the representative structure for the most
286	populated cluster for each of 4 independent replicate simulations. <b>B</b> , Representative

287	immunoblot showing relative expression of MyD88-AU1 and MyD88-GFP in THP-1
288	transductants, with vinculin as a loading control. C, NF-KB activity measured by secreted
289	alkaline phosphatase activity as reporter gene. Activity is relative to cells containing WT-
290	MyD88-AU1 & WT-MyD88-GFP. Each data point represents the average of the median
291	of 3 replicates from 3 independent experiments. <b>D</b> , Representative confocal images of
292	proximity ligation assay (PLA). Image 1, MyD88-KO; 2, WT-MyD88-AU1 and WT-
293	MyD88-GFP; 3, WT-MyD88-AU1 and S222R-MyD88-GFP; 4, S222R-MyD88-AU1
294	and WT-MyD88-GFP; and 5, S222R-MyD88-AU1 and S222R-MyD88-GFP. Blue,
295	DAPI and red, PLA event using anti-AU1 and anti-GFP antibodies. E, Average PLA
296	events per cell from 3 independent experiments. Error bars represent $\pm$ SD. *, p<0.05; **,
297	p<0.01; ***, p<0.001.

CM DOO

298

299 FIG E4. Dermal fibroblast neutrophil-attracting chemokine secretion and function. A,

300 unstimulated patient and control fibroblast secretion of CXCL1 and IL-8 over 24 hours.

301 **B**, unrelated health donor neutrophil chemotaxis over 4 hours in response to patient and

302 mother fibroblast-conditioned media. P, patient; M, mother. RLU, relative light units. For

303 A and **B**, each data point represents the median of 3 replicates, with results from 3

304 independent experiments (n=3) shown. Error bars represent ± SD. \*, p<0.05; \*\*\*\*,

305 p<0.0001.

306

FIG E5. SUDHL2 and patient EBV-LCL IL-6 and IL-8 expression, and STAT3 307

308 phosphorylation. A, Chemokine/cytokine gene and protein expression from U2932 and

309 SUDHL2 cell lines. B, Chemokine/cytokine protein and gene expression from EBV-

- 310 LCLs, without (Control) and with AS2444697 (200 nM for 16 hours) as indicated. P,
- 311 Patient; M, mother; HC, unrelated healthy control. C, Levels of P-STAT3 and total
- 312 STAT3 in SUDHL2 and U2932 cells. Representative immunoblot (left) with
- 313 quantification (right), from 4 independent experiments. Due to marked overexpression of
- total STAT3 in SUDHL2 cells, blot was run using 1:10 dilution of SUDHL2 protein
- 315 lysate. **D**, Levels of P-STAT3 and total STAT3 in EBV-LCLs from patient (P) and
- 316 mother (M). **E**, STAT3 phosphorylation in U2932 cells in response to 2 hour incubation
- 317 with conditioned media from SUDHL2 or U2932 cells. Conditioned media was used
- alone, or after human IgG (IgG) or tocilizumab (TCZ; 200 ng/mL) pre-treatment.
- 319 Relative STAT3 phosphorylation (P-STAT3) was determined as for **D**. **F**, STAT3
- 320 phosphorylation in EBV-LCLs from healthy control (HC) in response to conditioned
- 321 media from HC, mother (M), or patient (P). Conditioned media was used alone or after
- 322 IgG or TCZ pre-treatment, and relative STAT3 phosphorylation determined as described
- 323 in **E**. For **D**, **E**, and **F**, GAPDH used as a loading control. Error bars represent  $\pm$  SD. \*,
- 324 p<0.05; \*\*, p<0.01; \*\*\*, p<0.001.

TABLE E1. Summary of subject's laboratory values and peripheral leukocyte immunophenotyping

