THE JOHNS HOPKINS ARRHYTHMOGENIC CARDIOMYOPATHY (ARVC/ALVC/ACM) PRECISION MEDICINE CENTER OF EXCELLENCE

Winter 2025 *Volume 15, Issue 1*

Welcome to the Winter edition of our newsletter! We're posting a little early this year due to the timing of our annual seminar. As you know we typically hold our seminar the last weekend in April, but one of the major cardiology conferences took our week so we had to adjust a bit.

We're excited to host our 26th Annual ARVC/ACM Patient and Family Seminar on Saturday, April 5th, 2025. Our goal is to host a hybrid event using an interactive platform we have used previously (WHOVA) to increase engagement leading up to the seminar and even after the seminar is held. The event will also be livestreamed using the WHOVA platform. And if you can't attend in-person or watch live, the presentations will also be recorded for viewing later. Tickets will be limited, so registration for in-person attendees is open now, with virtual registration to open on or about February 15th. If you need to cancel your in-person registration, please let us know as soon as possible so we can make that ticket available to someone else.

Additional seminar details can be found inside along with some updates on what we've been working on this past year. Enjoy! Thank you for partnering with us!

2025 ARVC SEMINAR

Presented by
The Johns Hopkins ARVC Program

You and your family members are invited to join us for our annual Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) Seminar! This year the seminar will once again be held in-person, but it will also be livestreamed for those unable to join us in Baltimore. We will be utilizing the WHOVA platform where you will also have the opportunity to correspond with other attendees via chat groups. We hope you will consider joining in person to take full advantage of the opportunity to meet other individuals and families, participate in research opportunities, and interact with industry, specifically gene therapy companies.

We are thrilled to have two invited guest speakers, Sam Sears, PhD, cardiac psychologist, and Dominic Abrams, MD, MRCP, adult and pediatric electrophysiologist specializing in inherited cardiac conditions, including ARVC. In addition, we will have presentations from our own Johns Hopkins faculty; Andreas Barth, MD, PhD; Nisha Gilotra, MD; Konstantinos Aronis, MD, PhD; Cindy James, PhD; and Brittney Murray, MS, CGC. You won't want to miss this unique opportunity to meet and network with other families affected by ARVC/ACM and to learn the latest advances in the field. It will be exciting to share the collaborative efforts all around the world in solving the mysteries of ARVC.

Make plans to come into Baltimore early to attend a reception at the Hilton Garden Inn Friday evening (7pm-9pm). Heavy hors d'oeuvres will be served. This event is for patients and family members only. No industry representatives please.

Please register early! There is no registration fee for this seminar, but we continue to be mindful of our gathering capacity. You must register to attend (in-person and virtual).

WHEN: Saturday, April 5th, 2024 8:00am-5:00pm

COST: Registration is FREE. You just need to get here!

WHO: Patients and Families affected by ARVC, Healthcare Professionals

WHERE: Chevy Chase Conference Center Auditorium
Main level of Sheikh Zayed Tower
1800 Orleans Street
Baltimore, Maryland 21287

REGISTRATION: ALL participants must register! It is also helpful to list names of family members that will be attending with you so we can determine appropriate research opportunities. Register by March 29th.

https://tinyurl.com/ARVC2025

Additional Information

HOTEL ACCOMMODATIONS – RESERVE EARLY!!!
Hotel rooms are available (limited) at the Homewood Suites Baltimore Inner Harbor (625 South President Street, Baltimore, Maryland 21202) at a special rate of $171/night plus tax until March 14th, 2025 or as long as they are available.

Hotel reservations can be made through the Hilton Garden Inn Central Reservations Line at 888-429-7482. The group name is ARVC Program Seminar Group and the reservation link name is ARVC Program Seminar Group. Reservations can also be made through the online booking link:

https://group.homewood-suites.com/ksbvv6

The hotel front desk can be reached at 410-234-0999. Check-in 3pm / Check-out 11am. Self-Parking is available at a rate of $25 per day.

