American Heart Association.
Basic Cardiovascular Sciences

Chat Discussion
Wednesday, July 29, 2020

Concurrent Session 7A: HfpEF in Metabolic Diseases

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.
Jonathan Kirk	Good morning (for everyone who's in a time zone where it's morning)! I am Jonathan Kirk from Loyola University Chicago, and welcome to "HFpEF in Metabolic Diseases". We have 3 great talks in this session: Dr. Hossein Ardehali from Northwestern Medicine here in Chicago, Dr. Yajing Wang from Thomas Jefferson University, and Dr. Gopal Babu from Rutgers New Jersey Medical School.
Jonathan Kirk	I'll remind each of the speakers to keep their talks to less than 20 minutes. If they go over, I'll have to go back in time 4 weeks when they were recorded and activate a red blinking light indicating their time is up.
Gopal Babu	Thank you Dr. Kirk for moderating this session
Walter Koch	Hey Jonathan! and all
Jonathan Kirk	Thank you for participating Dr. Babu! I'm really looking forward to it.
Rong Tian	Good morning! Look forward to an exciting session
Farid Moussaviharami	Good morning everyone! Should be a great session.
Jonathan Kirk	For anyone with a question, please step up to the Chat Box. Please no YELLING, #hashtags, memes, or gifs. We should have some extra time at the end as well. Thank you and enjoy the session!
Adam Wende	Jonathan I love the joke, if only time travel were possible... Looking forward to another great session.
Venkatesh Sundararajan	Great session ahead!!! looking forward..
Qutuba Karwi	Hi everyone
Qutuba Karwi	Thanks Jonathan for moderating the session
Walter Koch	go get em Hossein!

Jiang Chang	Hi Hossein, great to see you again
Xinliang Ma	Hello, great to "see" all of you here...
Jiang Chang	Hi Wally, great to you again
Jiang Chang	Hi Ma, nice to you again
Paola Rosas	Hi everyone. This is Paola Rosas from UIC
Dhanendra Tomar	Looking forward to exciting session...
Suresh Palaniyandi	Hi All, Looking Forward a nice session
Joseph Wu	Looking forward to an exciting session on HFpEF!
Yajing Wang	it is nice to 'meet' everyone here
Jianyi Zhang	(thumbsup)
Walter Koch	looking forward to your talk Yajing!
Suresh Palaniyandi	Yes Joe, HFpEF
Walter Koch	Hey Jay !! congrats on being BCVS vice-Chair and Joe Wu thanks for your leadership last 2 years !!
Raj Kishore	Good to "see' you Hossein
Suresh Palaniyandi	good to meet you here Joe Wu, JC, Wally, Venkatesh and everyone
Yajing Wang	sure, thank you Wally!
Abinayaa Rajkumar	Hi everyone!
Joseph Wu	Thank you Wally!
Suresh Palaniyandi	Hi, Raj
Raj Kishore	hello suresh
Joseph Wu	Good to "see" you Raj!
Jonathan Kirk	I like this slide Hossein. When you start at the beginning, you really start at the beginning.
Raj Kishore	likewise Joe
Hossein Ardehali	hello everyone.
Liya Yin	@yajing, looking forward to your talk
Sakthivel Sadayappan	Thanks Hossein!! Excellent start!!
Hossein Ardehali	the thing about iron that is interesting is its role in evolution of life.
Steven Houser	Looking forward to your talk
Venkatesh Sundararajan	Hi Dr. Ardehali, very interesting topic
Xinliang Ma	Nice to see you Hossein! Great work!
Rongxue Wu	Nice to see you, Hossein
Yajing Wang	Liya, nice to 'meet' you
Priscila Sato	Does it matter if it is ferric or ferrous iron in mTOR signaling?
Hossein Ardehali	iron is converted from oxidized form into reduced form in our cells
Priscila Sato	thanks
Suresh Palaniyandi	Hi Hossein, important metal for every one not only "iron Man"
Sakthivel Sadayappan	Jonathan, We love the way you moderate the session!!

Gopal Babu	Hi Hossein, Any interplay between iron and calcium signaling?
Suresh Palaniyandi	Hi Sakthi, nice session and looking forward, my area of research, Thanks!
Jonathan Kirk	Thanks, Satkthi. Its easy to moderate a session with great speakers and an engaged audience. Great work organizing!
Rongxue Wu	Good to "see" you here, Wally
Hossein Ardehali	probably. we have not studied that, but there is evidence that they affect each other
Gopal Babu	Thanks
Venkatesh Sundararajan	@ Dr. Ardehali, does mitochondrial iron level influence mTOR activation?
Meenakshi Madhur	I may have missed this but what cell type are you studying? Could iron regulation be different in different cell types?
Suresh Palaniyandi	Hossein, is there a difference in iron metabolism in each cell types in heart like endothelial cells vs cardiomyocytes?
Walter Koch	You too Rosie!!
Hossein Ardehali	unlikely. we think the regulation is through leucine import into the cells and RAPTR.
Hossein Ardehali	yes, different cells have different levels of regulation, but similar mechanisms.
Suresh Palaniyandi	oh ok, that means it can be regulated by a common factors and mechanism, not cell specfic?
Paul Brookes	How specific is this for JmJCs? Are the other 70+ a-KG dioxygenases also involved? (TETs, ALKBs, PHDs/EGLNs)?
Joseph Wu	Outstanding talk and a great body of work Hossein!
Venkatesh Sundararajan	Thanks, Dr. Ardehali
Hossein Ardehali	great question Paul. we have also studied TETs and we think most of teh effect on MTOR is through JMJC proteins. TETs are also affected but they have other cellular effects.
Rajarajan AmirthalingamThanda	Dr. Ardehali, interesting talk,
WingTak Wong	Great talk
Hossein Ardehali	thanks Joe and Raj. all the work of Jason Shapiro, really bright student.
Paul Brookes	Thanks! Also, since most of these aKGH diox' enzymes use ascorbate as a co-factor, it provides some hints as to how ascorbate is so important for iron homeostasis. Cool work!
Hossein Ardehali	yes, that is why i always tell my patients to take Vit C with their iron supplements.
Gabriele Schiattarella	Very interesting talk. Does iron levels correlates with HFpEF? LVH perhaps?

Hossein Ardehali	yes, there is evidence that iron affects cardiomycyte relaxation and development of HFpEF.
Rajarajan AmirthalingamThanda	There is high ferritin content levels Covid-19 non-survivor compared to Covid-19 survived patients, any comments on this
Raj Kishore	cool data, Hossein
Hossein Ardehali	could be due to iron or it is just an acute phase reactant.
Rong Tian	very interesting, Hossein.
Guo Huang	Nice work, Hossein!
Jonathan Kirk	Regarding the different levels of regulation in different cell types, does this agree with clinical data, i.e., are different organs more/less sensitive to iron deficiency?
Ganesh Halade	Great talk, curious to know do any specific cell develop iron resistance?
Venkatesh Sundararajan	@Dr. Ardehali,Great work!!!
Farid Moussaviharami	Fantastic tyalk!
Jonathan Kirk	Hossein, thanks for the Fe-nominal talk!
Luke Potter	Very cool
Paul Brookes	Great work Hossein (and Jason)!
Qutuba Karwi	Very nice work Hossein! Congrats
Rongxue Wu	So happy for our lab, Hossein!
Ajit Magadum	Nice data Dr. Ardehali
Priscila Sato	Cool work
Brian Orourke	Congrats Hossein
Melissa Lieu	Is mTORC2 iron sensitive as well?
Laihua Xie	Great talk Hossein! Any comments on DMT1 may account for Fe uptake into cardiac myocyte?
Nicole Purcell	Great presentation!
Hossein Ardehali	yes,there is no disease with iron deficiency except for anemia. i have been a cardiologist fro 20 years and have never seen a patient with CM with iron deficiency unless they have significant anemia and get high output failure. our cells are protected from iron deficiency and we only get anemia.
Suresh Palaniyandi	Hossein, Did you check infiltrating cells such as platelets, RBCs, Macrophages contribute to iron-mediated relaxation issue in the heart?
Hossein Ardehali	mTORC2 is unlikely involved. we have checked it and if there is a regulation, it would be through indirect affect by AKT.
Yu Zhang	Very nice talk, Dr. Ardehali. I may have missed this, do you find iron deficiency in patients with metabolic disease that have HFpEF?

Shyam Bansal	Very interesting work, Hossein! Can you comment if Fe regulates HIF or vice versa as HIF is also an important regulator of mTORC?
Hossein Ardehali	Suresh, we have not. it its unlikely that they do.
Rongxue Wu	Hi Hossein, iron deficiency in Covid-19 are reported, have you done any research on that?
Hossein Ardehali	Yu, unlikely.
Hossein Ardehali	yes, iron regulates HIF through PhDs. jason checked all of his studies in ARNT KO cells to take HIF out of the equation.
Farid Moussaviharami	Hi Hossein, are the pathways you showed affected in the aging heart?
Shyam Bansal	Interesting! Thanks.
Kohta Ikegami	Hi Hossein, that you for the great talk. How does the JmjC reduction only repress mTOR factors given the global increase of H3K9me2 by ion deficiency?
Hossein Ardehali	hi Rosie, no we have not. i think it is an indirect effect of COVID 19. it is unlikelty that a virus affects iron levels.
Hossein Ardehali	Farid, likley. we are studying the role of iron in aging, but we have shown that only brain iron levels are affected by aging. whether it also affects the heart, i doubt it
Joseph Wu	Adipocyte dysfunction in cardiac injury is not well studied, thanks for covering this topic Yajing.
Farid Moussaviharami	Thanks Hossein!
Rajarajan AmirthalingamThanda	Hi Rosie, there are reports covid-19 non-suvived had more ferritin content compared to survived patients
Rongxue Wu	It is interesting, thank. Hossein
Yajing Wang	I agree, Joe, Thank you for your comment
Hossein Ardehali	great question Kohta. JMJC reduction has a global epigenetic effect. Jason showed that with his Chip-Seq data. what we know is that one of the effects is on mTOR which leads to significant metabolic changes
Rongxue Wu	Thanks
Melissa Lieu	Thank you, Hossein, Very interesting talk
Hossein Ardehali	Raj, the ferritin levels are likley indirect effects since ferritin is an acute phase reactant
Rajasekaran NamakkalSoorappan	Dr Hossein, Nice to see you again after your recent visit to UAB. Very impact-full IRON story. Congratulations!
Rajarajan AmirthalingamThanda	Thanks Hossein, and congratulations for your great talk
Rong Tian	Yajing, very novel findings! Do you know whether vis fat and subcu fat both contribute?
Raj Kishore	That's a great story Yabing. I am sure you investigated specific cargos in circulating exosomes

Viswanathan Rajagopalan	Very nice talk. Thanks.
Rajarajan AmirthalingamThanda	Great to see you Raj
Liya Yin	@Yajing, did you trace the specificity of exosome targeting to ischemic cardiomyocytes more?
Rongxue Wu	Good morning, Raj, K
Raj Kishore	morning Rosie
Yajing Wang	great question, Rong. in our study, we didnot seperate fat tissue from different place, so I do not know, but very likely they have similar effect.
Suresh Palaniyandi	Yajing, Cool data, My question is which cardiac cells and how you know the exosomes are specifically from adipose tissue? perhaps i missed it
Ronglih Liao	Great talks! learned a lot!
Mei Methawasin	@Yajing, can the exosome be delivered through the intravenous route ? will it be different from injection into the myocardium?, very interesting data.
Yajing Wang	Liya, excellent question, we didnot trace it, we use maker to pin down it from adipocytes.
Raj Kishore	Yajing: did you try to inhibit miR 130b directly in exosomes before cardiac treatments?
Rongxue Wu	Hi, Yajing, very novel findings! Does mir130 level change in patients with diabetes?
Liya Yin	@yajing, great talk
Jonathan Kirk	Yajing, this is really interesting. I've been banking epicardial fat from all of our heart transplant patients for the past couple years. If these samples would be of any help to you, please contact me.
Kimberly Ferrero	What a fascinating talk! Thanks, Yajing
sini sunny	Hi Yajing, nice information.
Yajing Wang	Suresh, we transplanted adipotissue from HFD to WT mice whose fat tissue was moved, to find the similar effect. Also injection of cultured adipocytes exo showed similar results.
Joseph Wu	Very interesting topic, really enjoyed your talk Yajing,
sini sunny	Whether there is any connection with lipid accumulation and exosome secretion in adipocytes?
Raj Kishore	Fantastic work, Yajing
Yang Xiang	very interesting! Yajing
Liya Yin	@Jonathan, That is a great idea because the epicardial fat has been implicated for cardiac protection@Yajing
Jonathan Kirk	Thanks, Yajing. Your talk was fat-tastic!
Farid Moussaviharami	Great talk.
Yi Tan	Yajing, very nice talk!