Total Leukeyre Count         605.725         398.104 x10 <sup>3</sup> nL           Neutrophil %         53.87.3         347.11%           Symphozyte %         78.10.2         4.7.12.5%           Moncyte %         78.10.2         4.7.12.5%           Eusephils         105.2         0.7.5.8%           Eusephils         0.1.0.5         0.1.1.2%           Eyrthrocyte Sedimentation Rate (ESR)         5.13         0.42 mmhr           Creactive Protein (CRP)         1.107.00         0.4.99 mgL           Otacocalian         Negative (CRP)         1.13.8.201.6         7.3.3.8.5 grint.           Netclar Anti-Bodies (ANA)         Negative (Negative (Negative (Negative < 20 U)         Negative (Negative < 20 U           Semm IgG1gMIgA         128.473.5         619.874/20.39/120-235         716.1711/15.188/47.249 mg/al.           Semm IgG1gMIgA         128.473.5         617.474/20.39/120-235         716.1711/15.188/47.249 mg/al.           Lef Subclassex. IgG1/IgG2/IgG3/IgG4         230.7864/20.39/120-235         716.1711/15.188/47.249 mg/al.           Lef Subclassex. IgG1/IgG2/IgG3/IgG4         230.7864/20.39/120-235         716.1711/15.188/47.249 mg/al.           Lef Subclassex. IgG1/IgG2/IgG3/IgG4         230.7864/20.39/120-235         716.1711/15.188/47.249 mg/al.           Lef Subclassex. IgG1/IgG2/IgG3/IgG4         230.786	Laboratory Test	Subject's Value Range	Reference Range
Neurophil %         Sign 57,3         34-71,1%         Management           Lymphogye %         30,53,63         19,34,17%           Monacyte %         78,10,2         47,12,5%           Easingphils         10-2,9         0,75,8%           Buoophils         0,10,5         0,11,2%           Erythrocyte Sedimentation Rate (ESR)         5,13         0,42 mm/hr           Creactive Protein (CRP)         1,10,7,00         0,4.99 mgl,           Osteocalcin         113,8,201,6         7,3 - 38,5 mg/ml,           Anti-Skaz Anti-Jo-J, Anti-Ska, Anti-Ska, Anti-Ska, Anti-Ska, Anti-Ska, Anti-Ska, Anti-Jo-J, Anti-Schan, Anti-Jo-J, Anti-Schan, Anti-Jo-J, Anti-Schan, Anti-Ska, A	Total Leukocyte Count	6.05-7.25	$3.98-10.04 \times 10^3/\mu L$
Tymphocyce %         30.5.36.3         19.3.51.7%           Murocyte %         78.10.2         47.12.5%           Eosinophils         0.1-0.5         0.1-1.2%           Eusphils         0.1-0.5         0.1-1.2%           Everythrocyte Sedimentation Rate (ESR)         5.13         0.42 mm/hr           C-reactive Protein (CRP)         1.10-7.00         0.4.99 mgl.           Anti-EMA Screen (Anti-RNP, Anti-Sm, Anti-SS-A,         Negative         Negative (20 EU           Anti-EMA Screen (Anti-RNP, Anti-Sm, Anti-SS-A,         Negative (20 U         Screen (20 CU           Anti-Histone / Anti-Scl-7.0)         Negative (Negative (21 U/Negative < 30 U	Neutrophil %	53.8-57.3	34-71.1%
Momographic         7.8-10.2         4.7-12.5%           Examphils         10-2.9         0.7-5-8%           Easinghils         0.1-0.5         0.1-1.2%           Creactive Fortein (CRP)         1.10-700         0.4-99 mgL           Oscocalcin         1.13.8-201.6         7.3 - 38.5 ng/mL           Anti-Nuclear Antibodies (ANA)         Negative         Negative <0.9 EU	Lymphocyte %	30.5-36.3	19.3-51.7%
Examphils         1.0-2.9         0.7-8.8%           Basephils         0.1-0.5         0.1-1.2%           Erythrocyte Sedimentation Rate (ESR)         5.13         0.42 mm/hr           Creactive Protein (CRP)         1.10-7.00         0.4.9 mg/L           Osteocalicin         113.8-201.6         7.3 - 38.5 ng/mL           Negative C         Negative C         0.9 EU           Anti-Non-Cerent (Anir, RVP, Anit-Sm, Anit-SS-A, Negative C         Negative C         Negative C           Anti-Histon (Anit-SDA)         Negative / Negative C         Negative C         0.10           Anti-Histon (Anit-SDA)         Negative / Negative C         Negative C         0.10           Seram (EgG/EgM/EgA)         128.4/33.5         90-180/10-40 mg/dL         0.10           Seram (EgG/EgM/EgA)         169/874/20-39/120-235         716-1711/15-18847-249 mg/dL         128/263/           IgG Subclasses, IgG/IgG/Ed/EgG/EgG/EgG4         367/140/27/3         299-934/82.516/20-103/20.7         121.7 mg/dL           Isobemagglutinins, anti-Avanti-B         Positive Positive         n/a         121.7 mg/dL         20.4           KG/Ed/EgG Ad         29.4         Reactive 2.5 AU/mL         Nati-Buble 2.5 AU/mL         Nati-Buble 2.5 AU/mL           Anti-Rubella EgG, Random         Negative C         Negative C	Monocyte %	7.8-10.2	4.7-12.5%
