Study Protocol

Title: “Kawasaki MATCH: A Clinical Decision Support Tool to Detect KD”

Parent Study: “Gene Expression in Kawasaki Disease and other inflammatory conditions”

Version date August 19, 2025

UCSD Human Research Protections Program
New Biomedical Application
RESEARCH PLAN

Instructions for completing the Research Plan are available on the HRPP website.
The headings on this set of instructions correspond to the headings of the Research Plan.
General Instructions: Enter a response for all topic headings.
Enter "Not Applicable" rather than leaving an item blank if the item does not apply to this project. Version date: 9/30/2013
RP Rev 19AUG2025

1. PROJECT TITLE

Study #140220: Gene Expression in Kawasaki Disease and other inflammatory conditions

2. PRINCIPAL INVESTIGATOR

Jane C. Burns, M.D.

3. FACILITIES

Rady Children's Hospital - San Diego

4. ESTIMATED DURATION OF THE STUDY

7 Years

5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

Kawasaki disease (KD) is an illness characterized by inflammation of blood vessels that supply the heart muscle (coronary arteries). There are other inflammatory conditions that also affect the heart in children. Multisystem inflammatory syndrome of children (MIS-C), which is a condition related to exposure to the SARS-CoV-2 coronavirus, is one of them. While the immediate effects of Kawasaki disease may not be serious, in some cases, there is permanent damage to the coronary arteries and heart muscle. Kawasaki disease affects children almost exclusively. Most patients are under 5 years of age and all races and ethnicities can be affected. Children with MIS-C tend to be older. This study will focus on identifying the proteins and molecular pathways that play a role in the disease process of KD and MIS-C with the goal of developing a diagnostic test for the disease, improving treatments, and finding the cause for the disease.

6. SPECIFIC AIMS

Hypotheses:

1) Identification of the gene expression pattern in whole blood and peripheral blood mononuclear cells (PBMC) during acute KD and MIS-C will contribute to our understanding of the pathogenesis of this disease.
2) Understanding the immune response will elucidate the mechanism of action of intravenous immunoglobulin (IVIG) and may inform us as to the nature of the trigger for KD
3) The characteristic pattern of gene expression in whole blood and PBMC and protein levels in serum, plasma, and urine from patients with acute KD and MIS-C will distinguish them from patients with similar-appearing non-KD illnesses. This distinction will allow us to develop a diagnostic test even if we remain ignorant as to the causative agent.

Aims:

1) To characterize the pattern of gene expression and protein biomarkers in blood from KD and MIS-C patients at different stages of disease.
2) To identify a unique pattern of RNA or protein(s) associated with acute KD and MIS-C by comparing the patterns during acute KD with patterns present in patients with known infectious and allergic conditions that appear similar to KD.
3) To develop a diagnostic test for KD and develop a natural language processing (NLP) tool to identify KD patients in the EMR
4) To understand the immune response in KD and MIS-C patients and the mechanism of action of IVIG
5) To evaluate adverse events related to treatment for KD and MIS-C.

6) To bank body fluids for future studies.
7) To determine the frequency of gallbladder hydrops in acute KD patients.
8) To record sociodemographic data and parent/guardian observations of signs/symptoms prior to admission to the hospital.
9) To evaluate the accuracy of a clinical decision support tool (previously known as KIDMATCH, now known as Kawasaki Match).

7. BACKGROUND AND SIGNIFICANCE

Kawasaki disease (KD) is an acute vasculitis of infancy and early childhood that has now replaced rheumatic fever as the leading cause of acquired heart disease in children in the United States and Japan (Taubert et al., 1991; Kawasaki et al., 1974). Although the acute illness resolves spontaneously, permanent damage to the coronary arteries occurs in 20-25% of untreated children. The cause of KD remains unknown and there is no specific laboratory test to identify affected children (Burns 2005). Nonetheless, high dose intravenous immunoglobulin (IVIG) administered within the first 10 days of fever significantly reduces the risk of coronary artery damage by unknown mechanisms (Newburger et al., 1991). KD thus presents a unique dilemma: the disease may be difficult to recognize, there is no diagnostic laboratory test, there is an extremely effective therapy, and there is a 25% chance of serious cardiovascular damage or death if the therapy is not administered.