Suresh Palaniyandi	Fat-tastic(haha) Kirk, lol
Yajing Wang	Mei, we direct inject to heart to foucus on the cardiac effect to research the direct effect on heart. tail injection do need more isolated exos.
Amadeus Zhu	Waiting to see what kind of pun Dr. Kirk comes up with for this talk :)
Mingfu Wu	Yajing, great work
Suresh Palaniyandi	Hi Gopal, Looking to learn about DMD., is it a HFpEF type in DMD?
Gopal Babu	Not really..but diastolic dysfunction is one of the major start point for HF in DMD
Yajing Wang	Raj, great questions, no, we didnot do specificly inhibit exo miRNA. We could colorbrate since I would like to know more how effectly inhibit it in exos. You are expert, no doubt.
Yajing Wang	Rongxue, yes, it did change in patients.
Yajing Wang	thank you, Liya, Kim and all
Kimberly Ferrero	@Amadeus -- we know Dr. Kirk is the king of sarco-sm with puns like that!
Yajing Wang	Jonathan, sure! We do need collorborate. Thank you!
Yajing Wang	Joe, thank you! I am so encourage by all of you and this sectiom. Appreiciate the opportunity!
Yajing Wang	Sini, great question, I do not know so far.
Elizabeth McNally	Did you look at respiratory function with SLN deletion?
Michelle Parvatiyar	Hi Gopal, Great talk! Do you think that co-segregating mutations in the sarcolipin locus that alter its expression may modify the severity of dystrophic diseases?
Gopal Babu	No
Gopal Babu	@Dr. McNally, no we did not study the respiratory function in these mice. We measured diaphrgam function in mdx:utr-/- and it was improved
Yibin Wang	Yajng, Congrats again! My question is do you know what is in the exosomes from normal fat that contributes to the protective effects?
Gopal Babu	@Michelle, I don't think so..however we haven't studied
Yibin Wang	great presentation and exciting science
Elizabeth McNally	better respiration —> better heart function. Might be really important in HFpEF. Definitely important in DMD.
Yajing Wang	Kirk, Suresh, lol, fat-tastic!
Sakthivel Sadayappan	Dr. Babu, Great to see you and thank you for your presentation.
Suresh Palaniyandi	It is a nice work and talk Gopal
Yajing Wang	Thank you for all your comments!
Gopal Babu	@McNally..We do have some data on other HF models which so SLN is important for HFpEF

Santosh Maurya	Dr Babu: Skeletal muscle specific SLN-overxpression mice do not develop any muscle dystrophy/atrophy. Please comment.
Gopal Babu	@SLN is abundant in the skeletal muscles of higher mammals..Also it may not have any effect on normal skeletal or cardiac muscle
Yibin Wang	@Hossein, Very exciting talk and discovery. I wonder if the same epigenetic factor regulates mTOR expression as well as LAT3? Or through different mechanisms?
Rachelle Crosbie	@ Dr. Babu. Really great talk. The effect of SLN on mdx:ur-nulls is very impressive, particularly with fibrosis reduction. Did you look at cardiomyocyte membrane damage?
Kimberly Ferrero	Dr. Babu, great talk! Curious, was that an increase in the ryanodine receptor in the mdx:utr-/- mice compared to WT? In your western blot series a few slides back. And if so, do you think it's related to the change in mito morphology?
Shyam Bansal	@ Dr. Babu: Did sarcolipin levels affect inflammation in the hearts/mucles/circulation?
Gopal Babu	@Rachelle..yes..it was better than mdx:utr-/-
Sakthivel Sadayappan	Dr. babu, Is there a difference in the level of SLN expression between mouse strains? Fvb/N versus C56BL6?
Sakthivel Sadayappan	in skeletal muscles
Grace Muller	Dr. Babu, is SLN more highly expressed in the atria? Were there any atrial pheotypes that you noted that were striking?
Gopal Babu	@Kimberly, We did not find any change in RyR
Rachelle Crosbie	very nice!
Gopal Babu	No Sakthi...
Elizabeth McNally	Hi Rachelle!
Rachelle Crosbie	Hi Beth!! great to see you here!
Jonathan Kirk	Gopal, that was a Darn Magnificent Discussion of sarcolipin in DMD. Thank you!
Susumu Minamisawa	Hi Dr. Babu, great talk! we also found the similar results in skeletal muscles of mdx/slnko mice. In the heart, gene dosage effect seems weak. Do you think that heterozyous deletion would be sufficient?
Joseph Wu	Greta talk Gopal!
Farid Moussaviharami	Great talk!
Gopal Babu	@Shyam..yes but we do not know the mechanisms
Jonathan Kirk	Thank you to all 3 speakers! We have 9 minutes for additional questions and discussion on all 3 talks.
Viswanathan Rajagopalan	Thanks Dr. Babu
Danish Sayed	Great talk Gopal
Jamie Francisco	Great talk Dr. Babu!
Shyam Bansal	thank you

Laihua Xie	Great talk Babu! Congrats...
Elizabeth McNally	Great talks all!
Charles Chung	Thank you all the speakers for introducing me to new concepts in metabolic diseases. -and Jonathan for showing off his better than moderate moderation skills!
Supriya Hota	Thank-you Dr. Babu! Are there any therapeutic drugs available to reduce SLN expression?
Venkatesh Sundararajan	Excellent work!!! Dr. Babu
Elizabeth McNally	Extra credit points to the moderator!
Liya Yin	Great session! Thank you
Gopal Babu	@Grace..there is a small upregulation in atria also..also sln+/- mice show improvement
Dominic DelRe	Great talk, Babu! Thanks to all speakers and to Jonathan for superb moderation!
Ganesh Halade	Nice talk Gopal
Gopal Babu	@Jonanthan..thanks
Venkatesh Sundararajan	Excellent moderating, Kirk
Grace Muller	Thanks for the talk!
Farid Moussaviharami	Dr. Babu, do you think the effects are specific to sarcolipin or any treatment that affects calcium levels?
Rajarajan AmirthalingamThanda	Great talk, Babu!
Jonathan Kirk	Dr. Babu, are there any known post-translational modifications on SLN that can affect function?
Gopal Babu	@Susumu..yes..heterozygous mutant is sufficient...complete KO is not good for diaphragm
Suresh Palaniyandi	Good session, Thanks speakers, moderator and the organizers
Gopal Babu	@J Wu..Thanks
Gopal Babu	Thanks Danish
Gopal Babu	Thanks Lai-Hua
Yajing Wang	Yibin, great question! We donot know so far. That is our future work....
Ganesh Halade	Question to Dr. Hossein - Great talk, curious to know do any specific cell develop iron resistance?
Gopal Babu	@Supriya..no we are screening for small molecules
Jun Feng	Thanks all presenters, great work. I would like to ask Dr. Wang about animal models of diabetic cardiomyopathy. It seems that Dr. Wang used a myocardial infarction model under HFD?
Hossein Ardehali	i am not sure what iron resistance means. but all of our cells are sensitive to the oxidative stress of iron excess.

Gopal Babu	@Farid...effects are becuase of Calicum normalization..we found some signaling pathways that are activated in the SLN deficient DMD hearts
Gopal Babu	@Jonathan...yes..nitration
Santosh Maurya	Dr Babu: Do you think inhibition of RyR-mediated Ca2+ leak would have similar effect as SLN deletion in DMD?
Gopal Babu	Thanks Sakthi, Loren and Jill .. Great session.. Thanks for the opportunity
Ganesh Halade	Thank you D. Hossein !
Gopal Babu	@Santosh...there are some studies on RyR leak and DMD
Sakthivel Sadayappan	Thanks to all the speakers for their excellent presentations and the star moderator, Dr. Kirk, for this wonderful session!!
Santosh Maurya	Thank you. Excellent work. A novel insight on SLN.
Yajing Wang	Jun, yes, you are right, we did infarction on diabetic model. the relationship between adipocyte and cardiomyoopathy is on going....
Jonathan Kirk	Thanks everyone!

Concurrent Session 7B: Cardiotoxicity of Cancer Therapeutics: Mechanisms and Potential Therapies

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.
Anand Singh	Good Morning Joe..
Richard Becker	Hi everyone! My name is Richard Becker, MD from University of Cincinnati Heart Institute. I am one of the moderators for session 7B: Cardiotoxicity of Cancer Therapeutics: Mechanisms and Potential Therapies. We have terrific speakers and great topics. Please feel free to post your questions to the speakers in this chat. Enjoy the session!
Bonnie Ky	Thank you, Richard! Welcome everyone! This is Bonnie Ky.
Richard Becker	Good morning Bonnie. Richard
Anand Singh	Thanks Richard, Looking forward for the awesome talks..
Keith Jones	Good morning everyone
Sumanth Prabhu	Looking forward to the presentations this morning!
Jil Tardiff	Fantastic and timely topic
Sumanth Prabhu	Keith, good to 'see' you
Joseph Wu	Looking forward to an exciting session on chemo cardiotoxicity!
Richard Becker	Off to a wonderful start.
Rong Tian	well said! Thanks to the organizers for a timely topic
Jil Tardiff	Part of our continuing efforts to include clinical investigators to help set the framework and present the primary questions that need new basic approaches to answer.
Jiang Chang	echo Rong Tian
Sumanth Prabhu	Great approach, Jil. You, Sakthi and Loren have put together an outstanding program.
Joseph Wu	I agree. Good way to start the session with a clinical talk, and no better choice of speaker than Bonnie (editor of JACC CardioOncology)
Jil Tardiff	The differences in those curves is truly interesting. These longitudinal studies are game-changing in cardiomyopathy studies
Matthew Wolf	Are the patents also undergoing cMRI to evaluate changes in myocardium, fibrosis, or edema? Just curious.
Sakthivel Sadayappan	Dr. Becker, Thank you for charing this exciting session.

