features are mostly compatible with macrophage activation syndrome (MAS) observed in other viral infections despite resulting in milder changes. Early detection and treatment of MAS may be associated with a better outcome. However, available criteria for MAS associated with other causes have not been helpful.

Objectives: To identify distinct features of MAS associated with COVID-19 using a large database enabling to assess of dynamic changes.

Methods: PCR-confirmed hospitalized COVID-19 patients followed between March and September 2020 constituted the discovery set. Patients considered to have findings of MAS by experienced physicians and given anakinra or tocilizumab were classified as the MAS group and the remaining patients as the non-MAS group. The MAS group was then re-grouped as the cases with exact-MAS and borderline-MAS cases by the study group. Clinical and laboratory data including the Ct values of the PCR test were obtained from the database, and dynamic changes were evaluated especially for the first 14 days of the hospitalization. The second set of 162 patients followed between September-December 2020 were used as the replication group to test the preliminary criteria. In the second set, hospitalization rules were changed, and all patients required oxygen support and received dexamethasone 6mg/day or equivalent glucocorticoids. Daily changes were calculated for the laboratory items in MAS, borderline, and non-MAS groups to see the days differentiating the groups, and ROC curves and lower and upper limits (10-90%) of the selected parameters were calculated to determine the cutoff values.

Results: A total of 769 PCR-confirmed hospitalized patients were analysed, and 77 of them were classified as MAS and 83 as borderline MAS patients. There was no statistically significant difference in the baseline viral loads of MAS patients compared to the non-MAS group according to the Ct values. Daily dynamic changes in the MAS group differed from the non-MAS group especially around the 6th day of hospitalization, and more than a twofold increase in ferritin and a 1.5-fold increase in D-dimer levels compared to the baseline values help to define the MAS group. Twelve items selected for the criteria are given in Table 1 below. The total score of 45 provided 79.6% sensitivity for the MAS (including borderline cases) and 81.3% specificity around days 5 and 6 in the discovery set, and a score of 60 increased the specificity to 94.9% despite a decrease in sensitivity to 40.8%. The same set provided a similar sensitivity (80.3%) in the replication, but a lower specificity (47.4-66% on days 6 to 9) due to a group of control patients with findings of MAS possibly masked by glucocorticoids.

Table 1. Preliminary Criteria for Macrophage Activation Syndrome Associated with Coronavirus Disease-19

1. Fever ($>37.0^{\circ}\text{C}$)
2. Ferritin concentration $> 550\text{ ng/mL}$
3. More than 2 times increase of ferritin concentration within 7 days of disease onset
4. Neutrophil count $> 6000\text{ cell/mm}^3$
5. Lymphopenia $< 1000\text{ cell/mm}^3$
6. Neutrophil/lymphocyte ratio > 6
7. D-dimer concentration $> 1000\text{ ng/mL}$
8. More than 50% increase of D-dimer concentration within 7 days of disease onset
9. CRP concentration $> 50\text{ mg/L}$
10. LDH concentration $> 300\text{ U/L}$
11. ALT or AST concentration $> 50\text{ U/L}$
12. Procalcitonin concentration < 1.2

1 point for each positive item assessed on Days 5-7. Score calculation: Total points / 12 x 100. Possible MAS ≥ 45 and Definite MAS ≥ 60

Conclusion: This study defined a set of preliminary criteria using the most relevant items of MAS according to the dynamic changes in the parameters in a group of COVID-19 patients. A score of 45 would be helpful to define a possible MAS group with reasonable sensitivity and specificity to start necessary treatments as early as possible.

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2021-eular.3113

OP0314

DOCK8 MUTATIONS IN COVID-19 AND MIS-C CYTOKINE STORM SYNDROME

R. Cron¹, M. Zhang¹, D. Absher², J. Bridges¹, A. Schnell³, P. Bhatraju⁴, A. Vagreicha⁵, S. Lozinsky⁶, S. Acharya⁷, C. Levy⁷, W. Chatham³. ¹University of Alabama at Birmingham, Pediatrics, Birmingham, United States of America; ²HudsonAlpha Institute for Biotechnology, Genomic Health Research, Huntsville, United States of America; ³University of Alabama at Birmingham, Medicine, Birmingham, United States of America; ⁴University of Washington, Medicine, Seattle, United States of America; ⁵Hofstra University, Pediatrics, Hempstead, United States of America; ⁶Hofstra University, Neurosurgery, Hempstead, United States of America; ⁷Hofstra University, Pediatrics, Hempstead, United States of America