Beginning in mid-March 2020, pediatricians in communities in Western Europe, the UK, and the Eastern U.S. that had been severely affected by the Covid-19 pandemic noted an increased number of children presenting with fever and evidence of severe inflammation who required admission to intensive care. A hallmark of these cases was heart failure leading to shock and the absence of significant pulmonary disease. In the US, the CDC named the condition *Multisystem Inflammatory Syndrome in Children (MIS-C).* The clinical presentation in these patients shared many features with KD. The inflammatory markers, however, were much higher even than KD shock syndrome, a variant of KD presenting with distributive shock and requiring inotropic and vasoactive support in the ICU. Some patients were polymerase chain reaction (PCR)+ for SARS-CoV-2 while most were virus-negative, but many had detectable antibody suggesting that MIS-C was an immune-mediated reaction to antecedent exposure to the virus. Curiously, while patients were being diagnosed with MIS-C, the numbers of children meeting clinical criteria for KD but with unusual features increased dramatically in these same regions. Data from the UK suggested that there was a lag of several weeks from the peak of Covid-19 in the adult population before children with MIS-C began to appear. Patients have responded to treatment with intravenous immunoglobulin (IVIG) sometimes with additional anti-inflammatory therapy and some have developed coronary artery aneurysms.

This proposal brings together an interdisciplinary team from academic centers throughout the U.S. and abroad to characterize transcript patterns, levels of candidate proteins, microbiome data from swabs, and PBMC and neutrophil populations in acute and convalescent KD and MIS-C patients and in children with other fever/rash illnesses. Biomarkers will be sought that distinguish KD and MIS-C from febrile controls. Healthy controls are also needed as many of these proteins have not been previously measured in children. In collaboration with Alessandra Franco at UCSD and other universities in the U.S. and abroad, the immune response and mechanism of action of IVIG will be characterized. In collaboration with climate scientists at UCSD, SIO, and other academic centers, we will analyze the distribution and timing of KD cases in our community through GPS mapping of patient's primary residence.

8. PROGRESS REPORT

We have now collected RNA, plasma, serum, and urine samples from 2612 patients which includes KD, MIS-C, and control subjects. A password-protected, web-based data entry system in REDCap now houses all data from the KD, MIS-C, and control subjects enrolled to date. This allows access of all investigators at UCSD and collaborating sites to de-identified individual patient data via the unique study number. Critical advances from

this research protocol to date include the following:

1) Elucidation of gene expression patterns in whole blood from KD patients over time
2) Identification of biomarker candidates for diagnosis
3) Creation of a diagnostic algorithm to aid clinicians in identifying KD patients (patent issued)
4) Elucidation of the critical role of dendritic cell and T cell regulation in downregulating inflammation in KD patients
5) Elucidation of the mechanisms of action of IVIG in KD patients
6) Epidemiologic studies suggesting clustering of KD cases in time and space

9. RESEARCH DESIGN AND METHODS

- Laboratory procedures and data collection:
- 12.5 cc of blood (2.5 teaspoons) (for RNA studies, plasma protein studies, serum antibody measurement, and *in vitro* studies of PBMC and cultured human umbilical vein endothelial cells (HUVECs)) will be drawn when phlebotomy is performed for routine clinical care from control and KD and MIS-C patients. For KD and MIS-C patients, this is usually at the time of admission, 24-48h after treatment and before discharge, at the 2- and 6-week clinic visits, and at one year. For healthy control patients undergoing orthopedic surgery, blood samples will be obtained at the time that an IV is started in the OR. Samples will be obtained before administration of IVIG for KD and MIS-C patients and serially thereafter when phlebotomy is necessary for routine clinical care. RNA will be extracted from whole blood and the plasma and serum frozen at -70°C. No further phlebotomy will be performed on control subjects. PBMCs and neutrophils will be studied in the Burns, Franco, and Croker Labs at UCSD.
- New information about diastolic dysfunction late after KD has spurred our interest in pursuing protein biomarkers that may signal cardiomyocyte damage in a subset of these patients. Blood samples from convalescent KD patients will be used for cardiac biomarker studies in collaboration outside companies who have specific assays for candidate biomarkers. Oxitope, Illumina, Anabios and OP2 are among the many companies with whom we are collaborating. Plasma and serum samples will be shared with Oxitope for the measurement of oxidized phospholipids using their in-house assay. RNA and plasma samples will be shared with Illumina.