Bonnie Ky	Thank you, Jill. Appreciate the feedback and the honor of this invite. I agree with others. Thank you for highlighting cardio-oncology and also bringing clinical investigators to the sessions.
Richard Becker	An honor and a pleasure Sakthi.
Bonnie Ky	Dear Matthew, in the Penn CCT cohort, we have not obtained cardiac MRIs. We only have cardiac MRIs in a small subset as part of another study of patients evaluating effects of radiation therapy.
Sakthivel Sadayappan	Dr. Becker leads the cardio-oncology program at University of Cincinnati Medical Center!
Bonnie Ky	Matthew (part 2) - I will say, however, the W. Greg Hundley has a strong body of work evaluating cardiac MRI and the changes seen in cardiac function seen with anthracyclines.
Matthew Wolf	thank you
Sumanth Prabhu	Bonnie, can you comment on the conceptual difference between direct cardiotoxicity (DOX) versus more of an interruption of cardiac homeostasis (herceptin), with implications for recovery
Fady Malik	Is background HF therapy initiated in these patients when the drop in EF is observed? Does that account for any of the recovery or is that in the absence of background therapy?
Jil Tardiff	It's like re-setting the baseline, kind of re-setting contractile reserve in genetic cardiomyopathies. Fascinating.
Bonnie Ky	Sumanth, thanks for that question. Certainly, the concept of recovery is more prevalent with trastuzumab. Actually, Joe Wu - if he's still on - had a great paper in Circulation detailing this and discussing metabolic modulation. See his Figure 6.https://www.ahajournals.org/doi/full/10.1161/CIRCULATIONAHA.118.037357
Madhumita Basu	Is there an increase in uncoupled endothelial nitric oxide synthase levels noticed?
Rene Packard	This is a terrific body of work - congrats.
Sumanth Prabhu	Thank you
Joseph Wu	Great talk, thank you Bonnie!
Bonnie Ky	Fady, great question. Yes, typically with a decline in EF, neurohormonal therapy is initiated. However, we are looking to evaluate the longitudinal data in greater detail with greater numbers. There are transient declines in LVEF that will also spontaneous recovery. I do think it depends upon the cardiotoxic therapy - i.e., doxorubicin or trastuzumab or radiation.
Hind Lal	Thanks @ Bonnie for the great presentation
Richard Becker	Thank you Bonnie. Terrific presentation.

Rong Tian	impressive work, learned a lot!
Ronglih Liao	congrats Bonnie for the outstanding work and thanks for sharing w/ us
Matthew Wolf	Fantastic talk.
Steven Houser	Very nice talk Bonnie
Jil Tardiff	This was great, Bonnie - thanks a million for participating.
Bonnie Ky	Madhumita, we have not specifically evaluated that question. If you have suggestions on how to quantify that, please let me know.
Bonnie Ky	Thank you Rene!
Ivor Benjamin	Excellent talk, Bonnie
Sumanth Prabhu	Outstanding presentation, Bonnie!
Bonnie Ky	Thank you, Joe!
Fuli Xiang	Excellent talk, I have learned a lot! Thank you Bonnie:)
Sakthivel Sadayappan	Excellent presentation, Bonnie!! Well done..
Xiongwen Chen	Hi Dr. Field. Good to see you here.
Sakthivel Sadayappan	I am a fan of Dr. Field's research!!
Loren Field	Ditto :)
Madhumita Basu	Sure! Thanks for an excellent presentation, Bonnie.
Steven Houser	Great to see you Loren
Bonnie Ky	Thank you all for the kinds words (I won't clog up the chat with individual thank you's) - again, I appreciate the invite and thank you for your inspiring science. Privileged to be part of this stellar group.
Huabo Su	Great to "See" you again Dr. Field
Loren Field	Hi Steve & Huabo
Zhaokang Cheng	Exciting research Dr. Field!
Jil Tardiff	Hi Loren - nice to "see" you. Did you see any diastolic dysfunction in your Dox mice? We did (actually very similarly to Bonnie's findings). We were perplexed at first.
Katherine Yutzey	Hi Loren, Could CM "atrophy" be lack of physiologic hypertrophy?
Loren Field	Hi Katherine - we see the same atrophy in adult hearts, as do many other labs using acute delivery
Loren Field	Hi Jil - not sure about dystolic - If Wuq is on-line (he did the analyses) he might be able to comment...
Jil Tardiff	Thanks!
Luay Boulahouache	Dr. Ky thank you for your presentation, I was wondering how did class 3 recover while class 2 failed to do so and maintained that moderate level
Anand Singh	What dose was used to treat animals with DOX
Bonnie Ky	Luay- given the significance of the magnitude of the decline, Class 3 were typically treated with cardiac medications. Given the "low level" declines in Class 2, which were still largely

	above the threshold of nomral, there was typically no meds initiated. These are also all core-lab quantified LVEFs.
Walter Koch	Hey Loren ! - hope all is well!
Guo Huang	Hi Loren, can you also see whether the mRNAs of Ku70/80 are also reduced in the late stage?
Loren Field	Anand - will look up and post it for you during the next talk...
Bonnie Ky	Jill, how did you measure diastolic dysfunction in the animals? We have also in some tumor-bearing animals treated with doxorubicin observed more of a HFpEF phenotype and with a relatively preserved LVEF.
Anand Singh	Thanks Loren..
Zhaokang Cheng	Dr. Field, Excellent talk! DNA-damaging chemotherapy selectively kills cells with higher proliferative activity. Could you comment how D2 heart has reduced level of apoptosis?
Fuli Xiang	Bonnie, may I ask what is the current major treatment for the onco-cardiotoxicity in patients?
Loren Field	70/80 went up in late stage wt but was about the same in late stage D2; barely detectable in saline treated animals
Loren Field	You to Wally!
Rene Packard	Measuring diastolic function in mice is feasible but difficult. To measure E/A they require significantly more / longer sedation which changes their heart rate and is problematic if doing a survival / longitudinal study.
Venkatesh Sundararajan	@Loren, Nice work!!! DOX also significantly accumulates within mitochondria. Did you see any effect on mitochondrial function ?
Joseph Wu	Great to "see" you Loren. Really enjoy hearing these interesting experiments and studies you're working on.
Heinrich Taegtmeyer	Very exciting, Loren!
Matthew Wolf	Do the S-phase events in the D2 mice correspond to an increase in ploidy, proliferation, or both? Just curious.
Luay Boulahouache	Thank you Bonnie!
Loren Field	Anand - mice got 5 weekly intra-peritoneal injections of 5 mg/kg DOX (25 mg/kg cumulative dose
Heinrich Taegtmeyer	Activation of the fetal gene program with atrophy?
Bonnie Ky	Fuli, can you please clarify? Do you mean what is the distribution of cancer therapies across all cancer patients? I have not seen that reported. But in general, the list of cardiotoxic therapies includes anthracyclines, trastuzumab, TKIs, proteasome inhibitors, immune therapy. There is an example though here - please see this central illustration.https://cardiooncology.onlinejacc.org/content/2/2/270
Anand Singh	@ Loren. Got it. Thanks.

Richard Becker	Loren, How is your group approaching the translation to patients treated with DOX? Richard Becker
Bonnie Ky	Rene, thank you.
Loren Field	Hi Venkatesh - we looked at a few mitochondrial markers but were never comfortable with the readout, so cannot answer your question with any degree of certainty
Coralie Poizat	Very nice work! I am wondering if the reverse proliferation of cardiomyocytes, which is clearly beneficial for Dox-induced cardiomyopathy, could be detrimental in clinical setting for cancer cells?
Hind Lal	Looking forward to your talk Carrie !!
Sakthivel Sadayappan	Loren, In some pilot studies that CDK 4/6 inhibitors can perform tumor suppressive and normal tissue protection during cancer therapy. Do you have any comments on using palbociclib, an CDK4/6 inhibitor, along with cancer drugs?
Sean Wu	Great talk Loren!
Sumanth Prabhu	Hi Carrie, look forward to your presentation!
Rene Packard	Thank you Dr. Field
Loren Field	Hi Joe - Hope you are well - I just changed an old Fiat motor and thought of you :)
Rong Tian	Great talk, Loren!
Ajit Magadum	Very exciting data Dr. Field.
Carrie Lenneman	Great set of talks by Loren and Bonnie.
Ronglih Liao	great talk Loren!
Venkatesh Sundararajan	@Loren, Thanks for the answer
Loren Field	Hi Matthew - there is cell division in the model (see increased CM number as the animals age) - I am sure that there is also ploidy increases occurring in the model as well.
Joseph Wu	Loren, send me photos :-)
Guo Huang	Nice work, Loren! Is it possible to express D2 in the heart to reverse the Dox-induced cardiotoxicity rather than to prevent it?
Loren Field	Hi Heinrich - hope you are well, and that we can meet up at a meeting in Germany some time soon!
Matthew Wolf	thank you, great presentation
Bonnie Ky	Great talk, Loren! I may reach out to you to discuss your acute/chronic models.
Richard Becker	Carrie, I love the time scale and history as a backdrop. Do anthracyclines exert vascular toxicity?
Fuli Xiang	Bonnie, I meant the treatment for the cardiac function impairment in the onco-patient:) The reason I am asking is that Entrasto only showed effect on the moderate EF group in

	HFpEF. I saw the different classes of your patient and wondered if it may also correlated to the treatment outcome.
Loren Field	Hi Zhaokang - the measurements were performed 1 week or 13 weeks after DOX treated - we did not look when the drug was onboard but I suspect that we would see more similar numbers as you suggest.
Carrie Lenneman	Yes we know that endothelial dysfuntion occurs very early during treatment, but we do not test for that on regular basis. EndoPat is a good way we have looked at early toxicity from Ac.
Zhaokang Cheng	Thank you Dr. Field for an excellent talk!
Loren Field	Sakthivel - we never tried the CDK4/6 inhibitors in our system but suspect that they would further impair the cyclin D2 phenotype.
Richard Becker	Have you been able to document impaired brachial reactivity that persists after treatment?
Bonnie Ky	Fuli, okay thanks! We have not systematically compared therapies. Honestly, our treatment for cardiovascular complications are not very targeted, with possibly the exception of what Carrie is showing here (although dex is prophylactic). Typically, we treat with neurohormonal antaongists... someone should do a trial with sGLT2i!! There is an entresto study in Norway - PRADA 2 by Torbjorn Omland underway. This is for anthracyclines.
Carrie Lenneman	No I have not looked at long term survivors vascular function, but definitely something we should do.
Loren Field	Guo - yes, I would thin that cell cycle induction post-DOX would reverse damage.
Guo Huang	@Loren, thank you. Hope to see you again soon.
Fuli Xiang	Thank you Bonnie:) Agree, sGLT2i rocks!
Ronald Vagnozzi	Hi Loren, thanks for a great talk. Wondering your thoughts on how much just reactivating the cell cycle might intrinsically protect myocytes in your model (for example via DNA damage pathway you showed), versus increasing myocyte number?
Carrie Lenneman	Agree with Bonnie - many new CV agents out that we need to examine the CV impact such as sGLTi.
Joseph Wu	Carrie, thank you for connecting clinical case presentations with the biology of cardiotoxicity
Carrie Lenneman	Thank you Joseph - cardio-oncology is the perfect field for translational research - bridge between bench and bedside.
Loren Field	Hi Richard - I think it would be really interesting to see if there are intrinsic variations in CM cell cycle activity vs. patients who recover better than others - the cleanest way to do it would be via the approach that Frisen and Bergmann used with C14

	incorporation. That would be a good proof of concept. Translation would require ongoing efforts from a lot of groups to promote CM renewal to work. ljf
Jil Tardiff	Beautiful talk, Carrie. So important to present these trajectories to drive home how dynamic the remodeling really is - important for basic scientists to visualize this process and not assume that the time course is inexorably downward or linear . Changes the perception of possible mechanisms
John Ralphe	Very nice talk Carrie- heartedly agree with Jill's previous comment!
Loren Field	Hi Ron - that is a good question, and I had not thought of it previously. Easy enough to test (ie just score the apoptosis rates in BrdU positive vs negative cells) - that being said, there are so few cells per section it would be a hell of a lot of screening...
Carrie Lenneman	It is very dynamic state of the CV system after cancer treatment. Agree we are finding ways to improve CV repair after cancer treatment.
Rong Tian	questions for all speakers: What is the state of art patient management for chemo cardiotoxicity?
Rong Tian	Oh, Carrie, your slide answers that!!!
Venkatesh Sundararajan	@Carrie, Very interesting topic and most wanted!!! connecting Oncology and Cardio- systems involved in two top leading causes of morbidity, Curious to know whether DOX resistance are reported in patients?
Rong Tian	Thx for a great talk, Carrie!
Rene Packard	Thank you to the speakers and organizers for a terrific session. The intertwining of basic science and clinical course was very informative.
Bonnie Ky	Rong, I think it depends upon what exact treatment you are talking. And also if you are talking prevention or management. I think a critical need in the field is risk-guided cardioprotection.
Carrie Lenneman	It really depends on the cancer treatment a patient is exposed to during treatment.
Bonnie Ky	Great talk Carrie!
Sumanth Prabhu	Outstanding talk, Carrie. Can you comment on endothelial predominance of effects (versus direct myocyte effects) and the implications for prognosis
Anand Singh	Great Talks on this session. Thanks
Joseph Wu	Great talk Carrie!
Richard Becker	We have time for questions and comments.
Fuli Xiang	Thank you Carrie. Very informative and inspirational talk!