Rasephils0.1-0.50.1-1.2%Erythrocyte Sedimentation Rate (ESR)5.130.42 mm/hrCreactive Protein (CRP)1.10-7.000.429 mg/LOsteocalchi1.13.8-201.67.3-38.5 mg/mLAnti-SNA Screen (Anti-RNP, Anti-Sn, Anti-SS, Anti-So, Anti-So-1, Anti-So-1, Anti-SC-70)NegativeNegative Anti-SNE, Anti-Go-1, Anti-SC-70)Negative / NegativeNegative Negative <20 EU	Eosinophils	1.0-2.9	0.7-5.8%
Erg/Incycle Sedimentation Rate (ESR)         5-13         0-42 mu/hr           Creactive Protein (GRP)         1.10-7.00         0-4.99 mg/L           Osteocalcin         113.8-201.6         7.3 - 38.5 ng/mL           Anti-Nuclear Antibodies (ANA)         Negative         Negative < 0.9 EU	Basophils	0.1-0.5	0.1-1.2%
$ \begin{array}{c} Creative Protein (CRP) \\ Osteocalcin \\ Osteocalcin \\ Anti-Nackear Antibodies (AVA) \\ Anti-Sha Screen (ATA) \\ Anti-Sta $	Erythrocyte Sedimentation Rate (ESR)	5-13	0-42 mm/hr
Oxteocalcin113.8-201.6 $7.3 - 38.5 \text{ ng/mL}$ Anti-Kucher Antibodies (ANA)NegativeNegative Anti-ENA Screen (Anti-RNP, Anti-Sm, Anti-SS-A,NegativeNegative Anti-Histone Anti-Anti-Anti-Sd-70)NegativeNegative Anti-Histone Anti-Anti-Anti-Sch70)Negative / NegativeNegative Anti-Histone Anti-Anti-Cyclic Citrullinated PeptideNegative / NegativeNegative Serum C3/C4128.4/33.590-180/10-40 mg/dLSerum C3/C4128.4/33.590-180/10-40 mg/dLGo Labclasses, IgG1/IgG2/IgG3/IgG4367/140/273289-9348/251620-103.20.7-Isohemacglutiniss, anti-Anti-BPositive/PositiveNcBeWCA-IgG1gMtENAPositive/PositiveNcCM VAb IgG1gM29.4Reactive > 10 U/LAnti-Rubela IgG, RandomNegativeNegativeAnti-Rubela IgG, Random0.14 (NegativeNegativeAnti-Rubela IgG, Random0.14 (Negative)Positive > 0.01 U/mLAnti-Rubela IgG, Random0.14 (Negative)Positive > 0.01 U/mL <td>C-reactive Protein (CRP)</td> <td>1.10-7.00</td> <td>0-4.99 mg/L</td>	C-reactive Protein (CRP)	1.10-7.00	0-4.99 mg/L
Anti-Nuclear Antibodies (ANA)NegativeNegative Negative Negative 0.9 EUAnti-SS-B, Anti-Jo-1, Anti-Scl-70)Negative / Negative Negative 10 / Negative 20 EUAnti-Histome / Anti-dsDNANegative / NegativeNegative Negative 10 / Negative 30 URheumatoid Factor / Anti-Cyclic Citrullinated PeptideNegative / NegativeNegative Negative 10 / Negative 20 USerum IgG/IgM/IgA19-874/20.39/120-23590-180/10-40 mg/dL128.4/33.590-180/10-40 mg/dLIgG Sabclasses, IgG/IgG2/IgG3/IgG41367/140/27/3289-93/482.516/20-103.2/0.7-121.7 mg/dLIgG Sabclasses, IgG/IgG2/IgG3/IgG4367/140/27/3121.7 mg/dLRebWCA-IgG/IgM/EBNANegative / Negative Negative Negative Negative Anti-Kubella IgG, RandomNegative Negative Negative <2.5 AU/mL	Osteocalcin	113.8-201.6	7.3 – 38.5 ng/mL
Anti-EMA Screen (Anti-RNP, Anti-SR-A, Anti-SR-A, Anti-Se-I, Anti-SR-A, anti-Se-I, Anti-Alge (JgM/IgA Science, IgG) (JgC) (JgA/GA Science, IgG) (JgC) (JgC) (JgC) (JgA/GA Science, IgG) (JgC)	Anti-Nuclear Antibodies (ANA)	Negative	Negative $< 0.9$ EU
Anti-SS-B, Anti-Jo-1, Anti-Scl-70)Negative / NegativeNegative < 1 U / Negative < 30 URheumatoid Factor / Anti-dsDNANegative / NegativeNegative < 1 U / Negative < 30 U	Anti-ENA Screen (Anti-RNP, Anti-Sm, Anti-SS-A,	Negative	Negative < 20 EU
Anti-Histome / Anti-dsDNANegative / NegativeNegative < 1 U / Negative < 30 URheumatoid Factor / Anti-Cyclic Citrullinated PeptideNegative / NegativeNegative < 15 U / Negative <20 U	Anti-SS-B, Anti-Jo-1, Anti-Scl-70)		
Rheumatoid Factor / Anti-Cyclic Citrullinated Peptide         Negative / Negative         Negative          <	Anti-Histone / Anti-dsDNA	Negative / Negative	Negative $< 1 \text{ U} / \text{Negative} < 30 \text{ U}$
Rheumatoid         Pactive / Negative			
Serum IG3/C4         128.4/33.5         90-180/10-40 mg/dL           JgG Subclasses, IgG1/IgG2/IgG3/IgG4         169-874/20.39/120-235         716-171/11/5-188/47-249 mg/dL           JgG Subclasses, IgG1/IgG2/IgG3/IgG4         367/140/27/3         289-934/82-516/20-103.2/0.7- 121.7 mg/dL           Isohemagglutinins, anti-A/anti-B         Positive/Positive         n/a           EBVCA-IgG/IgMEBNA         Negative/Negative/Negative         Negative <18/-236/<18	Rheumatoid Factor / Anti-Cyclic Citrullinated Peptide	Negative / Negative	Negative <15 U / Negative <20 U
