

Dear KD Families,

Hope you are enjoying a good summer and managing to stay cool. Lots of good news to share from the KD Research Center including research updates and news from Japan from the 12th International KD Symposium (IKDS) held in Yokohama, Japan.

The KDRC Team



Kawasaki Disease Research Center, Summer 2018



Reunion of past visiting scholars from Japan (IKDS 2018)



KD Symposium

The 9th Annual KD Symposium for Parents will be held on the UCSD campus on **September 29th**. As in the past, volunteers from Alpha Epsilon Delta UCSD will provide free babysitting and activities for children so that parents will be free to listen to the presentations. Registration information for this free event is attached. The presentations will also be streamed live via Facebook thanks to our talented KD parent, Beth Avant. We hope you will join us live either in person or on Facebook to hear updates about KD research.

Spreading the Word



Meeting of Japanese KD Climate Collaborators in Yokohama, June 2018

An important aspect of research is to share new information with colleagues around the world. This was a busy summer for our team with several invited presentations at the IKDS in Yokohama. Here are some highlights from our presentations in Japan.

- 1) A team of scientists from many different disciplines including oceanography, chemistry, environmental and climate science, bioinformatics, and molecular biology have collaborated to understand more about the cause of KD. The team reported an analysis of KD cases in the San Diego region that revealed clustering of KD patients in both time and space. The clusters were defined as at least 4 cases within a 7- day period and the geographical clustering was noted at distances between 20-100 km. There were distinct weather features of hotter temperatures and high pressure features over the Pacific Ocean that were associated with these clusters. This suggests that KD is not spread person to person, but rather results from an exposure acting over short distances. This would be most consistent with an agent spread as an aerosol carried by the wind.
- 2) A description of a computer-based physician support tool that can be adapted as a cell phone app was presented by Dr. Adri Tremoulet of the KDRC. This tool predicts the likelihood of KD based on a combination of 18 features including elements of the physical examination and routine laboratory testing. The tool was developed in collaboration with colleagues at Stanford University and was tested on data from colleagues from across the U.S. Dr. Tremoulet is now in discussion with the FDA regarding steps toward approval of this tool for use in emergency departments and Urgent Care centers. The hope is that this tool will help physicians identify infants and children who might have KD in a more timely manner. This tool could also be paired with a natural language processing tool developed by Dr. Tremoulet and her team that could be incorporated into the electronic medical record to recognize cases with possible signs and symptoms of KD. This tool could then alert the physician to run the physician support tool to assess the likelihood of KD.
- 3) In a collaboration with Boston Children's Hospital, data were presented that suggest that either infliximab or steroids were effective in reducing coronary artery dimensions in KD patients who presented with an initial echo showing dilated coronary arteries. In this retrospective study, steroids were more effective in suppressing fever compared to infliximab. Plans are underway for a large, multi-center study to formally test these two candidate therapies head-to-head.

- 4) Updates from the Adult KD study were presented by Dr. John Gordon of the San Diego Cardiac Center. Some patients with giant aneurysms have evidence of ongoing inflammation despite feeling well and having no symptoms. The significance of this inflammation signal is currently under investigation by the San Diego team.

Visiting scholars:



We hosted Stefanie Graeter from the laboratory of Stephan von Guten in Bern, Switzerland, in March who studied white blood cells from KD patients called neutrophils. Together, we are writing a summary of the role of neutrophils in KD and identifying gaps in knowledge that we then plan to address.



Dr. Shin Hoshino, a pediatric cardiologist from Shiga University of Medical Science, Japan, joined us in the spring and is studying biomarkers of persistent inflammation that may affect some patients with giant aneurysms .

Update on research studies at Rady Children's Hospital and the KD Research Center, UCSD:

- **Thirteen transcript diagnostic test for KD:** This collaboration with Prof. Michael Levin's lab at Imperial College, London, uses a signature of thirteen different RNA molecules in the blood of acute patients to diagnose KD. The paper was just published in JAMA Pediatrics. Researchers used a case-control approach, including children recruited from hospitals in the United Kingdom, Spain, Netherlands and US, with KD or similar illnesses. The majority of study participants with KD came from Rady Children's Hospital- San Diego. The overall study group comprised 404 children with infectious and inflammatory conditions (78 KD, 84 other inflammatory diseases, 242 bacterial or viral infections) and 55 healthy controls. The researchers looked for tell-tale transcription patterns in blood samples. Transcription is the first step in gene expression, in which information from a gene is used to construct a functional product, such as a protein. Next steps will be to seek an industry partner interested in developing this as a point-of-care test.
- **Anakinra clinical trial:** Anakinra, a recombinant molecule that is widely used to treat many inflammatory diseases in children, specifically blocks this pathway. Dr. Tremoulet received funding from the National Institutes of Health (NIH) for a pilot study of anakinra for children with early signs of coronary artery damage and the clinical trial is ongoing at Rady Children's Hospital and Boston Children's Hospital. Over a dozen patients have been treated thus far with no adverse effects and early results look promising. A new clinical trial to combine anakinra with atorvastatin has also been funded by the NIH.
- **Atorvastatin clinical trial:** Dr. Tremoulet has completed the two-center Phase I/IIa trial of atorvastatin (Lipitor®), a statin drug often used to lower cholesterol, to prevent further damage in KD patients with early signs of damage to the blood vessel wall. Drs. Jone and Dominguez at the University of Colorado were collaborators on the study. An exciting collaboration with the vascular biology laboratory under the direction of John Shyy at UCSD suggests that atorvastatin blocks certain cellular processes that damage the arterial wall. Further studies in mice and in cultured cells are being pursued to further our understanding of how atorvastatin may help KD patients.
- **Understanding how IVIG works:** Dr. Alessandra Franco, an immunologist collaborating with the KDRC, is continuing her studies of fragments of the IgG molecule that stimulate immune regulation and turn off the damaging actions of other cells of the immune system. These fragments, which could be synthesized for pennies, will be studied first in adult patients with rheumatoid arthritis. This may be an exciting breakthrough for treating inflammation in many different conditions including KD.



- **KIDCARE trial:** The team at the KDRC is leading a group of 30 sites across the U.S. in a study to compare two therapies that are widely used in KD patients whose fever returns after the first IVIG treatment: infliximab and a 2nd dose of IVIG. The study is funded by the Patient-Centered Outcomes Research Institute (PCORI) and incorporates parent observations of their child into the analysis of comparative effectiveness of the two different therapies. Samantha Roberts is the lead Study Coordinator at the KDRC who is working with Drs. Burns and Tremoulet to monitor and assist the 30 participating sites. She presented a poster describing the study at the IKDS meetings in Yokohama in June. The study aims to enroll 250 IVIG-resistant patients and will continue for several more years.