Bonnie Ky	Rong (continued): And risk guided can mean - clinical risk, risk by iPSC phenotyping, risk by imaging or risk by biomarker. We have 2 ongoing pilot studies of risk guided cardioprotection with biomarkers in one and clinical risk score in another. However, treatment for HF/cardiomyopathy is largely neurohormonal antagonists.
Sakthivel Sadayappan	Great session. Thanks to the speakers and moderator!!
Sumanth Prabhu	Thank you for these presentations!
Heinrich Taegtmeyer	To follow up on Sumanth's question: Can you comment on the loss of pericytes with sunitimib treatment? Beautiful talk!
Jil Tardiff	Bonnie - will be interesting to see how the genetic predisposition sorts out. Eventually "easy" to evaluate prior to therapy and let this information help select less "risky" drug combos.
Rong Tian	@Bonnie, thx! That is really helpful information for non-physicians.
Bonnie Ky	Jill, definitely. We are trying to do those studies... if only NIH will agree with us to its significant, impact and approach. ;)
Carrie Lenneman	It is thought that if we can detect endothelial dysfunction early that cardiomyocyte damage may be mitagated with anthracyclines. There is some nice work with statins and anthracyclines. For anthracyclines the myocyte death is not thought to be reversible. However with VEGF, Her2 antagonist and TKI CV effects are felt to be reversible because the cardiomyocyste damage is not seen.
Sean Wu	Thanks a lot Carrie for the clinical insights and the latest therapeutic approachs to cardio-oncology.
Jil Tardiff	Laughing - been there, done that. Going to reach out at some point, may have just convinced the NIH re: our work on potential genetic risk.
Richard Becker	If there are no additional comments or questions, I will offer a sincere “thank you” to our expert speakers who provided scholarly, thought-provoking and inspiring perspectives on the important topic Cardiotoxicity of Cancer Therapeutics: Mechanisms and Potential Therapies. I thoroughly enjoyed the session and trust that you, our attendees did as well. Enjoy the remaining sessions and have a great day. A special thanks to the BCVS organizers for bringing high impact to a virtual platform.
Bonnie Ky	Aarif Khakoo also had a nice paper on pericyte loss with sunitinib years ago in Sci Translational Med.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3833098/

Venkatesh Sundararajan	@ Thanks, Carrie
Carrie Lenneman	HT - great question about pericytes with suntent. Not sure it has been examined, something I need to investigate.
Rong Tian	Each class of drug has distinct mechanism of toxicity, would it be effective to develop mechanism specific biomarker and/or protection?
Maria Cimini	Dr. Lennmeman, are lymphatic vessels very impaired also?
Fuli Xiang	Bonnie and Carrie, I am wondering if the cardiac damage caused by the onco drugs are similar to the Methamphetamine-Induced Cardiomyopathy (MACM).
Jil Tardiff	Just a reminder - chat transcripts are also available to review, usually posted the next day!
Sean Wu	@Bonnie and Carrie - With the expanding use of immunotherapy, have you see any who had previous anthracycline toxicity that then receives immunotherapy? Is there additional risk that you anticipate for doing this?
Carrie Lenneman	Clinically speaking in breast cancer there is injury to lymphatics due to radiation and surgery. Not sure anyone has looked at the their response to various chemotherapies.
Bonnie Ky	Rong - Yes!!! That would be the goal! We have been limited in achieving these successes in cardio-oncology. But we are trying to discover more mechanistic biomarkers, certainly. Right now, clinically, we are using troponin and ntprobnp only. But we need more science and have been investigating oxidative stress markers (ADMA, MMA, etc).https://pubmed.ncbi.nlm.nih.gov/28683962/
Rong Tian	thx, Bonnie!
Bonnie Ky	Sean, this has not been studied systematically but one of my patients just did suffer from ICI myocarditis - normal LVEF - but also did have anthracyclines before. Anthracyclines cause "low level injury" - as manifested by our human data with echo and biomarkers. Whether somehow that translates to an inadequate compensatory response of some sort is not clear. Mechanisms of dysfunction here completely different though, as of course you know (better than me with the great work you are doing!)
Sean Wu	Thx Bonnie! Really enjoyed your talk.
Bonnie Ky	Thanks Sean! Great to chat with you!
Carrie Lenneman	Currently not known if immunotherapy after anthracyclines poses more risk. More systematic studies are greatly needed. We know CV ICI related effects appear to occur early after exposure and more common in combined immunotherapy.
Sean Wu	Ditto!

Carrie Lenneman	Thank you everyone!
Sean Wu	Thanks Carrie!

General Session 8: Molecular Mechanisms of Cardiac Hypertrophy (BCVS-HFA Joint Session)

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.
Rebekah Gundry	Hello everyone and welcome to this session. I am your moderator, Rebekah Gundry from the University of Nebraska Medical Center. We have three excellent talks lined up for you. If you have any questions, please post them in the chat and if they are not answered during the session we will have time at the end for questions. Enjoy the Session!
Qutuba Karwi	Hi Rebekah, thanks for moderating this session
Joseph Wu	Looking forward to the session Rebekah. Congrats to new job at UNMC! Joe
Rebekah Gundry	My pleasure, Qutuba! Thanks for joining us today!
Rebekah Gundry	Thanks, Joe! I am loving it here at UNMC!
John Ralphe	Hi Rebekah-- thanks for moderating!
Dhanendra Tomar	Looking forward to exciting session..
Rebekah Gundry	Thanks, John! Thanks for joining us today!
Laura Senatus	Looking forward to this session.
Jonathan Kirk	Hi Carter! Looking forward to your talk.
Niels Voigt	Good morning everyone. I am looking forward to an exciting session. Thank you Rebekah for moderating.
Sakthivel Sadayappan	Welcome everyone. This is the first time effort to have a collaborative session with the Heart Failure Association. A special thanks to Dr. Johannes Backs for the efforts.
Kimberly Ferrero	Thank you, Dr. Sadayappan! Looking forward to several great talks in this session.
Sakthivel Sadayappan	Thanks Carter!! Great start!!
Jiang Chang	Good morning very one
John Ralphe	Reverse C- and n-terminal designation...
Sakthivel Sadayappan	Thanks Rebekah for charing this session!!
Rebekah Gundry	Hi Sakthivel! My pleasure! Thanks for joining us today! It will be a fabulous session!
Elizabeth McNally	If there is C protein, Sakthivel is happy!
Sakthivel Sadayappan	Ha ha
John Ralphe	Some people are sooo easy!
Brett Colson	Lol!

Jianyi Zhang	(thumbsup)
Sakthivel Sadayappan	Brett, what are you doing here?
Maria Kontaridis	Hi John, nice to see you again! Great talk so far!
John Ralphe	Hi Maria! Good to 'see' you! Thanks!
Sakthivel Sadayappan	How much replacement of these mutant proteins?
Randy Faustino	Hi Carter! Great to (virtually) see you again, enjoying your talk :)
John Ralphe	This is complete replacement on the KO background, total cpro levels reach wild type control levels
Venkatesh Sundararajan	@ Great work!!! on an important protein, cMyBP-C
Joseph Wu	Great talk John and great to "see" you!
Rebekah Gundry	@John Ralphe - Can you comment on the ease at which your hPSC-CM engineering method can be implemented? If someone has a lot of experience with generating hPSC-CM, but not yet gone on to implement such 3D/force models, can you advise on the level of difficulty encountered when trying to get it up and running?
John Ralphe	Thanks Joe!
Brett Colson	Sakthi, here to expand my horizons to learn about this C protein I've been hearing about. Hi John! Great talk!
Ajit Magadum	Nice Work!
Jonathan Kirk	Carter, any comment on the change in Hill coefficient you observed?
John Ralphe	Students master the technical manipulations easily over 1-2 months generally. The equipment investment is approx 50K, and we use things off the shelf with minimal customization.
Rebekah Gundry	Thanks!
Hesham Sadek	Excellent talk. Are these predicted structural changes?
John Ralphe	The Hill coefficienty (and sensitivity shift) did not reach significance. This is also a measure of extracellular sensitivity so one more step removed form 'true' calcium sensitivity....
Jonathan Kirk	Oh - I thought I saw a star there - gotcha.
John Ralphe	nope- no real or implied star there :)
John Ralphe	Hesham- no predicted structural changes based on modeling we found completed by Zhang et. al.
Joseph Wu	Great talk again, thanks John!
Hesham Sadek	great, thank you
Ying Ge	Good job Carter!
Adam Wende	Nice study, thank you for sharing. Looking forward to seeing more in the future.
Renzhi Han	Nice work. Thanks for sharing
Jonathan Kirk	Great talk, Carter! Really interesting stuff.