Serum IgG1gM/IgA         619-874/20-39/120-235         716-1711/15-1884/7-249 mg/dL           IgG Subclasses, IgG1/IgG2/IgG3/IgG4         367/140/27/3         289-934/82-516/20-103.2/0.7- 121.7 mg/dL           Isobenagglutinins, anti-A/anti-B         Positive/Positive         Negative         18/2           EWCA-IgG1gM/EBNA         Negative/Negative         Negative < 18 / <36 / <18	Serum C3/C4	128.4/33.5	90-180/10-40 mg/dL
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	Serum IgG/IgM/IgA	619-874/20-39/120-235	716-1711/15-188/47-249 mg/dL
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	IgG Subclasses, IgG1/IgG2/IgG3/IgG4	367/140/27/3	289-934/82-516/20-103.2/0.7-
Isohemagglatinins, anti-A/anti-BPositive Positiven'a $EBVCA-IgG/IgM/EBNA$ Negative/Negative/NegativeNegative < 18 / $<36$ / <18			121.7 mg/dL
<i>EBVCA-IgG/IgMZENA</i> Negative/NegativeNegative < 18 / <36 / <18 <i>CMV &amp; b IgG/RM</i> 2.30/NegativePositive > 0.70 U/mL <i>Anti-Rubella IgG, Random</i> 29.4Reactive > 10 IU/L <i>Mumps Ab IgG, Random</i> NegativeNegative Negative <	Isohemagglutinins, anti-A/anti-B	Positive/Positive	n/a
CMV Ab $lgG/lgM$ 2.30/Negative         Positive > 0.70 U/mL           Anti-Rubella $lgG$ , Random         29.4         Reactive > 10 IU/L           Mumps Ab $lgG$ , Random         Negative         Negative < 0.8 AI	EBVCA-IgG/IgM/EBNA	Negative/Negative/Negative	Negative < 18 / <36 / <18
Anti-Rubella IgG, Random29.4Reactive > 10 IU/LMumps Ab IgG, RandomNegativeNegative Negative > 0.01 IU/mLAnti-Tetamis IgG, Random0.14 (Negative)Positive > 0.01 IU/mLNegative > 0.01 IU/mLNegative > 0.01 IU/mLNegative > 0.01 IU/mLAnti-Tetamis IgG, gost-re-vaccinationNegativeNegative N/aNegative N/aAnti-Varicella-Zoster Virus IgG, post-re-vaccination> 4000Positive > 165 IndexNegative > 165 IndexPositive anti-Pneumococcal Ab serotypes, Random1, 22Fn/aN/aNegative anti-Pneumococcal Ab serotypes, Random1, 22Fn/aN/aCD3 (% lymphocytes)73.5% (65.2-80.3)72.9% (69.6-70.3)CD4 (% CD3+)CD4 (% CD3+)51.6% (37.8-60.2)57.1% (40-72.3)CD9 (% CD3+)11.2 (9.94+12.6)11.7% (6.97-19.5)CD20+CD19+IgD-CD27+ Memory B Cells (%4.1% (2.41-5.15)23.3% (22.7-23.8)CD19+CD20-CD27+CD38+ Plasmablasts (%2.34% (1.64-2.86)40.7% (23.1-58.7)CD19+CD20-CD27+CD38+ Plasmablasts (%2.34% (1.64-2.86)40.7% (23.1-58.7)CD19+CD20-B Cells)CD14+CD16+ Monocytes (% total monocytes)0.0022% (0.0038-0.057)4.93% (2.61-8.66)CD14+CD16+ Monocytes (% total monocytes)0.0122% (0.0096-0.015)6.1% (3.7-85.1)2.7% (2.7-23.5)CD123+CD11-P Isparcenotion Colors)4.1% (8.69-5	CMV Ab IgG/IgM	2.30/Negative	Positive $> 0.70 \text{ U/mL}$
Mumps Ab IgG, Random         Negative         Negative          Negative	Anti-Rubella IgG, Random	29.4	Reactive $> 10 \text{ IU/L}$
Anti-Rubeola IgG, Random       Negative       Negative        Negative	Mumps Ab IgG, Random	Negative	Negative < 0.8 AI
Anti-Diphiheria Ab, Kandom       > 1.00       Positive > 0.01 IU/mL         Anti-Leamophilus Influenza Ab, Random       0.14 (Negative)       Positive > 0.15 mg/L         Anti-Haemophilus Influenza Ab, Random       0.14 (Negative)       Positive > 0.01 IU/mL         Anti-Haemophilus Influenza Ab, Random       0.14 (Negative)       Positive > 0.01 IU/mL         Anti-Varicella-Zoster Virus IgG, post-re-vaccination       Negative       n/a         Anti-Varicella-Zoster Virus IgG, post-re-vaccination       Negative       Negative         Positive anti-Pneumococcal Ab serotypes, Random       Negative       n/a         Negative anti-Pneumococcal Ab serotypes, Random       1, 22F       n/a         Peripheral leukocyte immunophenotyping       2, 3, 4, 5, 8, 9N, 12F, 14, 17F, n/a       n/a         CD3 (% Lymphocytes)       73.5% (65.2-80.3)       72.9% (69.6-70.3)         CD4 (% CD3+)       51.6% (37.8-60.2)       57.1% (40-72.3)         CD9 (% Lymphocytes)       11.2 (9.94-12.6)       11.7% (6.97-19.5)         CD19 (% Lymphocytes)       11.2 (9.94-12.6)       11.7% (6.97-19.5)         CD20+CD19+IgD-CD27- Naive B Cells (% CD19+       84.1% (79.5-87.2, 85.4)       56.8% (53.7-58.7)         B Cells)       CD19+CD20-CD27+CD38+ Plasmablasts (%       2.34% (1.64-2.86)       40.7% (23.1-58.7)         CD19+CD20-B Cells)       CD19	Anti-Rubeola IgG, Random	Negative	Negative < 25 AU/mL
