American Heart Association.
Basic Cardiovascular Sciences

Chat Discussion
Thursday, July 30, 2020

Concurrent Session 13A: Extracellular Matrix: Fibroblast and More

name	message
Joe Trusso	Welcome! Thank you for joining us. You should be hearing music play as we wait for the session to begin. If you do not, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Jianyi Zhang	(wave)
Sakthivel Sadayappan	(wave)
Xuejun Wang	(wave)
Jonathan Kirk	(wave)
Snekha Rajasekaran	Hi everyone!
Crystal Naudin	Hi!
Hind Lal	(wave)
Dominic DelRe	(wave)
Thomas Hund	(wave)
Katarzyna Cieslik	(wave)
Michelle Tallquist	(wave)
Farid Moussaviharami	Good morning!
Joy Lincoln	(wave)
Luke Potter	(wave)
Jiayi Yao	(wave)
Jiang Chang	good morning
Michael Czubryt	(wave)
Christopher Solis	(wave)
Jon Pagtakhan	(wave)
Jeff Molkentin	hello

Onur Kanisicak	Good morning everyone, welcome back to BCVS 2020. This is Onur Kanisicak from the University of Cincinnati. I will be moderating the Extracellular Matrix: Fibroblasts and More. It's my pleasure to introduce a great line of speakers, Dr. Wolfram Zimmermann, Dr. Michelle Tallquist, and Dr. Rongxue Wu.
Sadia Mohsin	Hello all
Jamie Francisco	(wave)
Cynthia StHilaire	Good morning from Pittsburgh
Jennifer Davis	hi all
Jennifer Davis	excited for a great session
Farid Moussaviharami	Should be a great session!
Pilar Alcaide	Hi Jen, Good to see you, I enjoyed your presentation on Tuesday!
Sumanth Prabhu	Looking forward to these talks!
Jennifer Davis	thanks Pilar
Pilar Alcaide	Looking forward to another great BCVS2020 session!
Yike Zhu	My screen seems to be frozen. How about yours?
Amadeus Zhu	refresh the page and it should work
Farid Moussaviharami	Seems Ok. You should refresh!
Yike Zhu	thanks! It works now
Jil Tardiff	Been looking forward to this one!
Daniel Turner	Did you find a difference in function depending on how many fibroblasts were used for the construct?
Ronglih Liao	Good morning everyone!
Wolfram Zimmermann	sorry - have issues with the internet
Wolfram Zimmermann	@Turner: yes; contractile performance depends critically on the amount of Fibs - reger to Tiburcy et al 2017 Circ
Abinayaa Rajkumar	Hello everyone,
Daniel Turner	Thank you! great presentation
Ronglih Liao	Very interesting work, Wolfram and great seeing you
Wolfram Zimmermann	Thanks Ronglih
Sumanth Prabhu	Is there an optimal stiffness for EHM - what proportion of fibroblasts?

Di Lang	Nice talk Dr. Zimmermann, how did you mix FB with CM? Is that randomly mixture? Have you test if FB and CM are coupled together and have electrical interactions?
Shyam Bansal	Great talk, Dr. Zimmerman! Is it possible to add a 3rd cell in this culture, say resident macrophages?
Heinrich Taegtmeyer	Great work. Were the organoides beating spontaneously?
Wolfram Zimmermann	depends on tissue format and on fibroblast source - aim at 50:50 first and then titer out the best composition - optimal for EHM is a starting population comprising 30% Fib
Wolfram Zimmermann	@Heinrich: yes they do
Michelle Tallquist	@ Wolfram: Is there any change in cardiomyocyte viability in the presences of fibroblasts?
Jennifer Davis	how much fibroblast proliferation is there in the tissued
Charles Chung	Very interesting data, Dr. Zimmermann. From a function perspective, my lab and others have seen collagen-dependence of force. Have you evaluated the collagen content or MMP/TMP expression in these engineered tissues?
Wolfram Zimmermann	@Bansal: yes any third forth and so in cell type can be added - all need to be optimized as to input content. Macrophages clear EHM from debris
Oscar Bartulos	Nice data Dr. Zimmerman. How the selection of CMs was done in the EHT and what could be the contribution of the selection method to the observed increase in force of contraction? (during the selection)
Katherine Yutzey	Could there be an age component of the HFF compared to other fibroblast types?
Maria Cimini	Dr. Zimmermann, did you try to vascularize the engineered tissue?
Michael Czubryt	Great work - do myofibroblasts show similar effects on EHM function, or is function impaired?

Wolfram Zimmermann	@Michelle: good question. Does not seem to be the case. But would have to looked at in more detail
Yike Zhu	Dr Zimmerman, have you dissociated the EHM to see if the CM contractility is improved at single cell level?
Sumanth Prabhu	Beautiful science, thank you Dr. Zimmerman
Amadeus Zhu	Dr. Zimmermann - very cool work! Did you characterize the fibroblasts phenotypically (e.g. staining for aSMA+ myofibroblasts)?
Jason Gardner	very interesting
Heinrich Taegtmeyer	Wolfram: What supports the crosstalk between the two cell types?
Wolfram Zimmermann	@Davis: no increase in Fibs - content remains stable
Daniel Turner	Very informative, thank you Dr. Zimmerman
Hind Lal	Hi Michelle-looking forward to your talk.
Shyam Bansal	Thank you for this interesting talk, Dr. Zimmerman!
Li Qian	Great talk and very interesting data, Wolfram! Thank you.
Michelle Tallquist	Hi Hind. Nice talk earlier this week.
Li Qian	Nice to "see" you, Michelle!
Wolfram Zimmermann	@ Charles: looked at this primarily in rat model - Tiburcy et al 2011 Circ Res. Rat and himan are very similar, but we did not study MMOs in human EHM
Onur Kanisicak	Beautiful data Dr. Zimmermann. Have you tried mixing fibroblast after they differentiate in culture? Do they need to be relatively quiescent during mixing with CMs?
Xiongwen Chen	Dear Dr. Zimmermann, did you see direct coupling via gap junction between cardiomyocytes and fibroblast? Is there any signal going through this route to regulate CM maturation?
Joseph Wu	Great talk Wolfram!

Xiongwen Chen	Dear Dr. Zimmermann, did you see direct coupling via gap junction between cardiomyocytes and fibroblast? Is there any signal going through this route to regulate CM maturation?
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Wolfram Zimmermann	At Omar: we culture fibs im 2D and use them after enzymatic dispersion in EHM
Wolfram Zimmermann	@Xiongwen: no Cx-mediated coupling between CM and Fibs
Jeff Molkentin	In vivo it is unlikely that fibros and CMs communicate directly, except for rare nanotube-like structures seen occasionally by EM. Otherwise fibrobalsts are outside the basal lamina and not in direct contact with CMs. Hence the EHM might be different, in that these cells might now directly touch....have you checked this>
Wolfram Zimmermann	Thanks all and good to see you Michelle
Michelle Tallquist	Nice talk, Wolfram.
Sathyadev Unudurthi	Hi Michelle, the Aorta in ablated hearts seems very enlarged... is this specific to this particular heart or do you see a change in the size of aorta and any other morphological changes in these ablated hearts?
Xiongwen Chen	Thank you, Wolfram and Jeff!
Di Lang	Since it seems there is no direct interaction between FB and CM, do you think it may be the chemicals secrete from FB that facilitate the improved functions?
Michelle Tallquist	That is the cross section of the heart. Aortic fibroblasts are not targeted significantly by this particular ablation model.
Jil Tardiff	Great lead-off talk , Wolfram, lovely work and accessible to non fibro-masters.
Sathyadev Unudurthi	Thank you Michelle