Rebekah Gundry	I particularly loved the successful implementation of Mass Spectrometry to find new proteins of interest! (hearteyes)
David Barefield	Hi Carter, great work, how many other missense mutations in that region might affect that binding pocket? It looks like most cardiomyopathy missense mutations are going to have different mechanisms of pathophysiology
John Ralphe	Thanks very much for the fedback! And I am also looking forward to seeing more :))
Sean Wu	Great talk!
Jie Xu	Great talk John! Really learned a lot!
Darshini Desai	Great talk, Dr .Carter! which is the better model to study the mechanism of hypertrophy 3D or 2D HiPSC-CMs
Prabhat Ranjan	Really interesting session
Shyam Bansal	@Katherine: Did you look at intermediate time-points? say p7?
Rebekah Gundry	Anyone else having interruptions in the streaming of this talk? or just my wifi....
Sean Wu	@Rebekah - ok for me so far
John Ralphe	David-- this is one of our principle theories- these mutations exert different effects on protein function dependeing on their location. How and why all roads then get to Rome (HCM) is an interesting question...
Katherine Yutzey	@shyam Its coming up later...
Shyam Bansal	(angelic)
Hesham Sadek	anyone else enjoying this format more than live lectures?
Sean Wu	@Katherine - I'm expecting a valve growing out of the myocardium any minute..
Shyam Bansal	(wave)
Jianyi Zhang	me(thumbsup)
Mingfu Wu	I enjoy this format very much
Ajit Magadum	@ Dr. Sadek. I love it.
John Ralphe	Darshinni-- I think 2D and 3D offer different opportunities and can in the end be quite complimentary. For iPS cells it comes down to having enough consistency and awareness of developmental status to be able to draw relevant conclusions.
Walter Koch	Heshem et al., please think about ways we can combine best of both worlds for future meetings !
Hesham Sadek	Will do
Zhaokang Cheng	@ Dr. Koch (thumbsup)
Suresh Verma	@ Prof. Sadek. Yes. But live are always best.... I agree with Prof. Koch.
Sudarsan Rajan	A copy of chat along with the transcript and notes, available in future will be worth it

Maria Kontaridis	Hi Katherine-beautiful work. What happens/role of early activated fbs if not to convert to myofibroblasts? Is this what defines physiological vs pathological response?
Nicole Purcell	Great talk Katherine! Good to see you.
Adam Wende	Sudarsan, I saw that Jil Tardiff mentioned the Chat transcript should be available within 24 hrs of the talk.
Sean Wu	@Hesham and Wally - I would love to have both live stream and in person available in future meetings so I can still network with colleagues in person yet not having to rush from one room to the next
Suresh Verma	@ Sean agree...
Sakthivel Sadayappan	Sudarsan: yes, all the chat conversations will be available to you!!
Katherine Yutzey	We think that the postn cells are active to make collagen, but maybe not the full pathology of an SMA myofibroblast. Postn and SMA may be different types of fibroblasts
Rebekah Gundry	I echo Sean Wu's request. I'd love to have live watch parties of pre-recorded talks - so time can be spent networking (not last minute talk edits) or rushing room to room.
Sudarsan Rajan	(thumbsup)
Ajit Magadum	(thumbsup)
Rebekah Gundry	and I really like the instant feedback from speaker on questions as you go along in the talk. And - I suspect that more questions are asked in a chat room format b/c it provides less intimidating format for asking questions - which might encourage some attendees who might be less likely to step up to a microphone in a big room
Hesham Sadek	Great talk Katherine! Do you think that this temporal pattern of proliferation fits with recent studies by Bin Zhou and Eldad Tzahor showing that fibroblast senescence is required for myocyte proliferation during neonatal heart regeneration?
John Ralphe	@Rebekkah Gundry-- When Ying Ge is your next door lab neighbor the potential to apply mass spec seems limitless!
David Wolfson	Dr. Yutzey, do you think the Postn and SMA fibroblasts originate from different populations or there are different transcriptional landscapes that prevent these Postn cells from transition to myofibroblasts
Michelle Tallquist	Are any of the periostin cells vsmcs? In the constitutive cres there are vsmcs lineage graced.
Katherine Yutzey	Hi Hesham, I do think that the fibroblasts could be involved in the loss of regenerative potential, but have not checked yet.
Rebekah Gundry	@John Ralphe - yes! Ying Ge rocks! And you also have a few other fabulous MS-neighbors so there is practically no limit to what you can to where you are!

Brian Orourke	Why only 50% reduction?
Joy Lincoln	@Katherine. Do you get more ECM when you ablate the Postn+ cells?
Katherine Yutzey	David, we have not seen SMA+ cells come from the Tcf21 or Postn+ in the developing heart. I am not sure if this is the same with injury.
Katherine Yutzey	Hi Joy, we did not see a change in the ECM overall, could be the we did not ablate enough cells...
Fuli Xiang	Beautiful work, Katherine!
Joseph Wu	Katherine, outstanding talk and a beautiful body of work on cardiac fibroblasts.
Katherine Yutzey	Hi Brian, I think the TAM/DTA system has some accessibility/variability issues which could be why not all the cells died.
Eric CordeiroSpinetti	Is there any functional advantage to express immature protein isoforms?
Walter Koch	Katherine - excellent data and talk !
Taejeong Song	Great talk Katherine!
Detlef Obal	great talk
Shyam Bansal	Interesting work, Katherine! Congratulation.
Joy Lincoln	Hi Katherine! Great talk and beautiful work as always! Any idea if the fibroblasts are secreting anything to regulate the CM?
John Ralphe	Beautiful work- great talk!
Madhumita Basu	Great talk, Katherine!
Adam Wende	Nice talk, thank you for reminding us that CM do not work in isolation.
Ajit Magadum	Nice work Dr. Yutzey.
Taejeong Song	#Katherine: Do you think the immature phenotype of the ablation heart is resistant to cardiac remodeling after injury?
Catherine Makarewich	Great talk Katherine!
Kohta Ikegami	@Katherine, are Postn+ CFs distributed fairly uniformly across the heart?
Suresh Verma	Excellent work Katherine.
Mingfu Wu	Hi Katherine, beautiful work! Congratulations!
Liming Pei	Excellent talk Katherine!
Michelle Tallquist	Nice talk, Katherine!
Katherine Yutzey	Hi Eric, I am not sure if there is advantage of the immature, but as the myocytes mature, the later is-forms are needed for increased cardiac output in adults. Could be related to the ability to divide.
Sean Wu	Wonderful talk Katherine! Any data you have on whether fibroblast paracrine effects vs direct cell-contact effects are involved in CM maturation?

Emmanouil Tampakakis	Hi Dr. Yutzey. Very interesting talk. Have you looked at vessel formation. NGF is produced primarily in coronary smooth muscle cells to regulate innervation. Also have you looked at heart size at P14 vs earlier time points?
Jie Xu	Thanks Katherine! Great talk!
Guo Huang	Nice talk, Katherine!
sini sunny	Hi Katherine, Whether there is persisting cardiac hypertrophy in all the developmental stage and how it is regulated?
Suresh Verma	Have you checked about paracrine mechanisms between FB-CM? May be via exosomes or extracellular vesicles
Katherine Yutzey	Hi Taejeong, We have not checked cardiac injury in the postnatal ablated hearts, but Onur Kanicak in Jeff's lab sees that posts-ablation in adults is protective (Nat Comm paper)
Guo Huang	When CMs are smaller while the heart size is about the same in the mutant mice at P14, do you expect more CMs in those?
Katherine Yutzey	Hi Kohta, the Postn+ cells are throughout the myocardium and also in the annulus and valves.
Guo Huang	those mutant mice?
Katherine Yutzey	Hi Sean, We are looking at potential paracrine effects now, there are some interesting candidate in the seq datasets.
John Ralphe	Is there any known correlation with perioperative volume changes (atrial dilation) and development of post-op AF?
Niels Voigt	Increased atrial size predisposes to AF. However, in our population atrial size was comparable in both groups
Katherine Yutzey	Hi Emmanouil, It did not look like vascular development or overall heart size were affected.
Katherine Yutzey	Hi Sini, We did not look beyond P30, but the ablated hearts showed some recovery at that point and there were not significant differences in heart weight/body weigh ratios.
Oscar Bartulos	@Dr. Yutzey: very interesting talk. Any idea if periostin positive cells have any role in cardiac conduction? (independent of potential interaction with TH+ neurons)
Katherine Yutzey	Hi Suresh, We have not looked at exosomes or extracellular vesicles, but we are very interested in figuring out the potential paracrine mechanisms going forward.
Hesham Sadek	Excellent talk Niels!
David Barefield	Hello Niels, were the kinetics in the time to peak strain measured regionally across the atria? Do these hearts have heterogenous depolarization/contraction across the atria?
Niels Voigt	Thank you Hesham.
Niels Voigt	@David: We only analyzed global strain in the atrial. However, heterogeneity may be disturbed due to alternans. See next slide...

Katherine Yutzey	Hi Guo, We were also puzzled about the discordance between the heart weights/ CM cell numbers and what we saw at the individual cell assays. Could be something else contributing to the heart weights that we have not figured out yet or the weight is not sufficiently sensitive to detect subtle differences. We are still trying to figure that out.
Farhan Rizvi	Exciting talk, what was the tissue you use for western are they patients' source who developed PoAF?
Guo Huang	Thank you, Katherine. Very intriguing! Look forward to more discoveries following this line.
Katherine Yutzey	Hi Oscar, While the conduction looked almost normal by EKG. We did not look at any more specific conduction markers. T
Niels Voigt	@ Farhan: Yes, all samples are right atrial samples obtained from patients undergoing open heart surgery. Patients had no documented AF episode before. We performed experiments blind and followed patients for 6 days after surgery.
Emmanouil Tampakakis	Thank you Dr. Yutzey. Very interesting. Happy to talk to your post-doc about postnatal cardiac innervation if interested.
Joseph Wu	Great talk Niels, very interesting topic on atrial cardiomyopathies.
Jianyi Zhang	(thumbsup)
Gopal Babu	Niels, Have you looked at sarcolipin levels in poAF, which is more abundant regulator in atria.
Niels Voigt	Dear Jo, Thank you!
Detlef Obal	Nils, great talk
Adrian Arrieta	@Dr. Yutzey: Hi Dr. Yutzey, excellent talk! Given the connection between myocyte hypertrophy and fibroblast activation and the presence of a stiffer substrate to which they attach, is there perhaps a way to measure the overall stiffness of hearts with fibroblast ablation as compared to control? (I hope that makes sense.)
Thomas Gillette	Great talk Niels
Niels Voigt	Gopal: Unfortunately there was no SLN antibody available. Any suggestion? mRNA expression was comparable.
Katherine Yutzey	Emmanouil, Thanks. He is very interested in the neural maturation angle these days.
Jianyi Zhang	(thumbsup)
Rebekah Gundry	Wow! What an outstanding set of presentations! We have time for a few more questions.
Niels Voigt	Thank you, Thomas!
Mebratu Gebrie	Great talk. Thank you.
Yunhui Xu	great talks. thanks
Jun Feng	Great talk Niel, Did you check any ion channel activity?

Emmanouil Tampakakis	Happy to talk to him. It is an exciting field
Yunhui Xu	very clear!
Thomas Gillette	Is it surprising that such a mild change in steady state levels of SERCA have that impact?
Niels Voigt	Detlef, thank you!
Katherine Yutzey	Hi Adrian, Would definitely be interesting to look at tissue stiffness with the ablation. Eldad Tzahor has been working in that area with interesting results.
Gopal Babu	Niels, mRNA levels sometime don't match with protein.. we have an antibody..happy to help.
Venkatesh Sundararajan	@Neils, Gute Arbeit !!!
Gabriele Schiattarella	Excellent talk, Niels! Wonder if the "outcome" of surgery impact on poAF development.
Adrian Arrieta	Thank you Dr. Yutzey!
Niels Voigt	@ Thomas, We were surprised by this as well but modelling data seem to follow represent our experimental work as well.
Niels Voigt	Venkatesh, Danke!
John Ralphe	Katherine-- the 3D microtissues arte made with added fibroblasts...might be a good model to in which investigate stiffness?
Katherine Yutzey	HI John,
Katherine Yutzey	I agree, some of this could be modeled in vitro.
Rebekah Gundry	Thank you to all the speakers for the fantastic presentations and to the attendees for the engaging discussions. Please be sure to check out the other oral and poster presentations coming up soon!!
Niels Voigt	@ Gabriele: Excellent point. Follow up for 6 days the outcome was comparable as well as operation time and time at the heart lung machine.
Yunhui Xu	Hi Niels, for your protein expression experiments, how many amounts of samples you got from your patient sample? Thanks
Niels Voigt	@ Yunhui: We receive about 300 mg and performed membrane fractionation. For each group we usually use 16 samples.
Yunhui Xu	thanks for your answer
Jared McLendon	Hi John Ralphe, what is the range of force (tenison) the 3d microtissue generate
John Ralphe	They generate 5 - 20 mN/mm2

Workshop 1: Nailing Your Statistics: Rigorous Analysis for Grants and Papers (hosted by Circulation Research)