Anti-Haemophilus Influenza Ab, Kandom       0.14 (Negative)       Positive > 0.15 mg/L         Anti-Fatamophilus Influenza Ab, Kandom       0.18 (Positive)       Positive > 0.01 IU/mL         Anti-HBs Antibody, Random       0.18 (Positive)       Positive > 0.01 IU/mL         Anti-Varicella-Zoster Virus IgG, pre-re-vaccination       Negative       Negative        Negative          Positive anti-Pneumococcal Ab serotypes, Random       1, 22F       n/a         Negative anti-Pneumococcal Ab serotypes, Random       1, 22F       n/a         CD3 (% lymphocytes)       73.5% (65.2-80.3)       72.9% (69.6-70.3)         CD4 (% CD3+)       51.6% (37.8-60.2)       57.1% (40-72.3)         CD4 (% CD3+)       51.6% (37.8-60.2)       35.9% (26.5-48.3)         CD19 (% lymphocytes)       11.2 (9.94+12.6)       11.7% (6.97-19.5)         CD20+CD19+IgD-CD27+ Memory B Cells (%       41.4% (34.7-46.2)       35.9% (25.7-83.8)         CD19 + CD20-CD27+CD38+ Plasmablasts (%       2.34% (1.64-2.86)       40.7% (23.1-58.7)         CD19+CD20-D20-CD27+CD38+ Plasmablasts (%       2.34% (1.64-2.86)       40.7% (23.1-58.7)         CD19+CD20-CD27+CD38+ Plasmablasts (%       2.34% (1.64-2.86)       40.7% (3.3-4.91)         CD19+CD20-CD27+CD38+ Plasmablasts (%       2.34% (1.64-2.86)       40.7% (23.1-58.7)         CD19+CD20-CD27+CD38+ Transitional B Cells (%<	Anti-Diphtheria Ab, Random	> 1.00	Positive $> 0.01 \text{ IU/mL}$
Anti-Ietanus IgC, Random       0.18 (Positive)       Positive > 0.01 IU/mL         Anti-Has Antibody, Random       Negative       Na         Anti-Varicella-Zoster Virus IgG, pre-re-vaccination       Negative       Negative       Negative          Anti-Varicella-Zoster Virus IgG, post-re-vaccination       Negative       Negative        Negative          Negative anti-Pneumococcal Ab serotypes, Random       Negative       Na       Na         Negative anti-Pneumococcal Ab serotypes, Random       n/a       1, 22F       n/a         CD3 (% lymphocytes)       73.5% (65.2-80.3)       72.9% (69.6-70.3)         CD4 (% CD3+)       51.6% (37.8-60.2)       57.1% (40-72.3)         CD8 (% CD3+)       11.2 (9.94-12.6)       11.7% (6.97-19.5)         CD20+CD19+lgD-CD27+ Memory B Cells (%       4.1% (2.41-5.15)       23.3% (22.7-23.8)         CD19 + CD20-CD27+CD38+ Plasmablasts (%       2.34% (1.64-2.86)       40.7% (23.1-58.7)         CD19+CD20-D22+CD38+ Transitional B Cells (%       5.21% (4.51-6.18)       4.05% (3.33-4.91)         CD14+CD16+ Monocytes (% total monocytes)       0.0132% (0.0096-0.015)       6.19% (3.78-8.51)         CD14+CD16+ Monocytes (% total monocytes)       0.0132% (0.0096-0.015)       6.19% (3.78-8.51)         CD14++CD16- Monocytes (% total monocytes)       0.0132% (0.0096-0.015)       6.19% (3.78-8.51) <td>Anti-Haemophilus Influenza Ab, Random</td> <td>0.14 (Negative)</td> <td>Positive <math>&gt; 0.15 \text{ mg/L}</math></td>	Anti-Haemophilus Influenza Ab, Random	0.14 (Negative)	Positive $> 0.15 \text{ mg/L}$
Anti-HBS Antibody, Kandom       Negative       n/a         Anti-Varicella-Zoster Virus IgG, pre-re-vaccination       Negative       Negative       Negative          Anti-Varicella-Zoster Virus IgG, pre-re-vaccination       > 4000       Positive > 165 Index         Positive anti-Pneumococcal Ab serotypes, Random       1, 22F       n/a         Negative       n/a       19F, 20, 22F, 23F, 6B, 10A, 11A, 7F, 15B, 18C, 19A, 9V, 33F         Peripheral leukocyte immunophenotyping         CD3 (% lymphocytes)       73.5% (65.2-80.3)       72.9% (69.6-70.3) (69.6-70.3) (69.7-19.5) (69.7-19.7) (70.7-10.7-10.7-10.7-10.7-10.7-10.7-10.7-	Anti-Tetanus IgG, Random	0.18 (Positive)	Positive $> 0.01 \text{ IU/mL}$
Anti-Varicella-Zoster Virus IgG, pre-revaccination Positive anti-Pneumococcal Ab serotypes, Random Negative anti-Pneumococcal Ab serotypes, Random Negative anti-Pneumococcal Ab serotypes, Random $1, 22F$ Negative $165$ Index n/aNegative anti-Pneumococcal Ab serotypes, Random Negative anti-Pneumococcal Ab serotypes, Random1, 22Fn/aPeripheral leukocyte immunophenotypingCD3 (% lymphocytes)73.5% (65.2-80.3)72.9% (69.6-70.3)CD4 (% CD3+)CD3 (% lymphocytes)CD3 (% lymphocytes)CD3 (% lymphocytes)CD3 (% lymphocytes)CD3 (% lymphocytes)CD3 (% lymphocytes)CD4 (% CD3+)CD2 (CD27+ Memory B Cells (%CD20+CD19+lgD-CD27+ Memory B Cells (%CD19+ B Cells)CD19+ CD20-CD27+CD38+ Plasmablasts (%CD19+CD20-CD27+CD38+ Plasmablasts (%CD19+CD20-CD27+CD38+ Plasmablasts (%CD19+CD20-CD27+CD38+ Plasmablasts (%CD19+CD20-CD27+CD38+ Plasmablasts (%CD14+CD16+ Monocytes (% total monocytes)0.0022% (0.0038-0.057)4.93% (2.61-8.66)CD14+CD16+ Monocytes (% total monocytes)0.0122% (0.0038-0.057)4.93% (2.61-8.66)CD14+CD16+ Monocytes (% total monocytes)0.0122% (0.0038-0.057)4.93% (2.61-8.66)CD14+CD16+ M	Anti-HBS Antibody, Random	Negative	n/a Na sting (125 kalor