Onur Kanisicak	Hi Michelle, great talk as always. Do you think in the absence of main PDGFra fibroblasts other cells may compensate for the collagen production?
Onur Kanisicak	Have you isolated other cells in the fibroablated hearts and compare gene expression?
Cynthia StHilaire	what is the turnover rate of collagen? is this the collagen from pre-ablation?
Cynthia StHilaire	kinda just answered that, lol
Jianyi Zhang	(thumbsup)
Eric Olson	Aloha Michelle. What happens when you injure the hearts of mice without fibroblasts?
Hind Lal	@Michelle-did you check the immune cell population and activation in this setting
Michelle Tallquist	@Onur: We thought the pericytes and VSMC could up regulate their production, but using the col-GFP we don't see that. We have started to isolate the other populations to look at expression.
Xiongwen Chen	Hi Michelle, did you look at the cross linkage between collagen proteins in your fibroblast hearts?
Suresh Verma	Have you used any injury model to see in these mice?
Michelle Tallquist	@Eric: Stay tuned!
Xiongwen Chen	@Michelle: did you look at the diastolic function, such as E/A ratio?
Grace Muller	Der. Tallquist, this is quite interesting. Have you considered crossing your mice with a known genetic disease model such as Duchenne Muscular Dystrophy that has pronounced increase in fibrosis?
Michelle Tallquist	@Hind: Immediately after ablation we see a small increase in neutrophils that normalizes within one week of ablation.
Hind Lal	Thanks
MariaPaola Santini	Hi Michelle, very interesting talk. is that a DTA mouse? If not, how long did you treat the animals with Diphteria Toxin? Further, did you try to induce MI?

Mingfu Wu	Hi Michelle, great talk and beautiful work as always!
Michelle Tallquist	@ Xiongwen: we have not explored the ultrastructure beyond scanning EM right now.
Shyam Bansal	Great talk, Michelle! May be i missed it but did you check if there were any arrythmias in fibroablated mice?
Suresh Verma	Nice work Mechelle. Have you checked endothelial cells and their quality in these ablated heart.
Michelle Tallquist	@Grace: we are very eager to investigate the benefits of fibroblast in other models. Duchenne's would be a good start.
Rajasekaran NamakkalSoorappan	Very nice talk Michelle, down-regulated genes are more implies suppression of some key pathways?
Xiongwen Chen	@Michelle: thank you. Very interesting study!
Dominic DelRe	Hi Michelle, beautiful work. Maybe I missed it - have you looked at diastolic function in fibro-ablated mice?
David Wolfson	Dr. Tallquist, did you see any changes in heart rate or arrhythmias? Do you see a drop in fibrosis that is traditionally seen in the SA and AV nodes?
Sumanth Prabhu	Why do you think there is overall lower rupture rate - seems counterintutive
Xiongwen Chen	@Dominic: I asked that too. Let us wait for her wander.
Rongxue Wu	Great job, Michelle, and great to see you again.
Xiongwen Chen	answer
Charles Chung	Excellent studies, Dr. Tallquist- Have you assessed developed pressure in the MI Model? E.g. are the ablated hearts simply producing less force, minimizing opportunities to rupture?
Michelle Tallquist	@ Xiongwen: Mark Ziolo just finished the PV loop measurements and we were all surprised to find that ablated hearts were not significantly different from controls.
Michael Czubryt	Great work Michelle
Detlef Obal	Great talk Dr. Zimmermann

Hind Lal	@ Michelle-Thanks for the great presentation and sharing unpublished data.
Xiongwen Chen	@Michelle, maybe you can push up the heart rate and probably see something.
Farah Sheikh	@Michelle: Great talk! I'm also curious if you have observed arrhythmias!
Michelle Tallquist	@MariaPaola: we used the DTA mice rather than the receptor mice.
Joseph Wu	Great talk Michelle!
Li Qian	Ditto!
MariaPaola Santini	thanks
Farid Moussaviharami	Great talk!
Sakthivel Sadayappan	Michelle Tallquist, Thank you for your excellent presentation.
Yi Hong	very interesting work. thanks
JoanHeller Brown	Great talk Michelle. Very clear and beautiful data !
Prabhat Ranjan	(thumbsup)
Jeff Molkentin	hello michelle and good talk!
Rajasekaran NamakkalSoorappan	Hi ROsy...good to see you
Venkatesh Sundararajan	interesting work, Michelle
Hind Lal	Hi Rosie..
Yike Zhu	DrTallquist, do you see any CM proliferation in MI model with fibroblast ablation? And have you looked at TAC model?
Nicole Purcell	Great talk!
Suresh Verma	Great to see you Rosie.
Jennifer Davis	great talk Michelle
Beverly Rothermel	Hi Michelle, nice to see you, and beautifully done work.
Michelle Tallquist	@Shyam: we have not explored this aspect in detail but would like to examine this aspect in the future.
Ronglih Liao	(thumbsup)
Austin Feeney	Great talk Dr. Tallquist. If I understood correctly, it appears that fibroablated mice have decreases in cell-based contractility, but increases in whole heart contractility (ejection fraction). How can this be explained? Does it relate to differences in chamber sizes?

Liming Pei	Excellent study and nice talk, Michelle. Considering the therapeutic potential of fibroblast ablation, have you tried in an inducible model that you remove some fibroblasts right after injury, to see whether acute fibroblast ablation is beneficial too?
Onur Kanisicak	Thank you Michelle for an excellent talk! Do you think that PDGFRa mediated ablation may selectively kill a specific fibroblast sub-population? And the remainder ones are low in Pdgfra and have different function? Or do you think this is simple a Cre efficiency issue? It would be interesting to check the transcriptome of the remaining fibroblasts.
Jil Tardiff	Thanks Michelle - nice work!
Chengxue Qin	Great Talk. Michelle
Jiang Chang	@Michelle very interesting observation. Great talk! That means majority of CF is not really useful?!
Yajing Wang	rongxue, great work!
Walter Koch	Hi Rosie - good start !!
Wolfram Zimmermann	Hi Jeff: we have never seen fibs and CM touch in EHM. And it is as you said-CMs in EHM dhow a dense basal membrane; fibs do not - similar as reported by us earlier in rat EHM (Zimmermann et al 2002 Circ Res)
Wolfram Zimmermann	Thanks Jil - tried my best
Jeff Molkentin	Thanks Wolfram!! great talk!
Rongxue Wu	Thanks Yajing!
Jeff Molkentin	so much love!!!!!
Rongxue Wu	Thank you for coming, everyone
Onur Kanisicak	@Jiang: Or maybe they are important in ways we haven't discovered yet? As you know Michelle showed that in the absence of fibroblast during development mice die...
Jiang Chang	@rosie enjoying your talk!
Xiongwen Chen	Rosie: Good presentation!