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.
Alicia Mattiazzi	I cannot see the video. Have you started?
Meenakshi Madhur	I do not hear music
Qutuba Karwi	same here
Jil Tardiff	Hi Alicia - it will start exactly at noon
Rongxue Wu	I can hear
Xuejun Wang	I hear it now.
JoanHeller Brown	Hi Alicia.. I think it has not started yet.. soon ! How are you???
Farid Moussaviharami	I hear the music.
Guo Huang	I can hear.
Claudia Preston	music just started on my end
Alicia Mattiazzi	Fine Joan! Thank you. Good to contact you. How are you?
Alicia Mattiazzi	I can hear also. Thanks
Rongxue Wu	I am looking forward to listening to the session
Ronglih Liao	good morning/afternoon to all
Rongxue Wu	good morning Rongli
Wenbin Liang	Hello everyone! thanks for this great event!
Sakthivel Sadayappan	Welcome everyone!!
Jiang Chang	Good morning everyone
Rong Tian	Really appreciate Circ Res to sponsor this session
Farid Moussaviharami	This is such an important topic.
Jennifer Below	Hi all!
Jil Tardiff	It will benefit everyone
Joseph Wu	Thank you Jane for moderating this important topic on statistical rigor.
Jeffrey Hsu	Very excited for this session!
Jil Tardiff	Hi Piper! Thanks again for doing this!
Jennifer Below	I'm the senior statistical editor for Circ Res, here to help answer your questions!
Venkatesh Sundararajan	One of the most awaited session!!
Jiang Chang	Really appreciate Cir Res to have this topic. Thanks Jane
Alicia Mattiazzi	Hi Jennifer!
Jennifer Below	Happy to be here Jil :)
Jane Freedman	Thank you Eric, Piper and Heather for wonderful talks!!!
Qutuba Karwi	Thanks to Circ Res for hosting this wonderful session

Jennifer Below	my covid office is a linen closet, in case that's not obvious
Jane Freedman	You're welcome. Let us know if you have questions, in general or specific to the journal.
Jil Tardiff	It's all about incorporating statistical analyses as part of the design of your studies. Not as an add-on.
Ying Ge	A timely session! Thank you Jane and all the statistical editors at Circ Res for the important info!
Gabriele Schiattarella	This is a crucial topic in science. Thank you for putting together this session. My question is: how to deal with (sometime requested) "power analysis" to estimate sample size for animals/cells experiments?
Jane Freedman	Well said Jil
Jennifer Below	this is a great question!
Jil Tardiff	Want to add that the chat transcripts will be made available after the sessions (usually by the next day).
Rajasekaran NamakkalSoorappan	I beleive this the first to have such a wonderful sessin/topic. Truly, appreciate the BCVS chairs and Co-chairs! Thank you so much!
DanielleJinkwang Kim	what are your thoughts on 'p=0.06' or something close to being significant and the authors say 'appears to be different' or 'trending towards ...'?
Jennifer Below	power can usually be determined for a given sample size, an effect size, and a significance threshold
Walter Koch	interesting Jil - I will keep it clean!!
Jiang Chang	What are criteria for exclusion of samples or animals?
Venkatesh Sundararajan	@Gabriele, I have the same question, but power analysis is more challenging when comes to a new study or experiment
Jil Tardiff	Whew, Wally ;-). Nice to see yo
Jennifer Below	indeed- because often you have to rely on estimates of effect size from other literature
Pilar Alcaide	Well said, Jiill: RE: incorporating statistical analyses as part of the design of your studies. Not as an add-on.
Walter Koch	you too and congrats on this week !
Pilar Alcaide	Great session, thanks for putting it together, and to the presenters and moderators!
Jennifer Below	which is why it's so important for authors to present effect sizes in addition to significance
Liming Pei	This is a great session. Thanks to BCVS to organize this.
Meenakshi Madhur	how do you deal with multiple comparison correction when you do something like RNA seq and you have 100s-100s of comparisons that you are making?
Heather Highland	@Jiang Chang, The exclusion criteria used are particular to a study, but need to be clearly stated. e.g. if some animals were

	excluded due to dying, or too small to do the procedure etc. These just need to be stated.
Meenakshi Madhur	100s-1000s
Jiang Chang	@Heather thanks
Jennifer Below	@meenakshi if there is an assumption of independence between tests, bonferroni is usually best
Heather Highland	@Meenakshi something like and FDR can be used and in the case of very small sample sizes it can be made clear this is hypothesis generating and many false positives are expected. That this is a very limited sample size must be clear.
Gabriele Schiattarella	I totally agree. in biology, we are usually far away to make assumption of normality. How do you consider your sample size being appropriate (is 10 mice better than 5 and 20 better than 10)?
Jennifer Below	in some cases false discovery rate can work well too
Meenakshi Madhur	Thanks Heather
Jil Tardiff	Great question, Gabriele - this one comes up all the time...
Maria Cimini	Which calculation do you recommend to verify the outliers?
DaoFu Dai	Hi Heather. Thanks for nice talk. Is conventional boxplot still acceptable for skewed data?
Heather Highland	@DanielleJinkwang Kim, present the p-values as they are. Use soft language and make statements acknowledging limited power due to the sample size.
Heather Highland	@DaoFu no. Box plots without superimposed points should be avoided.
Frank Li	is there any rule of thumb for using SD vs SEM? people (myself included) often fall into the trap that SEM makes things 'look prettier'
Ronglih Liao	Great section, thanks Jane and Circ Resfor organizing this section!(thumbsup)
Gabriele Schiattarella	What I trying to say is that sometimes reviewers ask for "please increase your n=number" just because probably they "feel" that more numbers will corroborate the data even in presence of the right statistical test
DaoFu Dai	Heather, can stata do superimposed points?
Jennifer Below	@Frank, either can be used- I'm actually more concerned when authors should be showing IQR
Heather Highland	@Gabriele Schiattarella, the limitations of statistical methods should be considered in the justification of animal sample size. Your power calculation should consider that if you only have a small number of animals per group, you will likely need to use nonparametric methods.
DanielleJinkwang Kim	Thank you, Heather!

Charles Chung	As an early career author, reviewer, and mentor, I often find my (and my trainee's education) is not sufficient in this area. I would very much appreciate if CircRes/AHA could develop some annotated examples of good and bad use of common statistics.
Heather Highland	@DaoFu Dai I haven't used stata for years so I am not sure how, but if it cannot I would suggest asking the company for support and adding this feature.
Gabriele Schiattarella	I think that we should always use non-parametric methods for experiments...
Jennifer Below	@charles, I hope that the forthcoming paper we are publishing that will outline our expectations for authors should help
Jane Freedman	Charles, you are in luck, these 3 outstanding stats reviewers are putting together a review for Circ Res
Jane Freedman	It will be linked with the AHAs broader guidelines
DanielleJinkwang Kim	Frank, excellent question. I always have issue with SD vs SEM. I thought studies with small sample size (<20) should use SEM as SEM accounts for the sample size, but was also told by one reviewer that I should use SD no matter what..
DanielleJinkwang Kim	waiting to hear what the panelists says..
Venkatesh Sundararajan	@Gabriele Schiattarella, Even minor difference makes significant if numbers are increased, but that is not the right way, I guess. Wondering if one need to do a pilot experiment, use the results for power analysis to define appropriate N number
Lindsey Fitzsimons	I agree with @Charles. Additionally, and even as a PhD Student, I too often find myself lacking the resources to expand my statistical rigor--any advise for those of us with limited resources/access to biostatistician expertise?
Jennifer Below	@gabriele, while they have their place- there are also times when normality is well established, and in these cases it's appropriate to use parametric tests
Charles Chung	Does CircRes/AHA have a preference between supplemental data (code, raw data, analytical outputs, etc) in journal submissions or those posted at doi-linked data archive websites?
Heather Highland	SEM vs. SD becomes less concerning when all data points are shown.
Paul Brookes	Frank - Re: SD vs. SEM, SEM is standard error of the means, so if the data points you are feeding in are themselves means (e.g. daily averages) then SEM is OK. If each data point is individual (say biological replicate) and not a mean of technical replicates, then SD should be used.
Paul Brookes	At least that's how it was taught to me (probably wrong!)

Jane Freedman	Charles, as long as the data is readily available, we don't typically have a preference
Jennifer Below	If you want to describe the spread and variability of the data, then you want SD. If you want to show the precision of the means or compare or test differences between means then you might choose SEM. But I agree with Heather- as long as you show all data points in addition to the mean and measure of variance, I'm happy.
Sakthivel Sadayappan	Some of the journals like JBC asks to provide a table for One-way and two-way ANOVA main factors and interactions!!
Heather Highland	@sakthivel, a table can be a clearer way to show the results of an ANOVA, we have not required this, but do require p-values are included somehow.
Jennifer Below	@lindsey, I feel your pain, I wonder if there are resources at your university? I am always happy to help when someone reaches out to me with questions
Sakthivel Sadayappan	Thanks Heather
Jennifer Below	and when @heather says "p-values" she means precise p-values
Jennifer Below	we often see p<0.05 or p<0.0001, which is not sufficient information for estimating effect sizes (which is essential for power calculations as we previously mentioned) or reproducing the work
Meenakshi Madhur	Great session!
Jane Freedman	Thank you Eric, Heather and Piper!
Jennifer Below	thank you all for coming today!
DanielleJinkwang Kim	Thank you!
Lindsey Fitzsimons	@Jennifer- tried that--- it proved WORSE because they couldn't understand some of the biological concept critical to understanding the study design (e.g. LVEF %) Normally it shouldn't necessarily matter (in principle, but the statistical design suggested made absolutely ZERO sense
Willard Sharp	thanks for a great session
Venkatesh Sundararajan	@ Jennifer, What the data says when p values is very close to significance but not
Amadeus Zhu	This was such an important session! Thanks for organizing it
SIKTA CHATTOPADHYAYA	Very informative, Thank you
Rene Packard	Thank you Circ Res and BCVS for a great session
Supriya Hota	Very helpful session! Thank-you Eric, Heather, and Piper!
Rachelle Crosbie	thank you-very helpful session.
Luay Boulahouache	Thank you, it was very informational!
Yajing Wang	great secction, I learned a lot!
Viswanathan Rajagopalan	Thanks for such an important session.