  Additional collaborations:
  - Plasma and serum samples from febrile control subjects, Kawasaki disease subjects, and MIS-C subjects will be shared with Juan Salazar, M.D., M.P.H. at the University of Connecticut. Material will be further distributed to Dr. Lynes at the University of Connecticut and Dr. Lawrence at Albany for this collaboration.
  - RNA and plasma samples will be shared with Charles Chiu, MD, PhD at UCSF.
  - Plasma samples from febrile control subjects, Kawasaki disease subjects, and MIS-C subjects will be sent to Iwijn De Vlaminck at Cornell for cell-free DNA and RNA analysis.
  - Dr. Mohit Jain at Sapient Bioanalytics, San Diego, who will perform metabolomics assays using Next Gen mass spectrometry on banked plasma samples at UCSD that were from KD patients and febrile controls at RCHSD.
  - Plasma and serum samples from febrile control subjects, Kawasaki disease subjects, and MIS-C subjects will be shared with Baylor College of Medicine.
  - Plasma and serum samples from febrile control subjects, Kawasaki disease subjects, and MIS-C subjects will be shared with SomaLogic who will perform proteomics. These data will then be shared with University of Pennsylvania.

  MTAs will be established for all send-outs as appropriate. A Moore clause has always been included in

the consent to cover the collaborations with commercial entities.

- KD and MIS-C patients only will have 1 cc of IVIG withheld in the RCHSD Pharmacy for testing glycosylation patterns of the IgG and other *in vitro* experiments. This sample will only be obtained from patients for whom the calculated dose (volume of a 10% solution) is less than the total amount prepared, which would otherwise be discarded.
- All patients: Throat or NP swabs will be sent to the Burns laboratory for microbiome studies.
- All patients: Urine for biochemical and molecular studies will be collected in a bag (infants) or in a cup for older children. If spontaneously voided urine is not available, we will not pursue urine collection further. Urine will be sent to the Burns laboratory for processing for biochemical and molecular studies.
- All patients: Any leftover patient samples obtained for routine care such as blood, urine, synovial fluid, or CSF.

FC and KD patients will be offered an ultrasound of the right upper quadrant to examine the gallbladder. This procedure will add approximately 5 minutes to the ED visit. Subjects may agree to the phlebotomy portion of the study but decline the ultrasound. Gallbladder hydrops is associated with the acute phase of KD and may be associated with an increase in ALT and GGT in the plasma and bilirubin in the urine. The incidence of gallbladder hydrops in KD has never been systematically assessed in a prospective study. The ultrasound examinations will be performed by ED physicians who are certified to perform ultrasound in the ED setting. The findings from the ultrasound will not be included in the medical record from the ED visit. This examination is considered research and will not generate any charges to the patient/family. Incidental findings will not be reported. Six attendings are certified for this ultrasound testing. Thus, patients will only be studied when these attendings are working in the ED. When available, a team member credentialed in biliary ultrasonography will obtain limited video and still images of the right upper quadrant in order to characterize biliary anatomy (presence of gallstones, sludge, pericholecystic fluid) and to measure gallbladder dimensions, wall thickness and diameter of the common bile duct. We will perform descriptive statistics of biliary features and measurements and will compare subjects with KD and febrile controls with regard to frequency of abnormal anatomic features and linear measurements of gallbladder and common bile duct.

- All patients:
  - Demographic and physical examination data: Patient's date of birth, sex, self-reported ethnicity of each parent, date of disease onset (first day of fever), date of study entry, and street address and zip code of primary residence will be recorded for GPS mapping (KD patients only). Physical findings typically associated with KD and specifically not associated with KD will be recorded (Burns et al., 1991). We will also record previous treatment received by patient (e.g. antibiotics).
  - Laboratory data: Laboratory data obtained as part of routine patient care will be recorded as available. All data from echocardiograms will also be entered. This information will be used to help categorize patients into disease groups and will include microbiology, virology, hematology, and clinical chemistry data. Culture and PCR results will be recorded.
- All patient data will be housed in a password-protected REDCap database with two-factor authentication required for access. All biologic samples will be stored in the KD Research Center Biobank housed on the UCSD campus, Biomedical Science Building, 2nd fl.
- Data analysis for diagnostic test development: This sub-study will use existing de-identified data and samples to test the performance of a diagnostic algorithm for KD that includes clinical and laboratory

data and new biomarkers for KD diagnosis. These de-identified data will be shared with colleagues at UCSD, USC, and Stanford University who are performing statistical analysis.