TRAVEL TIPS
The Baltimore/Washington International (BWI) Thurgood Marshall Airport is the closet international airport to Johns Hopkins (www.bwiairport.com). It is approximately 30 minutes from the seminar location.

Transportation from Hotel to Seminar – Uber and Lyft are recommended and is at your own expense. There is no bus transportation to and from the seminar.

PARKING AT THE SEMINAR
Parking is available at your own expense (max $15) in the Orleans Street Garage. There is a bridge that connects the garage to the main level of Sheikh Zayed Tower (4th floor).

SPECIAL EVENT
Join us for a Meet 'n Greet Reception, 7:00-9:00pm, on Friday, April 4th, 2025 in the Garden Grille and Bar at the Homewood Suites/Hilton Garden Inn. Please register for this event when you register for the seminar or contact Crystal. Patients and family members only. No industry representatives please.

CLINIC CONSULTATIONS – REQUEST YOUR APPOINTMENT NOW!!!
Dr. Hugh Calkins and the genetic counselors will be available Friday, April 4th and Monday, April 7th for consultations. Dr. Nisha Gilotra and Dr. Paul Scheel will also have a few clinic slots available. Diagnostic tests can also be arranged if necessary. We ask that if you live locally to please consider arranging your appointment at another time to allow new patients and patients traveling from a distance an opportunity to schedule. These appointments will be billed to your insurance. Please contact Crystal via email at ctichnell@jhmi.edu ASAP to schedule an appointment.

Share Your Story
Looking for patient/family stories to share! If you are interested in sharing your story for others to read, please make sure your story and any photos you'd like to include can fit on an 8x10 page. Stories need to be submitted to Crystal by March 21st.

QUESTIONS
Contact Crystal Tichnell, MGC, RN at 410-502-7161 or ctichnell@jhmi.edu

CLINICAL SERVICES AT JOHNS HOPKINS

The Johns Hopkins Arrhythmogenic Cardiomyopathy Program provides a variety of clinical services. We see patients for second opinion consultations to discuss diagnosis and management, genetic counseling and testing, routine ICD management and family member screening. We can also arrange concurrent cardiac testing.

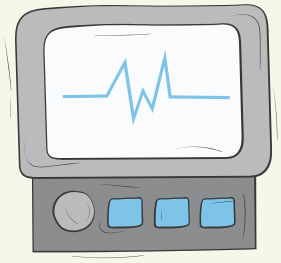
New patients are seen in consultation with Dr. Hugh Calkins and our clinical genetic counselor, Brittney Murray, to discuss test results, family history, and to provide guidance regarding further management. We see all of our patients for genetic counseling to discuss the diagnosis, the psychosocial impact of living with ARVC and with an ICD, as well as to discuss the benefits and limitations of appropriate genetic testing. In selected cases, we also offer catheter ablation as a treatment for difficult to manage ventricular tachycardia. All follow up patients will meet with Crystal Tichnell and Dr. Calkins to discuss current status and management recommendations. Appointments with our heart failure specialists, Dr. Nisha Gilotra and Dr. Paul Scheel, can also be arranged. All appointments are billed to your health insurance.

With the end of the COVID-19 state of emergency, licensure waivers have also ended. This means, per state laws, we are no longer able to offer telemedicine appointments with our physicians outside of Maryland. However, there may be some flexibility with our genetic counseling ONLY visits to be able to continue to offer this option. Please reach out to Crystal to see if you are eligible for a telemedicine appointment based on your appointment needs and physical location. Remember, even if your condition is stable, you should be checking in at least once every two years with repeat cardiac evaluations. It is best to respond to early changes in your health, rather than react to an urgent situation.

To schedule an appointment, contact Crystal at ctichnell@jhmi.edu or 410-502-7161.