Michelle Tallquist	@Wolfson: SA and AV node collagen remains intact but the density of fibroblasts is significantly reduced in these areas. Heart rate is same as controls. Have not performed EKG. Would like to challenge and explore this topic.
Jil Tardiff	Hi Jeff! Great to "see" you
Sakthivel Sadayappan	Thanks Rongxue for presenting your novel findings!
Pilar Alcaide	Very nice work, Rosie! Did you try agonist and antagonist ligands of AHR, upstream of ARNT, in barrier function?
Rongxue Wu	Thanks, xiongwen
Wolfram Zimmermann	@Michelle: great talk, have you considered to try CAR-T cell mediated Fib depletion (following the strategy of the Epstein lab)
Maria Cimini	Hi Rosie, greetings from Philadelphia, did you look the permeabilization/function of lymphatic vessels/endothelial cells, specifically in the KO mouse?
Liya Yin	@Rosie, great talk! Did you check the cerebral vessels?
Michelle Tallquist	@Sumanth: Rupture rate is not lower. It is not increased which was very surprising to us. We are currently ablating after injury to explore the rate of rupture if the hearts do not have time to adapt to the fibroblast reduced environment.
Xinliang Ma	Rosie: Nice work!
Wei Guo	Great work Rosie!
Rongxue Wu	Yes, Pilar, we did both agonist and arnt overexpression
Sumanth Prabhu	Thank you, Michelle. Very interesting set of studies!
Michelle Tallquist	@Charles: we have not explored the force production. What do you think would be the best way to do this?
Joseph Wu	Great talk Rose!
Rongxue Wu	Good to see you, xinling
Rajasekaran NamakkalSoorappan	Nice presentation and interesting observations Rosie! Congratulations!
Mingfu Wu	Rongxue, beautiful work! Congratulations!
Onur Kanisicak	Thank you for a great talk Dr. Wu!

Guo Huang	Great talk, Rosie!
Timothy Audam	interesting talks!
Zhongjian Cheng	@Rosie, wonderful talk! can protease inhibitor rescue ARNTdelection enhance EC permability
Jiang Chang	Beautiful work Rosie
Yi Hong	great talk. Rosie
Yibin Wang	@Rosie, Very exciting science and great presentation. Learnt a lot. Congrats!
Jil Tardiff	Great presentation and work, @Rosie - thanks for participating!
Xiongwen Chen	Good talk! Did you try stroke model or look at permeability at the BBB?
Ronglih Liao	nice work/presentation!
Charles Chung	@Michelle, I was thinking in vivo or isolated heart. Perhaps if mean arterial pressure is lower, that might be a correlate also?
Ke Cheng	Great talk Rongxue!
Onur Kanisicak	Thank you for all the speakers, Dr. Zimmermann, Dr. Tallquist, and Dr. Wu for an amazing session. Also, thank you for everyone attending for a great discussion and organizers for a successful BCVS 2020. Please continue to ask questions to our speakers as we have more time. Cheers!
Xuejun Wang	@Rosie, nice work and great talk, Congrats!
Michelle Tallquist	Hi everyone. Glad to "see" you.
Aijun Qiao	Great talk! Rosie.
Pilar Alcaide	Great talk Michelle!
Suresh Palaniyandi	Good talk Rosie, didn't you see this effect on non-cardiac vasculature by giving oral viral overexpression
Liya Yin	@Rosie, did you check what protein leaks most in ECKO? Thank you
Hind Lal	@ Onur-good to see you
Guochang Fan	Excellent work, Rosie.
Michelle Tallquist	@Yike: we have only explored the perinatal CM proliferation and there we do see reduced binucleation suggesting that proliferative capacity may be extended beyond the normal time window.
Onur Kanisicak	@Hind Good to see you too!! Cheers!

Rongxue Wu	Yes, we used both inhibitor and double knockout mice, and it showed reduced permeability in the KO mice after IR. I was not able to show those data due to the limited time.
Fuli Xiang	great talks from three excellent speakers! Thank you:)
Yike Zhu	Thank you Dr Tallquist!
Michelle Tallquist	@Yike: May try TAC in the future. We are curious to learn if the hypertrophy that we observe is maladaptive.
Sathyadev Unudurthi	Great job moderating the session @Onur
Fuli Xiang	Thank you Onur for organize such a great session!
Rongxue Wu	Thanks Dr. Fan. good to see you and thank you for your support
Wolfram Zimmermann	@Katherine: there seems to be an age component - „younger" fibs support better function.
Rajarajan AmirthalingamThanda	@Onur: Good to see you
Farah Sheikh	@Michelle- good to "see you" & great talk...wondering if you observed arrhythmias in your mice?
Sathyadev Unudurthi	@Michelle - Great talk Michelle, do you think that ablation of fibroblasts in the LV and RV could change the stiffness of the cardiac tissue and as a result, you could see changes in the structure of aorta and vasculature?
Onur Kanisicak	@Sathya: Thank you! Its my honor to introduce these great speakers. As evident from the interest I would suggest that we need more fibroblast talks in future BSVCs.
Michelle Tallquist	@Austin: Great question. We don't see increases in EF at baseline, but hearts do perform better than controls after injury.
Suresh Palaniyandi	Hi Roxie, didn't you see this effect on non-cardiac vasculature by giving oral viral overexpression systemically

Jijun Huang	Great talk Dr. Zimmermann! Nice to see you here! One question: You mentioned that fibroblast enhanced the CM Ca2+ handling, does cell-cell connection necessary for the effect?
Rongxue Wu	Hi, Liya, good question, we checked the different size of protein leakage but not a particular one.
Wolfram Zimmermann	@Bartulous: G418 - no contribution to contractile function under non-transgenic conditions
Wolfram Zimmermann	@Cimini: yes, can be done, but does not improve performance
Rongxue Wu	Good to "see" you Dr. Liao, and thank you for coming
Onur Kanisicak	@Wolfram: Have you tried to add endothelial cells in the mix?
Rongxue Wu	Hi, Xiongwen, Regarding BBB, no leakage was found in ARNT KO mice. However, we have another BBB related paper that will be published soon.
Michelle Tallquist	@onur: we would love to do single cell on the remain cells to explore this question. As for now we have performed ribotag to examine gene expression in the remaining alpha expressing fibroblasts and do not see significant increases in ECM transcripts.
Wolfram Zimmermann	@Czubryt: input Fibs show - because of their 2D propagation - myofibroblast properties (SMA, stress fibers). This phenotype reverses in EHM to a fibroblast phenotype and can be induced again by pro-fibrotic stimuli such as TGFb
Rongxue Wu	@.Yibin Wang, I appreciate your coming and encourage.
Rongxue Wu	Hi Yi Hong
Rongxue Wu	Thanks CJ
Rongxue Wu	Good you are hear @ Timothy AUdan
Onur Kanisicak	@Michelle: Thank you!
Rongxue Wu	Hi Guo huang
Wolfram Zimmermann	@Zhou: difficult to perform but interesting experiment, we have not done this comparision

Rongxue Wu	Thank you for everyone, if I missed anyone's question, please contact me rwu3@uchicago.edu
Rajasekaran NamakkalSoorappan	Nice presentation and interesting observations Rosie! Congratulations!
Wolfram Zimmermann	@Heinrich: „crosstalk“ appears via biomechanical condensation of ECM (important at early stages) and thus stiffening of the ECM, but paracrine factors can of course not be ruled out, seem however less dominant
Michelle Tallquist	@Sathyadev: That is a possibility that we have not explored yet.