Anti-Varicelia-Zoster Virus IgG, post-re-vaccination Positive anti-Pneumococcal Ab serotypes, Random> 4000Positive > 165 index n/aNegative anti-Pneumococcal Ab serotypes, Random1, 22Fn/aNegative anti-Pneumococcal Ab serotypes, Random2, 3, 4, 5, 8, 9N, 12F, 14, 17F, 19F, 20, 22F, 23F, 6B, 10A, 11A, 	Anti-Varicella-Zoster Virus IgG, pre-re-vaccination	Negative	Negative < 135 Index
Positive anti-Pneumococcal Ab serotypes, Random $1,22r$ $1,22r$ $1n^{2}$ Negative anti-Pneumococcal Ab serotypes, Random $2,3,4,5,8,9N,12F,14,17F,$ $n/a$ $19F,20,22F,23F,6B,10A,11A,$ $19F,20,22F,23F,6B,10A,11A,$ $7F,15B,18C,19A,9V,33F$ $19F,20,22F,23F,6B,10A,11A,$ Peripheral leukocyte immunophenotyping $51.6\% (37.8-60.2)$ $CD3 (\% lymphocytes)$ $51.6\% (37.8-60.2)$ $CD4 (\% CD3+)$ $51.6\% (37.8-60.2)$ $CD4 (\% CD3+)$ $51.6\% (37.8-60.2)$ $CD19 (\% lymphocytes)$ $11.2 (9.94-12.6)$ $CD20+CD19+lgD-CD27+Memory B Cells (\%$ $CD20+CD19+lgD+CD27-Naive B Cells (\% CD19+$ $CD19+B Cells)$ $CD19+CD20-CD27+CD38+Plasmablasts (\%$ $CD19+CD20-CD27+CD38+Plasmablasts (\%$ $CD19+CD20-B Cells)$ $CD19+CD20-B Cells$ $CD14+CD16-Monocytes (\% total monocytes)$ $CD14+CD16+Monocytes (\% total monocytes)$ $CD12+CD16+Monocytes (\% total monocytes)$ $CD12+CD16+Monocytes (\% total monocytes)$ $CD12+CD16-Plasmacytoid DCs (\% total DCs)$ $CD12+CD16-Plasmacytoid DCs (\% total DCs)$ $CD12+CD16+CPA+CD16+Monocytes (\% total DCs)$ $CD12+CD16+CPA+CPA+CPA+CPA+CPA+CPA+CPA+CPA+CPA+CPA$	Anti-Varicella-Zoster Virus IgG, post-re-vaccination	> 4000	Positive > 165 index $r/c$
Negative duit-Fneumococcut Ab services, Kandom $2, 3, 4, 5, 3, 9, 12F, 14, 11F, 17F, 17F, 17F, 17F, 17F, 17F, 17F$	Negative anti-Pheumococcal Ab serotypes, Random	$1, 22\Gamma$ 2 2 4 5 8 0N 12E 14 17E	n/a
Peripheral leukocyte immunophenotyping77, 57, 158, 158, 194, 9V, 33FPeripheral leukocyte immunophenotypingCD3 (% lymphocytes)73.5% (65.2-80.3)72.9% (69.6-70.3)CD4 (% CD3+)51.6% (37.8-60.2)57.1% (40-72.3)CD8 (% CD3+)CD19 (% lymphocytes)11.2 (9.94-12.6)CD19 (% lymphocytes)CD20+CD19+IgD-CD27+ Memory B Cells (%CD19+CD20-CD27+ Memory B Cells (%CD19+CD20-CD27+ CD38+ Plasmablasts (%CD19+CD20-CD27+CD38+ Plasmablasts (%CD19+CD20-B Cells)CD19+CD20+CD19+ B Cells (%S2.1% (4.51-6.18)4.05% (3.33-4.91)CD19+CD20+CD38+ Plasmablasts (%CD14+CD16- Monocytes (% total monocytes)S1.1% (76.8-86.1)75.7% (68.1-80.8)CD12+CD16+ Monocytes (% total monocytes)0.0022% (0.0096-0.015)6.19% (3.78-85.1)CD123+CD11c+ Manocytes (% total monocytes)0.0132% (0.0096-0.015)6.19% (3.78-85.1)CD123+CD11c+ Plasmacytoid DCs (% total DCs)Q27-23.5)37.9% (3.01-56.5)CD123+CD11c+ Plasmacytoid DCs (% total DCs)Q27-23.5)37.9% (3.01-56.5)CD123+CD11c+	Negative anti-Fneumococcui Ab serotypes, Kunaom	2, 5, 4, 5, 6, 9N, 12F, 14, 17F, 10F 20 22F 23F 6F 10A 11A	II/a
In the product of the		7F 15B 18C 19A 9V 33F	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Peripheral leukocyte immunophenotyping	1, 100, 100, 101, 77, 001	
$\begin{array}{c} CD4 (\% CD3 +) \\ CD8 (\% CD3 +) \\ CD8 (\% CD3 +) \\ CD9 (\% lymphocytes) \\ CD19 (\% lymphocytes) \\ CD20 + CD19 + lgD - CD27 + Memory B Cells (\% \\ CD19 + B Cells) \\ CD20 + CD19 + lgD + CD27 - Naive B Cells (\% \\ CD19 + B Cells) \\ CD19 + CD20 - CD27 + CD38 + Plasmablasts (\% \\ CD19 + CD20 - CD27 + CD38 + Plasmablasts (\% \\ CD19 + CD20 - B Cells) \\ CD19 + CD20 - B Cells) \\ CD19 + CD20 - B Cells) \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD19 + CD20 + CD38 + Plasmablasts (\% \\ CD14 + CD16 - Monocytes (\% total monocytes) \\ CD14 + CD16 + Monocytes (\% total monocytes) \\ CD123 + CD11c - Plasmacytoid DCs (\% total DCs) \\ CD123 - CD11c + Myeloid DCs (\% total DCs) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD1 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) $	CD3 (% lymphocytes)	73.5% (65.2-80.3)	72.9% (69.6-70.3)
$\begin{array}{c} CD8 (\% CD3 +) \\ CD19 (\% lymphocytes) \\ CD20 + CD19 + lgD - CD27 + Memory B Cells (\% \\ CD19 + B Cells) \\ CD20 + CD19 + lgD + CD27 - Naive B Cells (\% CD19 + \\ B Cells) \\ CD20 + CD19 + lgD + CD27 - Naive B Cells (\% CD19 + \\ B Cells) \\ CD19 + CD20 - CD27 + CD38 + Plasmablasts (\% \\ CD19 + CD20 - B Cells) \\ CD19 + CD20 - B Cells) \\ CD19 + CD24 + CD38 + Transitional B Cells (\% \\ CD19 + B Cells) \\ CD19 + B Cells) \\ CD19 + CD24 + CD38 + Transitional B Cells (\% \\ CD19 + B Cells) \\ CD19 + CD24 + CD38 + Transitional B Cells (\% \\ CD14 + CD16 - Monocytes (\% total monocytes) \\ CD14 + CD16 + Monocytes (\% total monocytes) \\ CD123 + CD11c - Plasmacytoid DCs (\% total DCs) \\ CD123 + CD11c + DCs (\% total DCs) \\ CD3 + CD4 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD4 + CCR5 + CD4 + T Cells) \\ CD3 + CD4 + CCR5 + CD$	CD4 (% CD3+)	51.6% (37.8-60.2)	57.1% (40-72.3)