A Gene-First Approach to Diagnosis

6th Zurich International Symposium on Arrhythmogenic Cardiomyopathies

September 19-21, 2024, Switzerland

In previous newsletters we discussed how the "one size fits all" approach of the current diagnostic criteria does not take into consideration the nuances of each gene specific cardiomyopathy. Therefore, we are working to update the diagnostic and management criteria using a gene-first approach given what we have learned about each of the different genotypes. For example, PKP2 has classic T wave inversions, arrhythmias, and primarily right ventricular dysfunction. On the other hand, DSP tends to affect the left side of the heart and may have a normal ECG. Furthermore, TMEM43 is highly arrhythmic often leading to sudden death among males.

Every 2 years, Professors Firat Duru, MD, Director and Corrina Brunckhorst, MD, Co-Director Cardiac Arrhythmia Division, University Hospital Zurich host an International Symposium on Arrhythmogenic Cardiomyopathy (ACM). This year, the focus was on the rationale for a new international expert consensus document on ACM, an effort led by Firat Duru and Hugh Calkins. This 2-1/2 day event was held in Zurich, Switzerland and involved 112 experts from around the world.

Experts were divided into groups addressing various topics including pathology, pathophysiology and mechanisms of disease, genetic basis, ECG, Echo, MRI, risk stratification, impact of exercise, pediatric population, as well as management including antiarrhythmic therapy, ACE/ARBs/Aldosterone inhibitors, ICDs, and catheter ablation. In addition, groups focused on each of the genetic causes of ACM including PKP2, DSG2, DSC2, DSP, PLN, TMEM43, JUP, DES, FLNC, and CDH2.

Each group of experts has started writing their chapters and sharing within the group. This is a huge effort and everyone involved has been so enthusiastic in putting this document together. We look forward to sharing our progress soon.

We are so grateful to the Georg and Bertha Schwyzer-Winiker Foundation who predominantly supported this symposium.


2nd Zurich International Symposium
on Arrhythmogenic Cardiomyopathies

RESEARCH OPPORTUNITIES

Clinical and Genetic Investigations of Right Ventricular Dysplasia (ARVD/C Registry)

This registry is the heart of our program and from which all of our research projects originate. This means eligibility for future clinical trials, including gene therapy, will require enrollment in our registry. You do not need to be a patient followed at Johns Hopkins to participate in our registry. Both children and adults either diagnosed with ARVC or a family member of someone diagnosed with ARVC are eligible to participate. Participation involves submission of past medical records and continued followup for at least 5 years (we will offer renewal for continued participation). A DNA sample may be collected for specific projects.

Reach out to Crystal at 410.502.7161 or ctichnell@jhmi.edu to join.

Seroprevalence Study of Pre-existing Antibodies against Adenovirus-Associated Virus Vector (AAV) in Patients with Plakophilin 2 (PKP2)-associated Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

This research study is sponsored by Tenaya Therapeutics, Inc. Eligible candidates will be invited to participate during their regular clinic appointment. The purpose of this study is to assess the prevalence of pre-existing antibodies against the AAV vector and to collect information about patients with PKP2 arrhythmogenic right ventricular cardiomyopathy (ARVC). Initial eligibility criteria include meeting definite task force criteria with a PKP2 pathogenic variant, being 18-65 years of age, and having a functioning implantable cardioverter-defibrillator (ICD). Participation involves donating a blood sample, completing quality of life questionnaires, and following up annually for 5 years. We will collect information from your existing medical records as well to help the sponsor learn about the natural history of ARVC. If you are eligible for this study you will be invited at your upcoming clinic appointment.

Stay Tuned for More Opportunities

FEATURED MANUSCRIPTS

Patient Perceptions of Emerging Gene Therapies for Arrhythmogenic Right Ventricular Cardiomyopathy

Circ Genom Precis Med. 2024 Nov 29:e004759.doi: 10.1161/CIRCGEN.124.004759.