- Data analysis for cardiovascular outcomes: De-identified patient data will be shared with IKDR Data Coordinating Centre (Hospital for Sick Children in Toronto) and IKDR Data Analytics Centre (Johns Hopkins University) for the International Kawasaki Disease Registry (IKDR) studies "IKDR – KD and COVID" and sub-study entitled "A data science approach to identify and manage Multisystem Inflammatory Syndrome in Children (MIS-C) associated with SARS-CoV-2 infection and Kawasaki disease in pediatric patients (NIH PreVAIL kIds program)" respectively where collaborators are performing an analysis of risk factors for coronary artery aneurysm formation and outcomes. No PHI will be shared. A DTA will cover the sharing of this information. The consent form already covers the sharing of data with collaborators.

- Data analysis for adverse events related to treatment for Kawasaki disease and MIS-C. We will utilize Clarity Reports built by Health Information Services to assist us with identifying side effects, conditions or events that may be related to the various treatment regimens for Kawasaki disease and MIS-C.

- Data analysis for developing a Natural Language Processing (NLP) tool: This sub-study will use existing data in the form of ED notes to develop an NLP tool that will distinguish KD patients from febrile controls. The NLP team at UCSD will use machine learning techniques to teach the computer to read ED and Urgent Care notes from children already enrolled in the study with signed informed consent for blood drawing. These notes will be anonymized and used for training the testing the NLP tool. Use of these data is already covered in the HIPAA authorization and the signed consent form so no amendments are necessary.

- Data analysis in partnership with our Machine Learning/AI team has created a physician support tool (Kawasaki Match – previously known as KIDMATCH). This tool is implemented into the RCHSD system and is currently being used for routine clinical care of subjects with febrile illnesses and suspicion for KD. Patient data (physical findings and laboratory data) will be entered into Kawasaki Match. Kawasaki Match will develop a risk score for KD. Treating study providers may or may not be offered the results of this algorithm. All data elements to be included are obtained as other parts of this study, no additional data will be obtained to run Kawasaki Match. Algorithm results will be provided only to members of the RCHSD Emergency Department Study Team (see 21 below). Providers will be queried regarding their confidence in diagnosis as well as usefulness of the algorithm on a visual analogue scale.

- Data analysis of Transition of Care survey: KD patients who are at least 12 years old and have a history of coronary artery aneurysms will receive a Transition of Care survey to assess their health literacy. This will be administered annually and their performance over time will be assessed. De-identified data will be analyzed.

- Proteomics will be performed on samples at SomaLogic. The data will be distributed to Dr. Burns' KD lab team as well as University of Pennsylvania, who will collaborate on data analysis.

10. HUMAN SUBJECTS

We plan to enroll 4,500 subjects in this study (includes KD patients, MIS-C, and controls) to allow for the collection of data and samples from cohorts that will support the many different aims in this study. We need to enroll healthy control children as the normal levels of many of these protein biomarkers have not been

determined in a pediatric population.

Inclusion criteria:

Four patient populations will be recruited for this study: patients with KD, patients with MIS-C. patients with infectious or allergic diseases that appear similar to KD (febrile control group), and otherwise healthy infants and children who are Orthopedic Surgery patients with no underlying disease or children who are having blood obtained for mandated lead screening.

Children from 1 month through 17 years of age will be recruited for all study groups (KD and MIS-C patients and control patients). Inclusion criteria for KD patients will be fever plus 4/5 standard clinical criteria (Kawasaki et al., 1974). On a case-by-case basis, KD patients who do not meet full criteria but who have supportive laboratory and echocardiographic data may also be enrolled at the PI's discretion. MIS-C patients may be SAR-CoV-2 antibody positive or negative. Patients must have blood samples drawn before IVIG administration.

Febrile control patients with diseases that appear similar to KD will be recruited from the Emergency Dept. (ED) at RCHSD. Eligible patients must have fever and one or more of the following clinical features: a) rash, b) conjunctival injection, c) red lips or oropharynx, d) swollen hands or feet. Infants <1 yr. with at least 7 days of fever and no obvious source of the fever will be enrolled even in the absence of physician signs suggestive of KD. All control patients must require phlebotomy as part of their clinical evaluation.