Concurrent Session 13B: Regulation of Small RNAs in Heart Failure

name	message
Joe Trusso	Welcome! Thank you for joining us. You should be hearing music play as we wait for the session to begin. If you do not, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Jaunian Chen	Good morning everyone. Welcome to Concurrent Session 13B on “Regulation of Small RNAs in Heart Failure”. I am Jaunian Chen from UCLA, your moderator for this session. We have two excellent talks scheduled. During the session, please feel free to contribute your thoughts or post questions in the Chat section. Enjoy the session!
Sakthivel Sadayappan	Thank you, Dr. Chen, for moderating this session!!
Yigang Wang	I am here!
Raj Kishore	good morning all
Walter Koch	hey Raj - guess you will miss faculty meeting - Ha!
Jaunian Chen	Good morning! looking forward to your talks!
Jiang Chang	Good morning Raj Yigang and Sakthi
Sakthivel Sadayappan	Hello Dr. Wang and Dr. Kishore, Thank you for your presentation!!
Walter Koch	oh no thats at noon - all good
Raj Kishore	I wont wally
Raj Kishore	thank you for invitTION sHAKTHI, jIL AND lOREN
Sakthivel Sadayappan	(shh)
Mohsin Khan	Hello everyone, Great session..Looking forward to the talks
Hind Lal	(wave)
Yigang Wang	Good morning Raj , Jiang, and Saktthivel
Sakthivel Sadayappan	Dr. Khan, How are you?
Keith Jones	Hi all
Willem DeLange	Good Morning!
Mohsin Khan	Doing well Sakthi. Wonderful meeting.. Congrats to you, Jill and Loren
Sakthivel Sadayappan	Hi Keith!!
Xinliang Ma	Hello Raj! Good to "see" you here
Raj Kishore	Hi Xin

Gang Fan	good morning
Keith Jones	Hi Sakthi! Hi Raj ,good "seein"everyone!
Venkatesh Sundararajan	Good morning all!
Jiang Chang	Thank you Jaunian for moderating the section
Venkata Garikipati	Hi Raj, Nice to see you
Rongxue Wu	Good morning, Raj. nice to see you
Rajarajan AmirthalingamThanda	Hi Raj, Good to see you
Gopal Babu	GM everyone
Loren Wold	Looking forward to watching Raj for 15 minutes!
Raj Kishore	ha Loren
Kimberly Ferrero	Are these from only male mice with MI, Raj?
Kimberly Ferrero	beautiful images by the way
Raj Kishore	in this cohort, yes, only male mice
Suresh Verma	Hi Raj, Nice to see you after some time. Nice work...
Ronglih Liao	indeed, good to see Raj and listen to his recent work on small RNAs
Ronglih Liao	Good morning everyone!
Raj Kishore	hi Ronglih
Suresh Palaniyandi	Hi Raj, if you don't have I/R injury, don't the exosomes damage just diabetic hearts (without any injury)?
Rajarajan AmirthalingamThanda	Hi Raj, did you get chance to check the RV function in the diabetic mice compared to normal mice
Liming Pei	Nice study, Raj. Have you test other diabetes models, such as high fat diet induced diabetic model?
Raj Kishore	potentially, though vascularity at that age was not different in noninjured mice
Raj Kishore	yes, high fat diet model has similar findings
Liming Pei	Nice. Thanks, Raj.
Raj Kishore	no we didnot look at RV functions
Yigang Wang	Raj : This is an excellent presentation
Rajarajan AmirthalingamThanda	Thanks
Liya Yin	Hi, Sakthi, Loren, Raj, Yi-gang,JC, Ma, Rosie,nice to "see" you all .this is a great session!
Raj Kishore	thanks yigang
Yigang Wang	Thanks Liya, good to "see" you
Saumya DAS	Nice talk Raj. Do you think miR-499 is 'more selectively' targeted to the exosomes in diabetic mice or is it stoichiometry

Raj Kishore	Soumya, all mirs are seen in diabetic muscle exosomes, but only 499 at higher levels, mir1 is downregulated
Raj Kishore	*myomirs
Yajing Wang	Raj, great work! I am wondering-are there any cluster with miR499 or family?
Liya Yin	@Raj,did you check miR21? Thank you. Great talk!
Yajing Wang	Hi, Liya, good to meet you!
Raj Kishore	we only focussed on myomiRs that were differentially regulated with diabetes
Joseph Wu	Great talk Raj!
Venkatesh Sundararajan	@Raj, Excellent work and talk!! Curious to know whether exosomes carry mitochondria within it? Have you found any mt related proteins or RNA in these exosomes?
Liya Yin	@Yajing, you can relax today. Great talk yesterday
Raj Kishore	Thanks Joe
Yajing Wang	liya, thank you! yes, i feel much relieved
Raj Kishore	Venkatesh: there is some evidence of mitochondria in exo, we havenot investigated that
Venkatesh Sundararajan	Thanks, Raj
Walter Koch	Great Talk as always - Temple Rocks!
Rajasekaran NamakkalSoorappan	Great talk Dr. Kishore!
Raj Kishore	Thank you wally and Raj
Ganesh Halade	@Raj - great talk !
Venkata Garikipati	Agreed Wally!
Shyam Bansal	Interesting work, Raj! Thanks,
Cindy Benedict	Nice talk Raj!
Mohsin Khan	Great Talk Raj.
Kimberly Ferrero	Definitely a great talk -- really proud to be part of CTM with science like this!
Yajing Wang	Ray, I like the name: my-o-miRNA
Rongxue Wu	Interesting findings, I enjoyed your talk, Raj
Zhongjian Cheng	Excellent talk Raj! You are true rocks!
Ajit Magadum	Excellent work and talk Raj..
Willem DeLange	Great talk- not my field at all, so please excuse my ignorance, Are miR499 and Myh7 expression co-regulated in any way?
Hind Lal	Great talk Raj, as always.
Raj Kishore	Willem: not that i know of
Sakthivel Sadayappan	Superb, Raj! Great talk as always!
Keith Jones	Hi Yigang!

Willem DeLange	Thank you
Yigang Wang	Nice job Raj.
Raj Kishore	Thank you all
Mohsin Khan	Hi Dr Wang.. Good to see you
Rongxue Wu	Good to see you Dr. Wang!
Yigang Wang	Good to be here!
Zhongjian Cheng	Nice to see you Yigang!
Sherin Saheera	Hi Raj..great talk!
Pilar Alcaide	Beautiful work, Raj!
Raj Kishore	hi sherin
Raj Kishore	thanks Pilar
Keith Jones	Interesting work Raj. have you figures out whether the circulating miR-449 is in EPCs or in exosomes in the blood? Or both?
Raj Kishore	Hi keith, it is enriched in plasma exosmes as well
Raj Kishore	and both
Keith Jones	INTERESTING, looked in diabetic human serum yet?
Sherin Saheera	Raj, I totally agree that exosomes are a promising treatment strategy. Do you think in any way these exosomes (let it be any from source) would have a deleterious effect, since they can carry redundant proteins form the parent cell?
Raj Kishore	On it, keith
Raj Kishore	thats what i showed you Sherin, depending on source they could be deliterious as well
Sherin Saheera	I think I missed it, I will go through the presentation. Thanks so much!
Yajing Wang	yigang, great model and great work!
Liya Yin	@Yigang, Great talk!Thank you
Yigang Wang	Thank you!
Di Lang	Thank you Dr. Wang, Great presentation!
Yigang Wang	Thank you
Raj Kishore	yigang: what percentage of CM proliferate? in vitro or in vivo
Yigang Wang	I will need to check for the exact number. We used both in vivo and in vitro
Liya Yin	@Yigang, You only injected twice Tamoxifen? Dosage? Thank you
Guo Huang	Nice work, Yigang!
Ronglih Liao	(thumbsup)
Raj Kishore	thats great work, yigang