$\begin{array}{c} CD19 (\% lymphocytes) \\ CD20 + CD19 + lgD - CD27 + Memory B Cells (\% \\ CD19 + B Cells) \\ CD20 + CD19 + lgD + CD27 - Naive B Cells (\% CD19 + B Cells) \\ CD20 + CD19 + lgD + CD27 - Naive B Cells (\% CD19 + B Cells) \\ CD19 + CD20 - CD27 + CD38 + Plasmablasts (\% \\ CD19 + CD20 - B Cells) \\ CD19 + CD20 - B Cells) \\ CD19 + CD20 - B Cells) \\ CD19 + CD24 + CD38 + Transitional B Cells (\% \\ CD19 + CD24 + CD38 + Transitional B Cells (\% \\ CD19 + B Cells) \\ CD19 + B Cells) \\ CD14 + CD16 - Monocytes (\% total monocytes) \\ CD14 + CD16 + Monocytes (\% total monocytes) \\ CD14 + CD16 + Monocytes (\% total monocytes) \\ CD123 + CD11c - Plasmacytoid DCs (\% total DCs) \\ CD123 + CD11c + DCs (\% total DCs) \\ CD3 + CD14 + CCR6 + (Th17) (\% CD4 Cells) \\ CD3 + CD$	CD8 (% CD3+)	41.4% (34.7-46.2)	35.9% (26.5-48.3)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	CD19 (% lymphocytes)	11.2 (9.94-12.6)	11.7% (6.97-19.5)
$\begin{array}{c} CD19+B\ Cells) \\ CD20+CD19+IgD+CD27-Naive\ B\ Cells\ (\%\ CD19+\\ B\ Cells) \\ CD19+CD20-CD27+CD38+\ Plasmablasts\ (\%\\ CD19+CD20-B\ Cells) \\ CD19+CD24+CD38+\ Transitional\ B\ Cells\ (\%\\ CD19+B\ Cells) \\ CD19+B\ Cells) \\ CD19+B\ Cells) \\ CD14++CD16-\ Monocytes\ (\%\ total\ monocytes) \\ CD14+CD16+\ Monocytes\ (\%\ total\ monocytes) \\ CD14+CD16+\ Monocytes\ (\%\ total\ monocytes) \\ CD123+CD11c-\ Plasmacytoid\ DCs\ (\%\ total\ DCs) \\ CD123+CD11c+\ Dls\ (\%\ total\ DCs) \\ CD123+CD11c+\ Dls\ (\%\ total\ DCs) \\ CD123+CD11c+\ Dls\ (\%\ total\ DCs) \\ CD3+CD1c+\ CR6+\ (Th17)\ (\%\ CD4\ Cells) \\ CD3+CD4+CCR6+\ (Th17)\ (\%\ CD4\ Cells) \\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ T\ Cells) \\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ Cells) \\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ Cells) \\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ T\ Cells) \\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ Cells) \\ CD3+CD4+CCR5+\ (Th17)\ (\%\ Cell$	CD20+CD19+IgD-CD27+ Memory B Cells (%	4.1% (2.41-5.15)	23.3% (22.7-23.8)
$\begin{array}{c c} CD20+CD19+IgD+CD27-Naive B Cells (\% CD19+\\ B Cells) \\ CD19+CD20-CD27+CD38+Plasmablasts (\% \\ CD19+CD20-B Cells) \\ CD19+CD24+CD38+Transitional B Cells (\% \\ CD19+CD24+CD38+Transitional B Cells (\% \\ CD19+B Cells) \\ CD14++CD16-Monocytes (\% total monocytes) \\ CD14+CD16+Monocytes (\% total monocytes) \\ CD14+CD16+Monocytes (\% total monocytes) \\ CD14+CD16+Monocytes (\% total monocytes) \\ CD123+CD11c-Plasmacytoid DCs (\% total DCs) \\ CD123+CD11c+Dcs (\% total DCs) \\ CD123+CD11c+Dcs (\% total DCs) \\ CD3+CD11c+Dcs (\% total DCs) \\ CD3+CD11c+Dcs (\% total DCs) \\ CD3+CD4+CCR6+(Th17) (\% CD4 Cells) \\ CD3+CD4+CCR5+CD127-Tran (\% CD4+T Cells) \\ CD3+CD4+CD25+CD127-Tran (\% CD4+T Cells) \\ CD3+CD4+CCR5+(Th17) (\% CD4+T Cells) \\ $	CD19+B Cells)		, , , , , , , , , , , , , , , , , , ,
$\begin{array}{llllllllllllllllllllllllllllllllllll$	CD20+CD19+IgD+CD27- Naive B Cells (% CD19+	84.1% (79.5-87.2, 85.4)	56.8% (53.7-58.7)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	B Cells)		
$\begin{array}{c} CD19+CD20-B\ Cells)\\ CD19+CD24+CD38+\ Transitional\ B\ Cells\ (\% \\ CD19+B\ Cells)\\ CD19+B\ Cells)\\ CD14++CD16-\ Monocytes\ (\%\ total\ monocytes)\\ CD14+CD16+\ Monocytes\ (\%\ total\ monocytes)\\ CD14+CD16+\ Monocytes\ (\%\ total\ monocytes)\\ CD14-CD16+\ Monocytes\ (\%\ total\ monocytes)\\ CD123+CD11c-\ Plasmacytoid\ DCs\ (\%\ total\ DCs)\\ CD123+CD11c+\ Myeloid\ DCs\ (\%\ total\ DCs)\\ CD123+CD11c+\ DCs\ (\%\ total\ DCs)\\ CD123+CD11c+\ DCs\ (\%\ total\ DCs)\\ CD123+CD11c+\ DCs\ (\%\ total\ DCs)\\ CD3+CD4+CCR6+\ (Th17)\ (\%\ CD4\ Cells)\\ CD3+CD4+CCR6+\ (Th17)\ (\%\ CD4\ Cells)\\ CD3+CD4+CCR5+\ CD127\ Tran\ (\%\ CD4+\ T\ Cells)\\ CD3+CD4+CCR5+\ CD127\ Tran\ (\%\ CD4+\ T\ Cells)\\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ Cells)\\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4\ Cells)\\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4+\ T\ Cells)\\ CD3+CD4+CCR5+\ (Th17)\ (\%\ CD4+\ Cells)\\ CD3+CD4+CC$	CD19+CD20-CD27+CD38+ Plasmablasts (%	2.34% (1.64-2.86)	40.7% (23.1-58.7)