Healthy control children will be enrolled at the time of surgery. A partial waiver of HIPAA consent is requested to obtain weekly schedule from the Orthopedic Surgery Office for patients who may be suitable for the study. Signed informed consent will be obtained from the parents by members of the research team, under the supervision of our KD nurse coordinator, Joan Pancheri. An alternative source of healthy controls are children having blood drawn for routine lead screening at RCHSD outpatient laboratory and children undergoing dental surgery at RCHSD.

Exclusion criteria:

All patients with pre-existing major medical conditions will be excluded. This includes patients with known genetic disorders (e.g., trisomy 21, cystic fibrosis), conditions requiring continuous medication (e.g. seizure disorder, asthma, heart disease), or known immune disorder (e.g. hypogammaglobulinemia, complement deficiency). Patients who have received oral steroids in the previous week will be excluded. For the healthy control cohort, patients who have serious underlying medical conditions will be excluded.

11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

Subjects will be recruited from the ED, inpatient units at RCHSD, and Orthopedic Surgery. For the Orthopedic Surgery control subjects, weekly logs for the OR will be reviewed to identify suitable candidate subjects. For Orthopedic subjects, the parents of the subject will be approached on the day of the surgery and offered participation. For the healthy controls who will be having routine lead screening, patients will be enrolled through the pediatrician's office in the MOB at the time of their well-child check by study personnel. Families with KD or MIS-C will be recruited by ED co-investigators when the child is admitted to RCHSD for evaluation and treatment or by Dr. Burns or Dr. Tremoulet in the case of direct admission that bypasses the ED.

12. INFORMED CONSENT

Study participation will be offered without regard to age, sex, or ethnic background. Child assent will be obtained for all study patients ≥ 7 yrs. and adolescent assent will be obtained for patients ≥ 12 yrs. presenting with features of either KD or MIS-C. An adult consent has been added for enrollment of young adults. Recruitment of human subjects with Informed Consent will be obtained by study personnel in the ED, the

hospital inpatient units, and the Orthopedic Surgery area. On occasion in the ED, no study personnel are available in which case one of the co-investigators (Drs. Burns or Tremoulet) is contacted by telephone. The Parent (child/ adolescent if applicable) is provided with the written consent form and HIPAA authorization by ED personnel and the co-investigator reviews the written informed consent document(s) over the phone and answers any questions. The parent (child/adolescent if applicable) then signs and dates the consent document(s) and the witness signature is obtained at a later date from the co-investigator who obtained the informed consent.

Consent will be obtained electronically (via RCHSD's RedCap) using an iPad, or on paper if an iPad is not available in the ED, and on paper only on the wards and in clinic. Electronic consents will be stored in Epic. Paper consents will be stored in a filing cabinet in a locked room that is only accessible to designated research staff at RCHSD.

A partial waiver of HIPAA authorization is requested to allow screening of suitable subjects to approach for enrollment as healthy controls. HIPAA authorization is obtained. All patient information is kept in a secure, password-protected computer file in Dr. Burns' office.

13. ALTERNATIVES TO STUDY PARTICIPATION

Alternative is to decline participation. This is not an intervention study.

14. POTENTIAL RISKS

The risks are bruising and discomfort at the venipuncture site associated with phlebotomy, local discomfort associated with swabbing of the nasopharynx, throat, and rectum. In addition, there is the potential for loss of confidentiality.

15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

Patient confidentiality will be protected by assignment of a unique study number to all data and samples. No publication or written reports will link patient data with a name. Entry into the computer data files will require a password. The patient's full name will not be entered into the file but a log sheet with the study number and name will be kept in the PI's office in a locked, password-protected computer file. The patient's full name is also logged into the RCHSD data base as required for all research subjects at RCHSD. Access to this database is password protected.

16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

Only members of the study team will have access to study files and documents. The coded list linking subject's names to their study number will be kept in a secure, password protected computer file as in Section 15. Participants will be afforded adequate privacy with the informed consent process, discussions with the study team, and with all study related visits and procedures. Parents are encouraged to be present for all study visit / procedures and may remain with the child per hospital policy. Study subjects may meet privately with the study doctor if requested.