Liya Yin	(thumbsup)
Zhongjian Cheng	wonderful talk Yigang! Thank you!
Yigang Wang	Raj: Increase in vitro ki-67 (CM increase) was 15%
Raj Kishore	thats impressive
Sherin Bakhashab	Thanks Raj and Yigang for great talks
Sakthivel Sadayappan	Thank you, Dr. Kishore and Dr. Wang. As we have no third presentation, please continue the discussion!!
Xinliang Ma	Yigang:
Venkata Garikipati	Nice work! Congratulations!
Mohsin Khan	Nice talk Dr Wang
Suresh Verma	Excellent talk Prof. Wang.
Xinliang Ma	Great work! Will contact you later to ask for some more specific questions.
Yigang Wang	Thank you for the wonderful moderation.
Jaunian Chen	Thank you to both speakers for delivering excellent talks. Also many thanks to all participants for your comments and active discussion. Please continue discussion using the Chat function.
Raj Kishore	Thanks Dr. chen
Yigang Wang	Tamoxifen dosage was 1 mg./g body weight.
Viswanathan Rajagopalan	Thanks for the wonderful session and the talks Dr. Kishore, Dr. Chen and Dr. Wang. Missed the early part. Looking forward to watching it.
Ke Cheng	Great talks! To both Raj and Yigang!(thumbsup)
Jiang Chang	Beautiful work Raj and Yigang
Yigang Wang	Thanks Ke and Jiang
Yigang Wang	Thanks Dr. Ma, Verma, and Khan
Guochang Fan	Congrats, Dr. Wang. Great presentation.
Guochang Fan	Missed your beautiful work, Raj.
Yigang Wang	Thanks Dr. Fan
Jianyi Zhang	(wave)

Concurrent Session 14A: Cardiac Arrhythmias: from Basic Mechanisms to Precision Medicine

name	message
Corey Dubois	Welcome! Thank you for joining us. You should be hearing music play as we wait for the session to begin. If you do not, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Wenbin Liang	Hello everyone!
Stacey Rentschler	Hello!
Steven Houser	Welcome to this exciting session on Cardiac Arrhythmias: From Basic Mechanisms to Precision Medicine. We have three great speakers in the session: Drs. Stacy Rentschler, Thomas Hund, and Francesca Stillitano. Each will speak for about 15 mins. Please post your questions and comments in the chat and the speakers will do their best to answer any questions. Thanks for attending and enjoy the session.
Thomas Hund	(wave)
Steven Houser	Looking forward to your talk Stacy
Wenbin Liang	Look forward to your talk, Stacey!
Thomas Hund	me too, Stacey
Steven Houser	Looking forward to hearing about your new work Thomas
Stacey Rentschler	Likewise!
Farah Sheikh	Great to "see you" Tom and Stacey! Looking forward to the talks!
Sakthivel Sadayappan	Dr. Houser, Thank you for charing this electrifying session!!
Walter Koch	Hi Stacey !
Wenbin Liang	look forward to three exciting talks today!
Stacey Rentschler	So great to "see" everyone!
Sakthivel Sadayappan	Stacey, Good to see you!!
Sean Wu	Hi Stacey!
Di Lang	Great talk Stacey, so nice to 'see' you again!!

Jil Tardiff	Such an under-studied topic. Atrial remodeling in virtually all cardiomyopathies is a big driver of clinical outcome.
Loren Wold	Thank you to the presenters, and our awesome chair, Dr. Houser!
Ronglih Liao	very nice work, Stacy!
Stacey Rentschler	Thank you so much!
Sean Wu	Agree w Jil! More molecular studies of AF and arrhythmia in general is needed.
Stacey Rentschler	I think it will be interesting to further elucidate different types of AF at a molecular level as a platform for understanding therapies
Sean Wu	Interesting finding on ploidy! Is there a correlation of duration of AF with degree of increase in ploidy?
Thomas Hund	Agree with Sean - would be interesting, for example, to look at ploidy in paroxysmal vs. persistent AF
Stacey Rentschler	The current study is probably not enough to answer that, we are harvesting more tissues from both paroxysmal and persistent now
David Barefield	Great study Stacey, it would be great to break down the AF monolith
Jil Tardiff	@Stacey- 100% . We still banter about whether the effect of sarcomeric mutations directly impact AF risk in HCM. After all these years!
Farah Sheikh	@Stacey- Did you look at pacemaker physiology in your optical mapping studies?
Jil Tardiff	Nice question Farah, exactly
Stacey Rentschler	yes, the heart rate is slower due to the "atrial myopathy".
JoanHeller Brown	Beautiful work Stacey and so well presented ! Perfect.
Stacey Rentschler	The loss of sodium current in the RA leads to a source sink mismatch and slow HR
Farah Sheikh	@Stacey-- follow up-- have you observed a change in the localization of the dominant pacemaker?
Stacey Rentschler	It seems to be slower but in the same location. Also, if we activate Notch only in the sinus node we did not see HR effects.
Farah Sheikh	@Stacey-- thank you!
Stacey Rentschler	There are human studies showing that SCN5a mutations can cause sick sinus syndrome, so we think this is the basis of the slow HR

Farah Sheikh	@Stacey-- makes sense..beautiful work!
Steven Houser	Very complex underpinnings for AF. Congrats on taking this approach to generate new hypotheses.
Joseph Wu	Great talk Stacey!
Michelle Tallquist	Nice talk, Stacey!
Stacey Rentschler	Thanks so much!
Loren Wold	Awesome talk Stacey!
Sean Wu	Great talk Stacey! So well presented.
Steven Houser	Great talk.
Elaheh Karbassi	Very cool talk! How long can you keep the tissue slices?
Ronglih Liao	Great talk!
Wenbin Liang	great talk, Stacey, as always!
Stacey Rentschler	We can keep the ventricular slices electrically viable for days, atrial not as long yet
Jil Tardiff	Super talk, Stacey - thanks!
Stacey Rentschler	We are now using the human slice platform to test SARS-CoV-2 therapeutics as well.
Maria Cimini	Dr. Rentschler, awesome talk! I may have missed it, does NICD have a role also on LV CMs?
Wenbin Liang	Stacey, did you see any sinoatrial node exit block?
Stacey Rentschler	Thanks Jil! Your former student Jesus Jimenez played a large role!
YangKevin Xiang	Stacy, do you mean the slices from human, can you do it on rodents?
Stacey Rentschler	We did not observe SAN exit block.
Wenbin Liang	Thanks, Stacey!
Stacey Rentschler	This slice technique can be applied to many species including rodents. We have mostly focused on human but other groups have looked at rodent tissue
Stacey Rentschler	NICD does have a role on LV CMS, we published this previously in Circ Res. It has different effects in each chamber
Maria Cimini	Thank you so much!
YangKevin Xiang	Great, thank you, Stacey! I remember Paul Simpson mentioned that rodent slices are very difficult to maintain in vitro.
Stacey Rentschler	Yes, rodent slices are actually more difficult technically
Stacey Rentschler	And the protocol is different for each species. We have also tried porcine and what works best for human is different than for porcine