$\begin{array}{llllllllllllllllllllllllllllllllllll$	CD19+CD20- B Cells)		
CD19+ B Cells)81.1% (76.8-86.1)75.7% (68.1-80.8) $CD14+CD16-$ Monocytes (% total monocytes) $0.0022%$ ( $0.0038-0.057$ ) $4.93%$ ( $2.61-8.66$ ) $CD14-CD16+$ Monocytes (% total monocytes) $0.0132%$ ( $0.0096-0.015$ ) $6.19%$ ( $3.78-8.51$ ) $CD123+CD11c-$ Plasmacytoid DCs (% total DCs) $12.7%$ ( $2.27-23.5$ ) $37.9%$ ( $3.01-56.5$ ) $CD123+CD11c+$ Myeloid DCs (% total DCs) $43.6%$ ( $19.1-88.5$ ) $45.3%$ ( $34.4-61.1$ ) $CD123+CD11c+$ DCs (% total DCs) $34.4%$ ( $8.69-54.3$ ) $0.73%$ ( $0.62-0.88$ ) $CD3+CD4+CCR6+$ ( $Th17$ ) (% CD4 Cells) $14.3%$ ( $9.19-19.7$ ) $8.39%$ ( $4.66-12.7$ )	CD19+CD24+CD38+ Transitional B Cells (%	5.21% (4.51-6.18)	4.05% (3.33-4.91)
CD14++CD16- Monocytes (% total monocytes) $81.1%$ (76.8-86.1) $75.7%$ (68.1-80.8) $CD14+CD16+$ Monocytes (% total monocytes) $0.0022%$ ( $0.0038-0.057$ ) $4.93%$ ( $2.61-8.66$ ) $CD14-CD16+$ Monocytes (% total monocytes) $0.0132%$ ( $0.0096-0.015$ ) $6.19%$ ( $3.78-8.51$ ) $CD123+CD11c-$ Plasmacytoid DCs (% total DCs) $12.7%$ ( $2.27-23.5$ ) $37.9%$ ( $3.01-56.5$ ) $CD123+CD11c+$ Myeloid DCs (% total DCs) $43.6%$ ( $19.1-88.5$ ) $45.3%$ ( $34.4-61.1$ ) $CD123+CD11c+$ DCs (% total DCs) $34.4%$ ( $8.69-54.3$ ) $0.73%$ ( $0.62-0.88$ ) $CD3+CD4+CCR6+$ ( $Th17$ ) (% CD4 Cells) $12.5%$ ( $6.26.8.15$ ) $9.70%$ ( $8.40.11.1$ )	CD19 + B Cells)		
CD14+CD10+ Monocytes (% total monocytes) $0.0022% (0.0038+0.057)$ $4.95% (2.61-8.66)$ $CD14-CD16+$ Monocytes (% total monocytes) $0.0132% (0.0096+0.057)$ $6.19% (3.78-8.51)$ $CD123+CD11c-$ Plasmacytoid DCs (% total DCs) $12.7% (2.27-23.5)$ $37.9% (3.01-56.5)$ $CD123+CD11c+$ Myeloid DCs (% total DCs) $43.6% (19.1-88.5)$ $45.3% (34.4-61.1)$ $CD123+CD11c+$ DCs (% total DCs) $34.4% (8.69-54.3)$ $0.73% (0.62-0.88)$ $CD3+CD4+CCR6+ (Th17) (% CD4 Cells)$ $14.3% (9.19-19.7)$ $8.39% (4.66-12.7)$ $CD3+CD4+CD25+ CD127$ Trag (% CD4+ T Calls) $7.25% (6.26.8, 15)$ $9.70% (8.40, 11.1)$	CD14++CD16- Monocytes (% total monocytes)	81.1% (76.8-86.1)	/5./% (68.1-80.8)
CD14- $CD10+$ Monocytes (% total monocytes) $0.0132% (0.0096-0.015)$ $6.19% (3.78-8.51)$ $CD123+CD11c-$ Plasmacytoid DCs (% total DCs) $12.7% (2.27-23.5)$ $37.9% (3.01-56.5)$ $CD123+CD11c+$ Myeloid DCs (% total DCs) $43.6% (19.1-88.5)$ $45.3% (34.4-61.1)$ $CD123+CD11c+$ DCs (% total DCs) $34.4% (8.69-54.3)$ $0.73% (0.62-0.88)$ $CD3+CD4+CCR6+ (Th17) (% CD4 Cells)$ $14.3% (9.19-19.7)$ $8.39% (4.66-12.7)$ $CD3+CD4+CD25+CD127$ Trag (% CD4+ T Calls) $7.25% (6.26.8, 15)$ $9.70% (8.49, 11, 1)$	CD14+CD10+ Monocytes (% total monocytes)	0.0022% (0.0038 - 0.057)	4.95% (2.61-8.66)
CD12s+CD11c- Plasmacytold DCs (% total DCs) $12.1%$ ( $2.27-23.5$ ) $37.9%$ ( $3.01-56.5$ ) $CD123-CD11c+$ Myeloid DCs (% total DCs) $43.6%$ ( $19.1-88.5$ ) $45.3%$ ( $34.4-61.1$ ) $CD123+CD11c+$ DCs (% total DCs) $34.4%$ ( $8.69-54.3$ ) $0.73%$ ( $0.62-0.88$ ) $CD3+CD4+CCR6+$ (Th17) (% CD4 Cells) $14.3%$ ( $9.19-19.7$ ) $8.39%$ ( $4.66-12.7$ ) $CD3+CD4+CD25+CD127$ Trag (% CD4+ T Calls) $7.25%$ ( $6.26.8.15$ ) $9.70%$ ( $8.49.11.1$ )	CD14-CD10+ Monocytes (% total monocytes)	0.0132% (0.0096-0.015)	0.19% (3.78-8.51)
CD125- $CD11c+$ Myeloid $DCs$ (% total $DCs$ ) $45.6%$ (19.1-88.5) $45.5%$ (34.4-61.1) $CD123+CD11c+$ $DCs$ (% total $DCs$ ) $34.4%$ (8.69-54.3) $0.73%$ (0.62-0.88) $CD3+CD4+CCR6+$ (Th17) (% $CD4$ Cells) $14.3%$ (9.19-19.7) $8.39%$ (4.66-12.7) $CD3+CD4+CD25+CD127$ Trag (% $CD4+$ T Cells) $7.25%$ (6.26.8.15) $0.70%$ (8.40.11.1)	CD125+CD11c- Plasmacytoid DCs (% total DCs)	12.1% (2.27-23.5)	5/.9% (3.UI-50.5)
CD125+CD11C+DCS (%  lotal  DCS) = 54.4% (8.69-54.3) = 0.75% (0.62-0.88) CD3+CD4+CCR6+(Th17) (% CD4 Cells) = 14.3% (9.19-19.7) = 8.39% (4.66-12.7) CD3+CD4+CD25+CD127 Trag (% CD4+T Cells) = 7.25% (6.26.8.15) = 0.70% (8.40.11.1)	CD125-CD11c+Myeloid DCs (% total DCs)	43.0% (19.1-88.5)	45.5% (34.4-61.1)
$CD_{3}+CD_{4}+CCR0+(1n1/)(\% CD_{4} Cells) = 14.5\% (9.19-19.7) \\ CD_{3}+CD_{4}+CD_{2}5+CD_{1}27 T_{reg}(\% CD_{4}+T_{cells}) = 7.25\% (6.26.8.15) \\ 0.70\% (9.40.11.1) \\$	CD2 + CD4 + CCP6 + (T-17) (0 / CD4 - C-112)	34.4% (8.09-34.3)	0.75% (0.02-0.88)
	$CD_{3+}CD_{4+}CD_{25+}CD_{127} T_{reg} (0 \le CD_{4+} T \le M_{2})$	725% (5.15-15.7)	0.37% (4.00-12.7) 0.70% (8.40.11.1)









MOSSHO MICHP