Emma M Schopp, Leonore Okwara, Crystal Tichnell, Amy Turriff, Brittney Murray, Andreas S Barth, Hugh Calkins, Leila Jamal, Cynthia A James

Background: No disease-specific therapy currently exists for arrhythmogenic right ventricular cardiomyopathy (ARVC), a progressive cardiogenetic condition conferring elevated risk for ventricular arrhythmias, heart failure, and sudden cardiac death. Emerging gene therapies have the potential to fill this gap. However, little is known about how adults with ARVC, or any other inherited cardiomyopathy or arrhythmia syndrome, appraise the risks and benefits of gene therapy research and which considerations may influence their decisions about clinical trial participation.

Methods: Twenty adults with clinically diagnosed and gene-positive ARVC participated in semistructured interviews that explored perceptions of gene therapy and hypothetical decision-making for gene therapy clinical trial participation. Interview transcripts were qualitatively coded and analyzed.

Results: Participants expressed enthusiasm for gene therapy with varied levels of personal interest in trial participation. Although clinical severity appeared to be associated with an elevated interest in early trial participation, participants anticipated weighing both personal and trial-specific factors including life stage, trial stage, risks, benefits, participation burden, study leadership, and anticipated cost of future gene therapy. Adaptation to living with ARVC and involvement in the ARVC patient community were also relevant to decision-making about trial participation. Potential ethical concerns included unquestioning trust in clinical teams collaborating on industry-led trials and vulnerability of those recently diagnosed or with high perceived severity of ARVC symptoms.

Conclusions: Several characteristics of the individual and trial warrant consideration during the informed consent process. Insights from this study may affect trial planning and communication with participants who have inherited cardiac conditions.

This article is available here: https://doi.org/10.1161/CIRCGEN.124.004759

Clinical features and outcomes in carriers of pathogenic desmoplakin variants

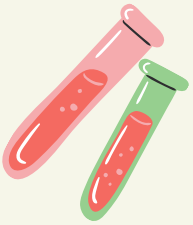
Eur Heart J. 2024 Sep 17:ehae571. doi: 10.1093/eurheartj/ehae571. Online ahead of print.PMID: 39288222

Gasperetti A, Carrick RT, Protonotarios A, Murray B, Laredo M, van der Schaaf I, Lekanne RH, Syrris P, Cannie D, Tichnell C, Cappelletto C, Gigli M, Medo K, Saguner AM, Duru F, Gilotra NA, Zimmerman S, Hylind R, Abrams DJ, Lakdawala NK, Cadrin-Tourigny J, Targetti M, Olivotto I, Graziosi M, Cox M, Biagini E, Charron P, Casella M, Tondo C, Yazdani M, Ware JS, Prasad SK, Calò L, Smith ED, Helms AS, Hespe S, Ingles J, Tandri H, Ader F, Peretto G, Peters S, Horton A, Yao J, Dittmann S, Schulze-Bahr E, Qureshi M, Young K, Carruth ED, Haggerty C, Parikh VN, Taylor M, Mestroni L, Wilde A, Sinagra G, Merlo M, Gandjbakhch E, van Tintelen JP, Te Riele ASJM, Elliott PM, Calkins H, James CA.

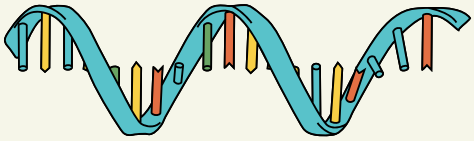
Background and aims: Pathogenic variants in the desmoplakin (DSP) gene are associated with the development of a distinct arrhythmogenic cardiomyopathy phenotype not fully captured by either dilated cardiomyopathy (DCM), non-dilated left ventricular cardiomyopathy (NDLVC), or arrhythmogenic right ventricular cardiomyopathy (ARVC). Prior studies have described baseline DSP cardiomyopathy genetic, inflammatory, and structural characteristics. However, cohort sizes have limited full clinical characterization and identification of clinical and demographic predictors of sustained ventricular arrhythmias (VAs), heart failure (HF) hospitalizations, and transplant/death. In particular, the relevance of acute myocarditis-like episodes for subsequent disease course is largely unknown. Methods: All patients with pathogenic/likely pathogenic (P/LP) DSP variants in the worldwide DSP-ERADOS Network (26 academic institutions across nine countries) were included. The primary outcomes were the development of sustained VA and HF hospitalizations during follow-up. Fine-Gray regressions were used to test association between clinical and instrumental parameters and the development of outcomes.