JoanHeller Brown	Thomas.. at what time after TAC did you do the gene arrays?
Thomas Hund	Hi Joan - 6 weeks post-TAC
Farah Sheikh	@Tom-- nice talk-- are you surprised to see STAT3 at the ICD given that it's a transcription factor?
Thomas Hund	Hi Farah- we were quite surprised. We searched the literature and didn't find that much on STAT3 localization in adult CMs - other studies have shown subpopulation at ID but we're still trying to understand the complex
Farah Sheikh	@Tom-- yes i wonder if there is a subpopulation there..have you fractionated cells into subcellular compartments to do western blots to follow up?
Thomas Hund	Farah, we've done some mostly focused on nuclear vs. extranuclear populations but need to do more.
Farah Sheikh	@Tom-- thanks! very interesting data! Congrats!
Sathyadev Unudurthi	Interesting work @ Tom
Thomas Hund	@Sathya, right back atcha!
Rajesh Kumari	Hi Dr. Thomas, great talk. I may missed it, what about the expression of Spectrin in cardiomyocytes and endothelial cells?
Shyam Bansal	Great work, Tom! Do you know if Fn14 is expressed on immune cells also? if yes, which ones?
Thomas Hund	@Rajesh, we've looked extensively at bIV-spectrin in cardiomyocytes but not so much in endothelial cells - important to consider.
Onur Kanisicak	Great work Tom and Sathya!
Steven Houser	Any idea what "type" of macrophages infiltrate the heart after TAC?
Joseph Wu	Great talk Tom!
Thomas Hund	hi Shyam,
Thomas Hund	Sathya is looking at the immune cell question.
Steven Houser	Great talk Tom
Loren Wold	Awesome talk Tom!
Thomas Hund	thank you, everyone!
Rajesh Kumari	Thank you.
Jil Tardiff	That was great, Tom - lovely work, congrats.
Stacey Rentschler	Awesome talk, Tom!
JoanHeller Brown	Very exciting Tom, thanks. Is there also an interaction with CaMKII in the fibroblast?
Sakthivel Sadayappan	Excellent presentation, Thomas! Thank you!!

YangKevin Xiang	Great talk. Tom. did you envision similar regulation of Stat3 by some signaling process such as CamKII in both CM and CF?
Wenbin Liang	Great talk, Tom!
Sakthivel Sadayappan	Hi Francesca!!
Jie Xu	Great work @Tom! Could spectrin be a signaling molecule for mechanical load as well? Very intriguing
Thomas Hund	@Joan, we have observed that CaMKII drives loss of bIV-spectrin in myocytes and are following up in fibroblasts.
JoanHeller Brown	Thanks..Kevin asked too !
YangKevin Xiang	ditto @Joan
Thomas Hund	@Jie, agree very much that spectrin is likely sensing/transducing mechanical load - we've observed an interaction also with mechanosensitive K channels
Michelle Tallquist	@tom: Was the fibroblast gene expression performed on cultured cells? Given the idea that spectrin is involved in mechanical stress sensing do you think the gene expression differences might be less if cultured on a soft substrate?
Jie Xu	Thanks Tom, very cool indeed
Thomas Hund	@Michelle, gene expression was performed on cultured cells at low passages. For HF fibroblasts, we didn't passage at all because we noticed that even 1 passage eliminated differences.
Thomas Hund	Follow up to Michelle question, would be cool to use Ribotag or something to get clearer picture of situation in vivo.
Evangelia Kranias	the humanized mice schematic is so interesting
Jie Xu	@michelle, great idea! Might need to both passive and active mechanical stimulation, i.e., soft/stiff substrate and stretching
Farah Sheikh	@Francesca-- nice to "see you"-- quick question: why do think there is no change in EF in the mice despite the changes in wall dimensions..did you measure strain?
Ronglih Liao	(thumbsup)
Francesca Stillitano	hi Farah, nice to see you too... yes, form MRI data EF was unchanged
Sakthivel Sadayappan	@Francesca (thumbsup)
Wenbin Liang	Great talk, Francesca!

Francesca Stillitano	thank you
Steven Houser	Francesca, great talk. Could you demonstrate a gene dosage effect on the arrhythmia reduction that you observed
Evangelia Kranias	Great talk and very effective slides!
Poonam Rao	Great talk
Francesca Stillitano	thanks
Steven Houser	Beautiful presentation. Very clear.
Alicia Mattiazzi	Excellent Talk!
Loren Wold	Excellent talk Francesca!
Sakthivel Sadayappan	Well done.. Excellent talk!
Ronglih Liao	another great section. well done!
Loren Wold	And the meeting is over! THANK YOU ALL for participating until the end. We couldn't have done this meeting without all of your support and interaction.
Francesca Stillitano	@steven what do you mean exactly by gene dosage?
Ronglih Liao	Thanks Loren!
Wenbin Liang	enjoyed all three talks today; thank the chairs for organizing a great event!
Rajesh Kumari	Hi Francesca, great talk. I may missed it, what is the PLN-R14del pathway for regulating arrhythmia?
Jil Tardiff	Thanks gain to all the participants both speakers and audience!
Francesca Stillitano	@ rajesh... we don't know yet, working on it
Joseph Wu	Great talk Francesca!
Francesca Stillitano	Thanks!
Rajesh Kumari	Ok, Thank you.
Thomas Hund	Thanks, everyone, for great session. Steve, thanks for moderating and kudos to Sakhti, Jil and Loren!
Ronglih Liao	well down! great section! thanks to Jil, Loren and Sakhti!\
Jie Xu	Great session. Thanks to the organisers!
Hind Lal	Thanks to BCVS 2020 program chairs and the organizing committee for the wonderful meeting.
Rajasekaran NamakkalSoorappan	Great Virtual Meeting - very good topics and better learning! Appreciate all the organizers!