17. POTENTIAL BENEFITS

There will be no direct benefit to the subject from participation in this study. No results will be shared with the patients or referring physicians since this information will be generated in the Burns Laboratory, which is a research laboratory, not a CLIA-certified laboratory.

18. RISK/BENEFIT RATIO

This project is categorized as a "minimal risk/no direct benefit" study: 45 CFR 46.404. The potential benefit to society with the generation of new information about KD and MIS-C and the potential to design a diagnostic test and identify children at risk for failing to respond to IVIG justify the minimal risks to the study subject and his/her family.

19. EXPENSE TO PARTICIPANT

None

20. COMPENSATION FOR PARTICIPATION

None

21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

All persons associated with this study have taken the CITI and HIPAA training.

Dr. Jane C. Burns is the Principal Investigator for the study. She is a UCSD faculty member in the Department of Pediatrics and a licensed physician in the State of California. Dr. Burns has medical staff privileges at RCHSD.

Burns Lab Team:

1. Jennifer Kim is a UCSD employee and the data manager for the KD Research Center. She will assist with data analysis and data entry.
2. Dr. Alessandra Franco is an immunologist and UCSD faculty member in the Department of Pediatrics and will perform the immunology studies. She will not be involved with direct patient care.
3. Dr. Chisato Shimizu is a Project Scientist at UCSD in the Burns Laboratory.
4. Ms. Sophia Hernandez is a laboratory technician in the Burns Lab who logs in and processes specimens.
5. Dr. Adriana Tremoulet is a Sub-investigator on the study. Dr. Tremoulet is a UCSD faculty member in the Department of Pediatrics and a licensed physician in the State of California. She has medical staff privileges at RCHSD and will be involved with KD, MIS-C, and control patient enrollment, data collection, data review and data analysis.
6. Ben Croker, PhD is a neutrophil researcher at UCSD who will be studying KD neutrophils.
7. Jonathan Lam is a PhD candidate with the UCSD Department of Biomedical Informatics. He will assist with data analysis.
8. Ellen Xu is a UCSD student and a research assistant on the AI Project
9. Alyssa Linkenheil, MD is a pediatric resident at UCSD and will assist with data analysis of the Transition of Care Study.
10. Shoko Yamazaki, MD is a visiting physician from Japan and will assist with data collection and entry.
11. Koichi Miyata, MD is a visiting physician from Japan and will assist with data analysis.
12. Corinna Puyat, MD is a resident at RCHSD and will assist the Burns Lab team with projects.

RCHSD Emergency Department Team:

The following physicians and Nurse Practitioner are employees of RCHSD Emergency Department. They are licensed in the State of California and will assist with the enrollment of subjects in the ED.

1. Dr. Michael Gardiner is a Sub-investigator on the study. Dr. Gardiner is a UCSD faculty member in the Department of Pediatrics and a licensed physician in the State of California. He has medical privileges at RCHSD and is an Emergency Department physician. He will assist with study enrollment, data collection, data review and data analysis.
2. Lukas Austin-Page, MD
3. Joe Bartoletti, MD

4. Amy Bryl, MD
5. Jennifer Case, MD
6. Elizabeth Chang, MD
7. Heather Conrad, MD
8. Gemmie Devera, MD
9. Joelle Donofrio Ödmann, DO
10. Kyna Donohue, MD
11. Atim Ekpenyong, MD
12. David Gutglass, MD
13. Scott Herskovitz, MD
14. Paul Ishimine, MD
15. Simon Lucio, MD
16. Katherine Mandeville, MD
17. Michelle McDaniel, MD
18. Ashley Metcalf, MD
19. David Mills, MD
20. Margaret Nguyen, MD
21. Mylinh Nguyen, MD
22. Kathryn Pade, MD
23. Brian Park, MD
24. Dunisha Ranasuriya, MD
25. Fareed Saleh, MD, MHA
26. Stephanie Schroter
27. Kristy Schwartz, MD
28. Vanessa Tamas, MD
29. Andrew Tang, DO
30. Nicole Titze, MD
31. Stacey Ulrich, MD
32. Tatyana Vayngortin, MD
33. Caroline Vega, MD
34. Yvette Wang, MD
35. Karen Yaphockun, DO
36. Elise Zimmerman, MD

Gallbladder ultrasound team: John Kanegaye, MD, Kathryn Pade, MD, Mylinh Nguyen, MD, Atim Ekpenyong, MD, Shahfar Khan, MD, and Nicole Barbera, DO, faculty members in the UCSD Department of Pediatrics, Division of Emergency Medicine and attending physicians in the Emergency Department at RCHSD, are credentialed in Emergency Ultrasonography and will participate in recruitment and enrollment of subjects, collection of clinical data, and acquisition of ultrasound images.