Heather Highland	Thank you all for your great questions we will be on for a bit longer to answer remaining questions
Jennifer Below	please do reach out if we can help
Charles Chung	Thank you. One more question- Does CircRes have guidance on other requirements, e.g. does it suggest including F-values/df-values when reporting ANOVA p-values?
Paul Brookes	Regarding multiple corrections for OMICs data, can the speakers recommend any specific online tools, beyond the standard "go do a Bonferroni"?
Jil Tardiff	Take advantage of this assembled expertise everyone ! And thanks again to the Circ Res team
Ronglih Liao	very import and useful informations! Thanks !
Jennifer Below	ha great question @paul
Heather Highland	@charles, more information and transparency is always preferred!
Lindsey Fitzsimons	Thank you to all the organizers and presenters and support staff!!! I would LOVE to see more of these sessions includes in future conferences! Or even an "Ask a statistician" lunch!
Jennifer Below	often we don't even adjust p-values in OMICS, but rather, we adjust the alpha (p-value threshold needed to reach significance)
Martin VilaPetroff	Great Session, my conclusion is that every lab should have a statistician to advise on each project.
Jil Tardiff	Oh, great point, Piper
Rong Tian	Is it meaningful to distinguish p<0.01 vs. p<0.001? If so, under what circumstances?
Charles Chung	I second that suggestion for more sessions and "ask statistician" sessions! Thank you all for this session, helpful.
Jennifer Below	@martin, I hope not! most of what we see are t-tests, anova, Mann-Whitney, etc
Heather Highland	@Rong, this is important for lit-review meta-analyses and if a reader wishes to further adjust for multiple testing.
Jennifer Below	which are pretty straightforward
Lindsey Fitzsimons	@Charles was very affirming to have you voice your thoughts- thank you!
Paul Brookes	Thanks Jen = and therein lies the problem. Say nominal p 0.05, 1000 genes tested (1000 hypotheses), so adjusted p value is 0.05/1000 = 0.00005 and now nothing reaches that new threshold. It's not a very useful modification to make, if it results in no usable conclusions. Surely there has to be something better than Bonferroni.
Jennifer Below	but if you are doing more complex systems, yes, making a friend who is a statistician can be really helpful

Daniel VelezRamirez	Is Dunnett's test always the best option when comparing treatment(s) with a control?
Martin VilaPetroff	(thumbsup)
Jennifer Below	@Paul when tests are not independent, bonferroni can be too conservative
Jiang Chang	Now I need add a budget for a statistician in future r01
Jennifer Below	and FDR can be more appropriate
Paul Brookes	Agree 100%
Heather Highland	@Paul this is when an FDR can be useful. You can say here are our top results we know 20% are likely false positives but it gives us direction for more focused future work.
Venkatesh Sundararajan	@ Jennifer, I like the answer-making statistician as a friend, make life more easier.
Paul Brookes	Thanks to all the speakers - more of this sort of thing at future meetings please!
Heather Highland	@Jiang also ask the statistician to help with design instead of saying here is the data make this work.
Jennifer Below	but, speaking from my world of computational human genetics, seeing manhattan plots that look more like Akron, Ohio plots is something I really understand <3
Jil Tardiff	That is an excellent point by Heather! Like they said - make it part of design
Lindsey Fitzsimons	Will there be any shift with incentivizing budgeting a statistician in on grants? Given that the overall rigor/expectations are evolving/refining so much?
Rong Tian	Will Circ Res develop a stats checklist for study design?
Jennifer Below	on the study sections that I sit, I see a lot of positive feedback when statisticians or bioinformaticians are included in budgets, yes
Jennifer Below	@rong, yes, an updated author checklist will be part of our upcoming paper, and will be posted on the circ res website
Jiang Chang	Echo Jil
Pilar Alcaide	Great session! Taking notes for planning next year's BCVS and include your suggestions!
Nicole Purcell	This has been great and love the idea of luncheon with statisticians or another workshop
Lindsey Fitzsimons	Thank you @Pilar! Very much looking forward to following this programming specifically!
Rong Tian	@jennifer, that is fantastic! Perhaps to persuade all CV journals for a similar checklist
Joseph Wu	Thanks to all the speakers in this session. Very helpful for PIs and trainees alike.
Jianyi Zhang	(thumbsup)

Jijun Huang	Great session! Thanks for the organizers and all speakers! One suggestion: could Circ Res publish an Editorial to summarize common mistakes in submitted manuscripts?
Rajesh Kumari	Its a great session. Thank you all
Jane Freedman	Jijun, we are doing that. It will come out in early 2021 to synch with the larger AHA statement on stats
Jijun Huang	That's great! Thanks Jane!

Session 9A: Outstanding Early Career Investigator Award Competition

name	message
Vincent Nelson	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.
Hesham Sadek	Hello everyone and welcome to this session. I am your moderator, Hesham Sadek from UT Southwestern Medical Center. We have three excellent talks this session. If you have any questions, please post them in the chat. Enjoy the Session!
Qutuba Karwi	Hi Hesham, thank you for moderating this session
Sumanth Prabhu	Hello Shyam. Congratulations on your selection as a finalist for the Early Career Award! Looking forward to the presentation!
Shyam Bansal	Thank you, Dr. Prabhu!
Konstantinos Drosatos	Looking forward to watching the talks!
Danish Sayed	Hi Shyam, looking forward to your presentation
Raj Kishore	good luck to all presenters
Suresh Verma	Congratulations Shyam. Looking forward for your talk.
Shyam Bansal	Thank you for moderating this session, Hesham!
Raj Kishore	good luck Shyam
Rajarajan AmirthalingamThanda	Congratulations to all for selection as a finalist for the Early Career Award!
Rajasekaran NamakkalSoorappan	Hi Shyam Good luck with your presentation and Q&A as well!
Sumanth Prabhu	Hello Konstantinos
Hind Lal	Shyam-Very best for the presentation and competition
Qutuba Karwi	Good luck to all finalists!
Shyam Bansal	Thanks, Suresh and Raj
Rajasekaran NamakkalSoorappan	Best of luck for all Finalists
Rajarajan AmirthalingamThanda	Congratulations Shyam,
Jane Freedman	Congratulations to the finalists!
Danish Sayed	Congratulations to all finalists
Li Qian	Good luck to all finalists!
Sakthivel Sadayappan	All the best and good luck to our early careers!!
Maradumane Mohan	Congrats Sham
Carolina Gonzalez	Good luck to all the finalists!
Shyam Bansal	Thank you everybody
Joseph Wu	Congrats to all finalists! Thanks for moderating Hesham :-)

Adam Wende	Congratulations to the finalists. Looking forward to hearing about their work.
Loren Wold	Best of luck to all of the finalists!!!!!!!
Wolfram Zimmermann	Congrats to the three finalists
Maria Cimini	Best of luck to the presenters
Emmanouil Tampakakis	Thank you all
Meenakshi Madhur	Congrats and good luck all
Nicolas Christoforou	Congratulations to all finalists. Good luck!
Rong Tian	excited to hear from all finalists!
Sadia Mohsin	Good Luck to all finalist. Looking forward to your talks!!
David Paik	Thank you Dr. Sadek for moderating. Looking forward to the talks
Ameen Ismahil	Hi Shyam, Congratulation !!!!
Ronglih Liao	Congrats and good luck to all finalists !
Mohsin Khan	Congrats to the finalists. Looking forward to the talks
Maria Kontaridis	Congratulations, Shyam!
Shyam Bansal	Thanks, Maria
Maria Kontaridis	Excited to hear the talks from all the finalists! congratulations to all!
Sakthivel Sadayappan	Congratulations, Shyam!
Sakthivel Sadayappan	The OSU!!!
Venkatesh Sundararajan	Great work and talk!!! Shyam, nice to see you
Shyam Bansal	Thanks Sakthi and Venkatesh
Meenakshi Madhur	Did you use male or female mice for the initial sequencing and ingenuity pathway analysis?
Shyam Bansal	Male mice
Shyam Bansal	All studies were done using male mice except where specified
Raj Kishore	Shyam: did these Mi studies also include estradiol supplementation?
Shyam Bansal	No... we did not include this group. But we are including that also as a control now
Sathyadev Unudurthi	Hi Shyam, does this drug reduce proinflamamtory cytokine secretion only by inhibiting proliferation or can this inhibit proinflammatory secretion independent of proliferation?
Raj Kishore	great story
Jie Xu	Hi Shyam, great work! Did you check to see pharmacokinetics to see how long the drug stays in the mice and how well are the target of the drug engaged over time after dosing?
Shyam Bansal	This drug did not inhibit proinf cytokines after PMA/Iono activation

Pilar Alcaide	Great presentation Shyam, on congrats on being a finalist. Did the drug had any systemic effect on T cell death in the heart or elsewhere?
Shyam Bansal	Yes, this drug has almost 18-20 hr half-life
Shyam Bansal	and the dosing was done everyday
Eric CordeiroSpinetti	Is there any difference between male/female mice treated with the drug?
Suresh Verma	Shyam: are you planning to study other injury models like I/R or TAC with this drug?
Shyam Bansal	In-vitro assays showed no effect on T-cell death at this dose
Rajarajan AmirthalingamThanda	Hi Shyam, great talk, did you get chance to check half life
Khanh Ha	what would be the best half-life for these drug ?
Sumanth Prabhu	Very interesting results, Shyam! the differential effect of the drug early versus late post-MI suggests change in T-cell phenotype. Can you comment on this
Khanh Ha	thanks Shyam
Meenakshi Madhur	Did you look at IL-17A/Th17 cells?
Shyam Bansal	We did not do HF studies using female mice. But we did find similar inhibition of T cells isolated from female mice
Rajarajan AmirthalingamThanda	is there any toxicity level invivo or ivitro
Shyam Bansal	Yes, I plan to study it with TAC also..
Poonam Rao	What was the dose that you used?
Khanh Ha	Also again how did you guys come up with the structure of these drug again?
Shyam Bansal	Yes, half-life is 18-20 hrs
Khanh Ha	Like how did you come up with the modifications and design?
Rajarajan AmirthalingamThanda	Thanks Sham
Adrian Arrieta	Excellent talk Dr. Bansal. Does your drug affect regulatory T-cell proliferation?
Dhanendra Tomar	Great work Shyam, congratulations!!
Pilar Alcaide	Is it possible the drug induces T cells anery?
Sathyadev Unudurthi	DId you notice lower cardiac fibrosis in drug treated animals Shyam?
Ganesh Halade	Nice talk Shyam - congratulations !
Prabhat Ranjan	Nice talk. Congratulations..!!
Shyam Bansal	@ Dr. Prabhu:Yes, I think there are significant phenotype differences in T-cells between the early and late stages.
Mingfu Wu	Beautiful work Shyam, congratulations!!
Suresh Verma	Excellent work. Congratulations!!!

Adam Wende	Great work. Glad to see your transition to The OSU is going well.
Loren Wold	Great job to my academic office neighbor, Shyam!
Sumanth Prabhu	Wonderful presentation Shyam. Novel work!
Shyam Bansal	@Meena: Th17 cells were also reduced. This drug inhibited polarization of all T-cell subsets
GRACIOUS ROSS	Nice Work! Shyam(thumbsup)
Hind Lal	Outstanding work. Congrats
Naresh Kumar	Very nice talk, Dr. Bansal!!
Farah Sheikh	Nice presentation and findings, Shyam!
Shyam Bansal	@ Rajarajan: No apparent toxicity was observed
Ameen Ismahil	Great work Shyam!!!
Zhongjian Cheng	Great job Shyam! Congratulations!
Shyam Bansal	@ Poonam: 60 mg/kg/d; gavage
Santosh Maurya	Outstanding presentation, Shyam.
Yike Zhu	Dr Shyam, have you tried drug treatment before MI? Would that protect cardiac function?
Ronglih Liao	congrats! strong work!
Danish Sayed	Nice! Keep up the great work Shyam
Sakthivel Sadayappan	@ Hesham, you are doing a great moderation!! Thank you!!
Meenakshi Madhur	Great work!
Shyam Bansal	Khanh: DDI here at the OSU has been working on this structure from several years. A paper is coming-out soon
Khanh Ha	Thank you
Wolfram Zimmermann	Nice work - are there any sex associated differences? differences
Khanh Ha	was that structural diverssity based?
Shyam Bansal	Adrian: Yes, it reduced Treg levels also but increased Foxp3 expression in Tregs
Hesham Sadek	Thanks Sakthi!
Meenakshi Madhur	Any effect on CD8 T cells?
Shyam Bansal	@Pilar: We have not looked into that yet. But its a great question
Shyam Bansal	@Sathya: Interestingly we did not see reduction in fibrosis/markers
Adrian Arrieta	Very cool! Thank you Dr. Bansal.
Wolfram Zimmermann	EC50 (>3 μM) is suboptimal for clinical translation. Any idea how to optimize PK/PD?
Pilar Alcaide	Thank you Shyam. Your TCR data may point in that direction. Congratulations on an outstanding presentation and beautiful work!
Madhumita Basu	Great work, Shyam! Congratulations again.
Poonam Rao	Great work.