Concurrent Session 14B: Systems Approaches to Cardiac Disease: Novel Mechanisms

name	message
Corey Dubois	Welcome! Thank you for joining us. You should be hearing music play as we wait for the session to begin. If you do not, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Chengxue Qin	Welcome everyone, I am Chengxue Helena Qin, a translational cardiovascular pharmacologist from Monash University in Melbourne. I am the moderator for this session "Systems Approaches to Cardiac Disease: Novel Mechanisms"
Xuejun Wang	(wave)
Chengxue Qin	Please feel free to post your question to the speakers on this chat. There will be a 15min Q and A session at the end as well. Thanks for joining us.
Chengxue Qin	(wave)
Kate Weeks	Hi Helena!
Jil Tardiff	Looking forward to these presentations!
Sakthivel Sadayappan	Chengxue Qin, Thank you for moderating this inspiring session from Australia..
Jeff Molkentin	Hi Jil!!!
Chengxue Qin	Hello Kate OMG.... you are up too:)
Jil Tardiff	Jeff!
Chengxue Qin	Thanks Sakthivel.
Chengxue Qin	We have three great speakers lined up for the session: Jenny Kanter: She is currently a Research Assistant Professor at UW Medicine Diabetes Institute at the University of Washington. Brian O'Rourke: He is the Vice Chair of Basic and Translational Research, Professor of Medicine, Department of Medicine at Johns Hopkins University Catherine Makarewich: She is the Assistant Professor, UC Department of Pediatrics, Cincinnati Children's Hospital Medical Center
Detlef Obal	exciting to hear about the new approaches
Sakthivel Sadayappan	Hi Jenny, Great start!
Xiongwen Chen	I am looking forward to all the great talks!
Jianyi Zhang	(thumbsup)

Venkatesh Sundararajan	@Jenny, is this from human samples?
Chengxue Qin	Great start Jenny. Does ApoC3 increase in T2D as well as T1D?
Jenny Kanter	Some of the data is from human samples.
Venkatesh Sundararajan	@Jenny, Thanks, the venn diagram one
Jenny Kanter	Yes, APOC3 is elevated in T2DM too, both mouse models and humans
Jenny Kanter	The Venn diagram is both mice and humans.
Chengxue Qin	Great Thanks
Venkatesh Sundararajan	@Jenny, Thanks!
Santosh Maurya	Did you measure cardiac TG levels?
Jenny Kanter	We have not measured cardiac TGs, no. We know that the T1DM model has a modest cardiac function impairment (by echo)
Ronglih Liao	Nice work, Jenny!!
Heinrich Taegtmeyer	Amazing work, and amazing experimental strategies. Long live metabolism
Jenny Kanter	Long live metabolism!!
Farid Moussaviharami	Very cool data Jenny!
Chengxue Qin	How does the liver look with APOC3 antisense treatment?
Jenny Kanter	As far as we can tell, the livers are normal. Liver enzymes are normal and no increase in liver TG
Chengxue Qin	Thanks:)
Farid Moussaviharami	Do you think the results will be the same if it is added to statins? I am thinking about it for our patients who should be on treatment already.
Venkatesh Sundararajan	@Jenny, do you think there might be any modifications of APOC3 by high glucose, for e.g., glycosylation, that leads to its accumulation?
Jenny Kanter	I don't know if the data would look the same with statins, but we hypothesize that APOC3 aso targets mostly TG-rich particles (VLDL, remenants) and thus would be a useful tool in addition to statins. But we have not tested it yet
DaoFu Dai	Great talk Jenny. Good to see you
Jenny Kanter	There might be modification to APOC3, perhaps by glucose. In humans it's glycosylated.
Viswanathan Rajagopalan	Great work.
Chengxue Qin	Great talk Jenny:) Very interesting work
Venkatesh Sundararajan	@ thanks, Jenny. Interesting work!!!

Jenny Kanter	Thanks you all for listening, and for your comments! I really appreciate the opportunity!
Rajasekaran NamakkalSoorappan	Dr. Brain R, Great science as always!
Yajing Wang	Jenny, great work!
Rajasekaran NamakkalSoorappan	Does ROS accumulation in the mitochondria could inhibit SOD activity, thereby it is more toxic situation in the matrix?
Brian Orourke	Yes, SOD can be inactivated by H2O2
Heinrich Taegtmeyer	Brian, compelling lines of reasoning. Long live metabolism - again!
Rajasekaran NamakkalSoorappan	Thanks Dr. Brian OR
Elizabeth Murphy	Brian,
Elizabeth Murphy	Brian, nice talk. Any thoughts on why the MCU-KO mice did not show a difference in TAC. How does this fit with your data.
Jeff Molkentin	Your western was from total heart?
Jeff Molkentin	30% increase
Brian Orourke	Yes western was from total heart
Jeff Molkentin	So do you know that each infected cell has increased MCU?
Jeff Molkentin	And how much?
Brian Orourke	when we look at isolated mitochondria about 40% of the population is transduced but we were unabel to sort them to do westerns
Jeff Molkentin	Got it!
Brian Orourke	So it could be that individual cells have up to 80% increase
Xiongwen Chen	Is it possible to sort the mitochondria with enhanced MCU expression (MCU can be tagged)?
Mei Methawasin	@Brian, I have a naive naive question. What is the difference between mitochondrial dysfunction in systolic vs diastolic failure models?
Chengxue Qin	@Brian, great work. Just wondering if is there a particular complex in the mitochondria that the intervention affects?
Brian Orourke	Regrading tish's question. I think GP, which has a positive force frequecny and loading response and higher Na, tends to have a much lower SR load in HF

	so it could contribute to lower loading of mitos than mice
Brian Orourke	We needed a special high sensitivity cytometer for flow but it doesn't have a sorter - yet. in development.
Heinrich Taegtmeyer	Do substrates matter? eg. glucose/pyruvate vs. fatty acids/ketone bodies?
Brian Orourke	We have not yet examined Mito Ca uptake in a pure diastolic HF model. Tried to feed high fat but did not get much of a phenotype in Guinea pig
Jeff Molkentin	EMRE is matched to MCU in a stoichiometric relationship. Do you see increases in EMRE with your MCU overexpression?
Brian Orourke	I believe that the the more reduced state of fat metabolism could partly mitigate the problem but we have little information about it. Fine line between lipid protection versus toxicity I think.
Joseph Wu	Great talk Brian!
Venkatesh Sundararajan	@Brian, Great work!! Do electron complex chain activities influences mitochondrial calcium levels and vice versa? Have you measured in these models?
Dhanendra Tomar	Dr. O'Rourke, did you check the protein levels of MCU regulators in over expression condition?
Chengxue Qin	Another great talk. Thanks Brian
Brian Orourke	Chengxue, I think there are multiple targets of oxidation related to ROS overflow.
Michael Regnier	Brian, great talk! Nice quality work.
Chengxue Qin	Thanks @Brian
Santosh Maurya	Will inducing SR-Ca2+ leak improve HF phenotype in MCU-overexpressed hearts?
Kevin Casin	Great work Brian! Nice to virtually see you again!
Qutuba Karwi	Very nice work Brain! Congrats
Matthew Wolf	Are there genetic variants in human MCU and do they correlate with heart failure outcomes?
Miao Cui	Hi Cat! Good to see you!
Guo Huang	Nice to "see" you, Cat!
Catherine Makarewich	Thank you! Happy to be here
Brian Orourke	IN the ACi model we do not see any signifcant change in the stoichiometry of the regulatory subunits. Need to measure ratios in the population of mitos that are transduced but need sorting to do it right.