Kathryn Hollenbach, PhD, MPH is a UCSD Research Associate in the Department of Pediatrics. She will be working with the Emergency Department Research Associates to identify subjects for enrollment into the study. She will oversee notifying the IRB regarding all changes in personnel and CITI training.

Rady Children's Team

1. Sherrie Bandy, MS, is a senior clinical research coordinator at RCHSD. Ms. Bandy will be the lead coordinator for the study and will assist with the enrollment of subjects, data collection, IRB submissions and the maintenance of regulatory and other research records for the study.
2. Joan Pancheri, RN, BSN, CCRC, is a clinical research nurse coordinator and licensed RN in the State of

California. Ms. Pancheri is the back-up research coordinator for the study and will assist with the enrollment of subjects, data collection, IRB submissions and the maintenance of regulatory and other research records.

3. Manaswitha Khare, MD is a hospitalist at RCHSD and a licensed physician in the State of California. Dr. Khare will assist with subject enrollment and specimen collection.
4. Kirsten Dummer, MD, is a pediatric cardiologist in the Division of Cardiology in the Dept. of Pediatrics. Dr. Dummer will assist with echo and MRI interpretation for the KD and MIS-C patient populations.
5. Alexis Quade, MD is a UCSD Resident in the Department of Pediatrics who will be assisting with data analysis.

22. BIBLIOGRAPHY

Burns JC, Mason WH, Glode MP, Shulman ST, Melish ME, Meisner C, Bastian J, Beiser AS, Meyerson HM, Newburger JW and the U.S. Multicenter Kawasaki Study Group. Clinical and epidemiological characteristics of patients referred for evaluation of possible KD. J Pediatr. 118:680-686,1991.

Burns JC and Glode MP. Kawasaki Syndrome. Seminar series. Lancet 2004;364: 533-543.
Cummings CA and Relman DA. Using DNA microarrays to study host-microbe interactions. Emerg Infect Dis. 2000;6:513-525.
Kawasaki T, Kosaki F, Okawa S, et al. A new infantile acute febrile mucocutaneous lymph node syndrome (MCLS) prevailing in Japan. Pediatrics 1974;54:271-6.

Newburger JW, Takahashi M, Beiser AS, et al. Single infusion of intravenous gamma globulin compared to four daily doses in the treatment of acute Kawasaki Syndrome. New Engl J Med. 1991; 324:1633-9.

Popper SJ, Shimizu C, Shike H, Kanegaye JT, Newburger JW, Sundel RS, Brown PO, Burns JC, Relman DA. Gene expression patterns in Kawasaki disease reveal underlying processes. In press, Genome Biology.
Sherlock SG. The Stanford microarray database. Nucl Acids Res. 2001;29:152-155.

Taubert KA, Rowley AH, Shulman ST. A nationwide survey of Kawasaki disease and acute rheumatic fever. J Pediatr 1991;119:279-82.

23. FUNDING SUPPORT FOR THIS STUDY

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NIH –NHLBI HL103536
Gordon and Marilyn Macklin Foundation
The KD Foundation
PCORI
NIH-1R61HD105590 – 01 (PreVAIL)

24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT

Signed with Stanford University for transfer of RNA, plasma, and urine. Signed with Columbia University for all patient samples. Signed with Imperial College, London, for transfer of clinical samples.

25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER

N/A

26. IMPACT ON STAFF

All nursing intervention required for participation in this study will be provided by the research nurse at

RCHSD. Health Information Services will assist when Clarity Reports are needed to assess adverse events.

27. CONFLICT OF INTEREST

None

28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES

N/A

29. OTHER APPROVALS/REGULATED MATERIALS

None

30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

No surrogate consenting or decisional capacity assessments will be used.