Results: Eight hundred patients [40.3 ± 17.5 years, 47.5% probands, left ventricular ejection fraction (LVEF) 49.5 ± 13.9%] were included. Over 3.7 [1.4-7.1] years, 139 (17.4%, 3.9%/year) and 72 (9.0%, 1.8%/year) patients experienced sustained VA and HF episodes, respectively. A total of 32.5% of individuals did not fulfil diagnostic criteria for ARVC, DCM, or NDLVC; their VA incidence was 0.5%/year. In multivariable regression, risk features associated with the development of VA were female sex [adjusted hazard ratio (aHR) 1.547; P = .025], prior non-sustained ventricular tachycardia (aHR 1.721; P = .009), prior sustained VA (aHR 1.923; P = .006), and LVEF ≤ 50% (aHR: 1.645; P = .032), while for HF, they were the presence of T-wave inversion in 3+ electrocardiogram leads (aHR 2.036, P = .007) and LVEF ≤ 50% (aHR 3.879; P < .001). Additionally, 70 (8.8%) patients experienced a myocardial injury episode at presentation or during follow-up. These episodes were associated with an increased risk of VA and HF thereafter (HR 2.394; P < .001, and HR 5.064, P < .001, respectively).

Conclusions: Patients with P/LP DSP variants experience high rates of sustained VA and HF hospitalizations. These patients demonstrate a distinct clinical phenotype (DSP cardiomyopathy), whose most prominent risk features associated with adverse clinical outcomes are the presence of prior non-sustained ventricular tachycardia or sustained VA, T-wave inversion in 3+ leads on electrocardiogram, LVEF ≤ 50%, and myocardial injury events.



Gene Therapy Clinical Trials



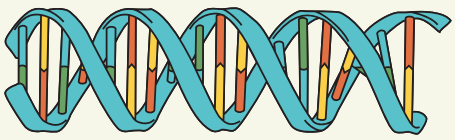
The first in human gene therapy clinical trials are currently underway. As you consider the question of whether you should participate, it would be prudent to first determine if you meet the strict entry criteria for the study. Current gene therapy trials require patients to be diagnosed with ARVC, have a PKP2 pathogenic variant, and an ICD in place. There are many other inclusion/exclusion criteria as well, which may vary between trials. It is appropriate to weigh options between trials as you decide if participation is right for you.

Assuming you meet enrollment criteria, it is then a difficult personal question whether you should participate. Participation in any study is a personal decision and participation in an early phase "first in man" gene therapy trial is a big decision. Before enrolling in a gene therapy trial, you should have a good understanding of the study goals and take into consideration what the expectations are of you, and what the risks and benefits of the study are before you agree to participate. Gene therapy trials will have strict protocols and it will be very important for you to be able to adhere to them. Participation is not for everyone, and that's okay. Each individual has different experiences/circumstances, including varying degrees of symptoms, medications and subsequent side effects, ICD shocks, catheter ablation procedures, etc. that play into how significantly ARVC has impacted their life. Each individual also has different tolerances for risk and different motivations for their decision to participate in an early phase gene therapy trial.

If you are interested and meet the initial eligibility criteria, we are happy to set up a zoom call to discuss gene therapy trials in greater detail. The ARVC Program at Johns Hopkins will be enrolling for both the Tenaya and Lexeo PKP2 Gene Therapy Trials. Email Crystal at ctichnell@jhmi.edu for more information.