Rajasekaran NamakkalSoorappan	Hello Catherine, Good intro...and clean DWORF model
Walter Koch	dont know how many "last talks" at BCVS people have attended so for this format that is an improvement !!
Viswanathan Rajagopalan	Nice point Dr. Koch.
Julia Liu	Brian, this probably also relies on sorting, but does the MCU overexpression significantly increase the levels of matrix calcium?
Brian Orourke	Inducing more SR Ca leak would make things worse.
Brian Orourke	Matt, I am not aware of MCU mutations linked to HF. Thanks
Adam Wende	Nice story. How long did it take you to find the cell with a heart in it?
Catherine Makarewich	haha! Thank you, Adam. We actually did not notice this for a while and published the images upside down-someone pointed it out to us at a later date!
Detlef Obal	Nice talk, Cat
Adam Wende	On a more serious note how many lncRNA do you think fit this classification of actually encoding small proteins? Have you or anyone done the in silicons screen?
Brian Orourke	Julia, we measured matrix Ca in response to pacing in an earlier slide and it was enhanced with MCU overexpression. No major change in baseline mCa
Joanne Garbincius	Interesting work, Cat. Any insight into how DWORF's targeting to SERCA may be regulated?
Onur Kanisicak	Great work, Cat!
Hind Lal	Hi Cat-good to see you.
Beverly Rothermel	Hi Cat, Will DWORF also compete with sarcolipin for SERCA biniding and regulation?
Catherine Makarewich	@Adam, There have been many studies that have tried to address this and depending on which paper you read the estimations range quite a bit. I would estimate there are a few hundred of these out there
Julia Liu	Thanks, Brian! Great talk!
Catherine Makarewich	@Joanne-Thank you. We don't know much about the signals that regulate the targeting of DWORF to SERCA, but we do know through mutagenesis/binding experiments that DWORF binds to the same residues on SERCA as PLN.

Manuel Rosagarrido	Very nice talk, Cat! Did you guys study DWORF transcriptional regulation?
Evangelia Kranias	Great talk, Cat! Congrats!
Catherine Makarewich	Hi Bev! We have in vitro data that indicates that DWORF can compete SLN off of SERCA as well
Detlef Obal	where the westerns done from whole heart or risk zone?
Gopal Babu	Hi Catherine, what is the level of Dworf in atria compared to the ventricles?
Catherine Makarewich	Thank you Manuel. We have some ongoing work aimed at addressing the transcriptional regulation of DWORF, but we do not have any conclusive data at this time.
Chengxue Qin	Great story, very clear and impressive phenotype:)
Samadrita Bhattacharyya	Hi Cat. Great Talk. Hi from UTSW Dallas. How conserved are micropeptides? And why do you think evolution needs such micropeptides?
Elizabeth Murphy	Great talk Cat!
Nicole Purcell	Great talk Cat! Good to see you.
Joseph Wu	Great talk Cat!
Jennifer Davis	Great work Cat! Soo good seeing you!
Catherine Makarewich	@Detlef-Westerns were done from whole heart extracts
JoanHeller Brown	Cat.. Very nice and convincing work. Wondering whether you arethinking the effect of DWORF and Ca signaling drives HF through effects that are independent of gene expression or due to changes secondary to some Ca dependent signaling?
Elizabeth Murphy	Great session everyone! thanks to all the speakers.
Julia Ritterhoff	Do you know if DWORF downregulation is a common feature in HF remodeling (ischemic vs. non-ischemic)? And did you look at arrhythmias in your gene therapy models?
Eric Olson	Nice to see you Cat. Great talk!
Brian Lin	@Cat. Great talk,really cool stuff. Does your AAV.cTNT.DWORF treatment elicit any immune responses?
Mebratu Gebrie	Great presentation!
Venkata Garikipati	Great talk!
Xiongwen Chen	Hi Cat. Good to "see" you. Did you see if DWORF over expression increased SR load or arrhythmias?

Guo Huang	Nice talk, Cat! Was AAV-Dworf injected before or after MI?
Glynnis Garry	Awesome talk Cat!
Yike Zhu	Dr Makarewich, wonderful talk! I wonder whether you have tried to give the mice purified microprotein of DWORF?
Brian Orourke	Wonderful work Cat!
Danish Sayed	Nice work Cat! May be I missed . Did you check the expression levels in human heart tissue
Michael Czubryt	Excellent work Cat!
Detlef Obal	Well done
Kimberly Ferrero	Fantastic talk, Cat! Congrats on starting your own lab, too!
Jennifer Davis	Awesome session!
Kate Weeks	Fantastic talk, thanks Cat!
Viswanathan Rajagopalan	Wonderful work. Congrats.
Grace Muller	Dr. Makarewich, that was a great presentation. Thank you!
Rushita Bagchi	Great session!
Ajit Magadum	Nice talk..
Catherine Makarewich	Hi Sam-great to hear from you. Micropepetides are very well conserved, just like larger protein coding genes. Looking for signatures of evolutionary conservation is actually how we have discovered most of them.
Chengxue Qin	Does DWORF have any polymorphism? How is it lelve in human
Taejeong Song	Great talk. Congratulation Cat!!
Qutuba Karwi	Very nice story Cat! Congrats and good to see you
Brian Orourke	Hope to see everyone in person soon!
Adam Wende	Great talk and nice way to end the meeting. Thank you to all the organizers and speakers. Went better than I had expected.
Wei Guo	beautiful work! Congrats Cat!
Gabriele Schiattarella	Fabulous talk, Cat and great to "see" you! Wondering if all the positive effects of DWORF on cardiac function are 100% dependent from calcium-related effects or there are some not-calcium-effects of DWORF.
Rong Tian	great session!
Chengxue Qin	Thank you very much for participating in this session. Thanks for our great speakers. Great to "see" you all.

	Stay healthy and enjoy the rest of the session and the summer/winter. Hope to see you next year.
Catherine Makarewich	Thank you for all the questions! I will try to address them all.
Mebratu Gebrie	Thank you BCVS 2020 Scientific sessions. Wonderful event!
Mebratu Gebrie	Thank you all
Catherine Makarewich	@Julia-We have looked at MI, TAC, and several genetic mouse models of heart failure (MLP KO, Calcineurin Tgs) and have seen a robust down regulation of DWORF protein
Ronglih Liao	well done, thanks to program co-chairs, Jil ,Loran & Skhti! and all for running in
Catherine Makarewich	Hi Joan-thank you. At present, I think the effects we are seeing are independent of gene expression and due to changes in calcium signaling
Catherine Makarewich	Thanks Eric!
Yike Zhu	Dr Makarewich, have you checked whether the DWROF has any effect at its mRNA level?
Catherine Makarewich	@Brian-We did not see any adverse immune response in our animals
Catherine Makarewich	Hi Wen-DWORF overexpression does increase SR load but we have not seen any evidence of arrhythmias
Catherine Makarewich	Hi Guo-AAV was injected before MI. We are currently repeating these experiments with deliver post-MI
Guo Huang	Look forward to more exciting findings from your group @Cat!
Catherine Makarewich	Hi Yike-We did some very preliminary work trying to use purified DWORF protein but had a hard time with these. DWORF is VERY small (34aas), and the majority of the protein is a hydrophobic transmembrane domain. It is very difficult to work with in this sense.
Catherine Makarewich	Hi Danish-In human heart failure samples we see a reduction in DWORF expression
Danish Sayed	(thumbsup)
Yike Zhu	(thumbsup)Thank you Dr Makarewich
Catherine Makarewich	Hi Helena-We are actively looking for mutations in DWORF that could be linked to HF but have not found this data yet
Chengxue Qin	Thanks Cat. Really interesting area:)

Catherine Makarewich	Thanks Gabriele! And thank you for your help with our initial DWORF Tg/MLP studies. We cannot say for sure that what we see if 100% dependent on calcium related effects and are trying to follow up on a lot of additional things now
Chengxue Qin	Hi all, there is moderated poster sessions, check them out too
Catherine Makarewich	Thanks Guo!