Background: We recently identified *DOCK8* as a novel gene associated with cytokine storm syndrome (CSS)¹. Heterozygous missense mutations in *DOCK8* diminish NK cell lytic function and contribute to increased pro-inflammatory

cytokine production (CSS). CSS is a potential complication of COVID-19 with severe consequences². Children are at risk of a SARS-CoV-2 post-infectious CSS, multisystem inflammatory syndrome in children (MIS-C)³. Host genetic factors associated with COVID-19 CSS and MIS-C CSS are unknown.

Objectives: The goals are to identify and functionally study rare mutations in *DOCK8* in patients with SARS-CoV-2 COVID-19 and MIS-C.

Methods: To date, 16 adult patients enrolled in a COVID-19 CSS clinical trial at UAB had whole genome sequencing. Four (25%) had rare heterozygous *DOCK8* mutations (3 missense, 1 intronic). A COVID-19 CSS adult patient in Seattle also had a *DOCK8* missense mutation. In addition, *DOCK8* missense mutations were identified in five children (UAB & Northwell) hospitalized with MIS-C. *DOCK8* mutations, or wild-type (WT) sequence controls, were introduced into human NK-92 cells by FOAMY virus transduction. WT and mutant *DOCK8*-expressing NK-92 cells were incubated with K562 target cells and compared for cytotoxicity and degranulation (CD107a).

Results: One COVID-19 patient *DOCK8* mutation (Gly523Arg) reduced NK cell degranulation by 30% and cytotoxicity by 23% (n=3) (Figure 1). Similar studies of 3 MIS-C patients with *DOCK8* missense mutations (Arg899Trp, Ala2Thr, Pro-687Leu) revealed up to 31% reduced NK cell degranulation and 48% reduction in cytotoxicity by 3 distinct mutations (n=3). Two-way ANOVA analysis revealed statistically significant ($p<0.05$) differences in NK cell degranulation and lysis for four unique *DOCK8* mutations.

Conclusion: Heterozygous *DOCK8* missense mutations may contribute to severe COVID-19 and MIS-C CSS by partial dominant-negative effects yielding decreased NK cell cytotoxicity.

REFERENCES:

- [1] Schuler GS, Cron RQ. The genetics of macrophage activation syndrome. *Genes Immun* 2020;21:169-181.
- [2] Cron RQ, Chatham WW. The rheumatologist's role in COVID-19. *J Rheumatol* 2020;47:639-642.
- [3] Reiff D, Mannion ML, Samuy N, Scalici P, Cron RQ. Distinguishing active pediatric COVID-19 from MIS-C. *Pediatr Rheumatol Online J*, in press.

Disclosure of Interests: Randy Cron Consultant of: SOBI, Novartis, Pfizer, Sironax, Grant/research support from: SOBI, Mingce Zhang: None declared, Remy Cron: None declared, Devin Absher: None declared, John Bridges: None declared, Amanda Schnell: None declared, Pavan Bhatraju: None declared, Anshul Vagreicha: None declared, Shannon Lozinsky: None declared, Suchitra Acharya: None declared, Carolyn Levy: None declared, Winn Chatham Grant/research support from: SOBI.

DOI: 10.1136/annrheumdis-2021-eular.1865

Metabolic pathways during the regulation of inflammation and immunity

OP0315

EFFECTOR CD4 T CELLS REQUIRE SURVIVIN FOR REGULATION OF GLUCOSE METABOLISM AND IFNG PRODUCTION

M. Erlandsson^{1,2}, K. M. Andersson¹, N. Oparina¹, S. Töyrä Silfverswärd¹, M. I. Bokarewa^{1,2}. ¹Gothenburg University, Rheumatology and Inflammation Research, Gothenburg, Sweden; ²Sahlgrenska University Hospital, Rheumatology clinic, Göteborg, Sweden

Background: Interferon-gamma (IFN γ) producing effector T cells play the leading role in triggering and perpetuation of inflammation in rheumatoid arthritis. Inflammation leads to metabolic reprogramming of T cells and high energy consumption supporting proliferation and IFN γ production. Being a part of chromosomal passenger complex, oncoprotein survivin is essential for cell proliferation. It has also been identified as a marker of severe therapy-resistant rheumatoid