Visit: **https://www.clinicaltrials.gov/** for a list of trials currently recruiting.
Consider using search terms such as PKP2, DSP, ACM, ARVC, Arrhythmogenic Cardiomyopathy

We hope this information is helpful as we navigate these new opportunities together.



ARVC PROGRAM INFO

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Nisha Gilotra, MD—Heart Failure
Paul Scheel, MD—Heart Failure
Konstantinos Aronis, MD—Ablation
Jonathan Chrispin, MD—Ablation
Caridad de la Uz, MD—Pediatrics
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Cynthia James, ScM, PhD—Genetic Counselor
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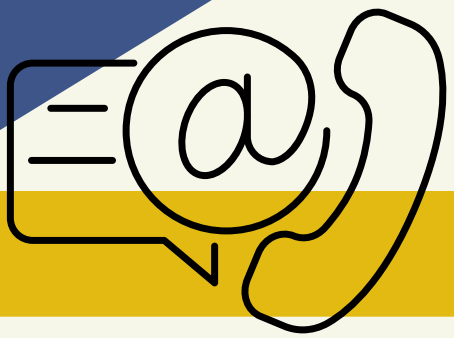

Staff Updates

Meet Katie

Katie Nunez joined the team in June as our research program coordinator, replacing Catherine Pendleton. Katie attended Towson University and graduated with honors with a bachelor's degree in molecular biology, biochemistry, and bioinformatics. During her time at Towson, she was on the swim team and took part in undergraduate research using a mouse model of septic shock. She then took on a role at the NIH as a post-baccalaureate research fellow in the laboratory of clinical immunology and microbiology. Her research was focused on T-cell mediated clearance of established viral infections. At the NIH she was exposed to genetic counseling research and moved back to the Baltimore area to be a part of our team. She plans to attend graduate school to obtain her Master's in Genetic Counseling and a Ph.D. in human genetics.

JOHNS HOPKINS
MEDICINE

Support of the Johns Hopkins ARVC Program Ensures Success

As a charitable, tax-exempt organization, Johns Hopkins Medicine relies on donations to make a difference in the lives of our patients. Supporters of Dr. Calkins and the team of experts in the ARVC Program are partners in the mission to provide exceptional personalized care, discover better ways to diagnose and treat our patients, and provide educational and training programs for medical professionals, patients, and families. Here are some of the ways that you can help:

Make a Personal Donation

Donations of all sizes, one-time or recurring, make a difference. There are a variety of ways to make a gift to support efforts in the ARVC Program:

- Make an outright gift of cash or securities
- Become a monthly donor
- Give in honor or in memory of a loved one
- Give through IRAs, wills and trusts
- Leverage workplace matching gift programs

To make a gift by credit card, visit our online giving form via the QR code

To make a gift by mail, please make a check payable to Johns Hopkins Medicine and indicate the "ARVC Program" on the memo line. Mail to:

Johns Hopkins University and Medicine
Attn: Heart and Vascular Institute
PO Box 49143
Baltimore, MD 21297-9143

https://secure.jhu.edu/form/heart
*Choose "**ARVC Program**" from the drop down menu*

Launch a Personal Fundraising Campaign

There are many opportunities to become involved in raising awareness and much-needed funds on behalf of the Johns Hopkins ARVC Program:

- Create an online giving page and leverage social media
- Ask friends to make contributions in lieu of gifts
- Host your own event or auction
- Plan a fundraising event in your community or school
- Contribute a portion of your company's sales

The Johns Hopkins Heart and Vascular Institute Development Office is here to help!
We welcome your questions, concerns, ideas, and feedback. Please contact Shannon Brockman, Associate Director of Development,
at 443-687-2947 or s.brokcman@jhumi.edu, for more information.