Shyam Bansal	No we did not try before MI time-point. We believe T-cell activation early after MI is required for adequate healing. That also explains increased mortality at 7d post-MI treatment
Sathyadev Unudurthi	That's interesting Shyam....so you see the same levels of increased fibrosis in hearts in drug treated mice, as seen in controls, but we see that the EF is preserved in drug treated mice?
Yike Zhu	Thanks Dr Shyam
Li Qian	Great work, nice presentation and questions well handled, Shyam! Congrats!
Shyam Bansal	@Wolfram: Could you please elaborate your question? Do you mean in T-cell biologu?
Poonam Rao	Did you find an initial decrease in EF after MI?
Hee Cho	@Shyam, congratulations for your great story! Wonder if you can measure serum concentration of your drug over time and look at its metabolites for optimizing the drug candidate.
Shyam Bansal	@Khanh: Yes, my collaborator is further optimizing this molecule to increase potency
Sakthivel Sadayappan	Emmanouil, Congratulations and all the best!
Shyam Bansal	@Meena: It decreased splenic T-cells numbers but no effect in circulating T-cell numbers or frequency...somewhat mixed effects
Sathyadev Unudurthi	Great work and great talk Shyam... Congrats
Emmanouil Tampakakis	Thank you
Li Qian	Great to see you, Emmanouil! Enjoy your recent work on this cool direction, congrats on being a finalist!
Shyam Bansal	@Wolfram: Yes I agree. its sub-optimal. My collaborator is designing other molecules with increased potency.
Shyam Bansal	@Sathya: yes, but this is preliminary and we need to add more numbers to confirm
Shyam Bansal	@Poonam: Do you mean with Drug treatment? If so, we did not do echo at other time-point. Only 8 weeks time-point was tested
Shyam Bansal	@Hee Cho: DDI here at OSU is doing detailed kinetics related to this drug
Shyam Bansal	Thank you everybody.
Wolfram Zimmermann	pH3 and Ki67 data was quite similar - tyically i67 is higher - please explain.
Li Qian	Are these CMs still functionally competent (upon ablation of sympathetic innervation)?
Emmanouil Tampakakis	We found that ki67 was higher. I only presented pH3 and Edu data
Wolfram Zimmermann	the FACS plot indicated Ki67 on the x-axis??
Emmanouil Tampakakis	That was mislabeling which I omit to say

Emmanouil Tampakakis	My apologies Dr. Zimmermann for the confusion
Matthew Wolf	Do beta-adrenergic receptor antagonists recapitulate the effects of ablation of sympathetic innervation in neonatal hearts?
Katherine Yutzey	Nice work!! Do you see any effect on glial cells or fibroblasts?
Emmanouil Tampakakis	Hi Li. We have not analyze the function on neonatal CMs but I anticipate it will likely be affected given the down regulation of Calcium handling and Structural genes
Li Qian	Thanks, Emmanouil! Interesting work!
Emmanouil Tampakakis	Dr. Wolff. Bernard Kuhn showed similar data in b-adrenergic DKO mice
Matthew Wolf	thank you
Guo Huang	Nice work, Emmanouil! In your nerve ablated mice, Per1 is reduced by 60% and Per2 is reduced by ~40%. I wonder whether Per1 +/-, Per2 +/- mutant mice have phenotypes.
Emmanouil Tampakakis	We do think that a-drenergic receptors mediate partly our phenotype
Xinliang Ma	For Emmanouil: Does sympathetic innervation defect occur in human disease with heart development defect?
Emmanouil Tampakakis	Dr. Yutzey. We have not focused on fibroblasts of glial cells but I think they should be affected. Based on RNA-Seq data some of fibroblast specific genes were actually increased
Emmanouil Tampakakis	Hi Guo. We did not see the same phenotype in the Het mice. They are redundant so you do need a DKO system to study them
Hee Cho	@Emmanouil, great work! What would happen if you overexpress Per1/Per2 genes in the context of inhibition of sympathetic inhibition in vivo?
Ricardo Frausto	Emmanouil, cell cycle genes are notoriously decoupled from their protein abundances. Since the proteins are the ultimate effector molecules in cell cycle regulation, did you look at protein levels encoded by the cell cycle genes?
Chulan Kwon	Great job Emmanouil! Well done!
Loren Wold	Excellent talk Emmanouil!
Matthew Wolf	great talk!
Raj Kishore	Great job, Emmanouil
Jil Tardiff	Nice job!
Ronglih Liao	Great job! congrats!
Guo Huang	@Emmanouil, sorry, I meant Per1+/-;Per2+/- double het mutant mice because the expression of Per1 and Per2 would be more like that in your nerve-ablated mutant mice.
Suresh Verma	Outstanding Job Emmanouil!!
Guo Huang	Great talk, Emmanouil!
John Ralphe	Very nice work! Great job!

Yike Zhu	Interesting topic Dr Emmanouil! Have you looked at the metabolic changes in CMs with defected sympathetic innervation as there is known circadian control of CM metabolism?
Mohsin Khan	Great Work Emmanouil.. interesting data foe Wee1
Emmanouil Tampakakis	Dr. Ma, HLH patients appear to have impaired b-adrenergic signaling. Prematurely born babies have reduced innervation. The same for babies undergoing neonatal surgery
Suresh Verma	What is your view about CM proliferation in reference to day vs night as per1/2 alters their expression with light cycle.
Jennifer VanEyk	Have you looked to see if glycosylation of NGF is intact and or important to these effects?
Xinliang Ma	Excellent!
Emmanouil Tampakakis	Dr. Cho we have not done this. Interesting question.
Emmanouil Tampakakis	Dr. Frausto, very interesting point. We are in the process of testing protein expression. Had to slowed down due to COVID-19
Beverly Rothermel	Have you looked at multiple time points to see what the effect on amplitude of gene cycling is? If one looks across a 24 hour period is amplitude of all circadian genes dampened?
Emmanouil Tampakakis	Guo, I have not tested the het mice.
Maria Cimini	Emmanouli, I may have missed this, but, is there any increase in immune cell population in NGF depleted mice?
Danish Sayed	Hi Emmanouil, Great work. Have you checked if Glucocorticoid signaling is intact in these mice. We know that GR activation induces Per expression
Sakthivel Sadayappan	Yang Zhou, Congratulations and all the best!!! Congratulations to your mentor, Dr. Jianyi Zhang!!
Li Qian	Yang, congrats on this beautiful new work at UAB! We are all very proud of you. Lab folks say hi and remotely cheer for you!
Hind Lal	Congrats @ Yang Zhou...UAB
Emmanouil Tampakakis	Dr. Verma, this is an interesting question. Circadian genes, in the heart follow their own independent cycle irrespective of the CNS circadian cycle mediated by the hypothalamus. Also mouse pups do not have their own day-night cycle. So I am not sure there will be an effect of day-night light in neonatal heart regeneration. In oncology there is a school of thought about treating patients with chemotherapy at night time because cancer cells are more prone and less proliferative.
Jiang Chang	Congratulate Yang Zhou and mentor Jay!
Yang Zhou	Thank you, Li! Great to 'see' you here. Say hi to the lab!
Hind Lal	Congrats to Dr. Jay Zhang for these great studies..

Emmanouil Tampakakis	Dr. Romethel I agree. We are in the process of doing this now. We believe that there is likely dampening of circadian cycle in CMs and potentially prolongation
Rong Tian	@Li, @Yang congratulations! Very happy to see Yang's achievement!
Suresh Verma	Thanks Emmanouil. I agree. Good Luck.
Emmanouil Tampakakis	Dr. Cimini, we have not looked but I think there is an effect as RNA-Seq data is very suggestive of that. We would like to test this as well
Li Qian	@ Yang We all miss you so much already.:-) But thrilled to see your recent achievement so quickly!
Li Qian	@ Rong Thanks!
Emmanouil Tampakakis	Dr. Sayed, very good question. We have not tested GR signaling but I do not think that at these early time points can potentially mediate the Per1/Per2 induction but it is an interesting question
Wolfram Zimmermann	Any evidence for contractility in the TBX20 expressing human iCM
Emmanouil Tampakakis	Thank you all for your questions and comments. Very exciting session
Walter Koch	great session - congrats to all speakers !
Shyam Bansal	Thank you, Dr. Koch!
Wolfram Zimmermann	RyR1 would be more indicative for skeletal muscle diff - any RyR2 changes
Kimberly Ferrero	What a great session; thanks everyone!
Wolfram Zimmermann	Congratulations to all three speakers - well done and well deserved to be selected as finalists
Yang Zhou	Dr. Zimmermann. Not yet, we are trying to do electrical stimulation. The RyR2 also changes, but lower fold change.
Shyam Bansal	Thank you, Dr. Zimmermann!
Mingfu Wu	@Li @Yang Great work! Congratulations!
Emmanouil Tampakakis	Thank you Dr. Zimmermann. Excited to be part of this
Rose Belfer	Thanks Dr. Zimmerman!
Li Qian	@ Mingfu Thanks! It's all Yang's independent work at UAB as AP (without me). Very proud of her.
Jennifer VanEyk	Very nice work. What will be your approach to determine the direct downstream targets of TBX20 and also how TBx20 is regulated
Zhaoning Wang	Hi Yang, very cool discovery! Does TBX20 accelerate the reprogramming process? (Can you detect beating iCMs in a earlier timepoint than control?)
Guo Huang	Nice work, Yang. Congratulations!
Chulan Kwon	Great work, Yang!

Miao Cui	Nice presentation, Dr. Zhou. Do you think the function of TBX20 function is context dependent? I recall Dr. Yutzey group showed that TBX20 overexpression increases adult cardiomyocyte proliferation. This effect was not observed in the reprogamming setting.
Yang Zhou	I will do the Cut&Run for TBX20 and identify the direct target. @Dr. VanEyk
Ronglih Liao	Congrats to all three finalists! great job!
JoanHeller Brown	Wonderful talk Yang, congratulations on this work !
Detlef Obal	wonderful talks
Poonam Rao	Congrats to all 3 finalists. Wonderful job by all
JoanHeller Brown	Indeed, all were really impressive !
Yang Zhou	@ Miao Cui. Yes, it is context dependent. We actually see the reduced proliferation in reprogramming setting.
Hee Cho	@Yang, wonderful work and congratulations! Do you think Tbx20 is working as mostly a transcriptional activator in your experimental setting? Hesham's recorded question appears to be on the same topic of activator vs. repressor roles of Tbx20.
Joseph Wu	Great presentation by all 3 finalists, very impressive data!
Jijun Huang	Congratulations, Yang! Wonderful work!
Danish Sayed	Great talks from all three presenters
Yang Zhou	@ Zhaonign Wang. Yes, it's kind of acceleration. We haven't see any beating so far, but we see earlier upregulation of cardiac genes during this process.
Suresh Verma	Great work Yang.
Li Qian	@ Hesham, great job in moderating too!
Chulan Kwon	ditto
Jennifer VanEyk	well done everyone!
Venkata Garikipati	Awesome talks! Congratulations to all the three presenters
Venkatesh Sundararajan	Congratulations!!! all speakers
Emmanouil Tampakakis	Thank you Dr. Sadek.
Hesham Sadek	Three excellent presentations. Congratulations Shyam, Emmanouil, and Yang
Suresh Verma	Great session Hesham. All are excellent talks
Shyam Bansal	Thank you, Dr. Sadek and the audience for great questions/comments and support

Session 9B: Metabolism and Redox Mechanisms in Heart Failure

name	message
Vincent Nelson	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.
Paul Brookes	AHA needs to up their music game! Give us some Weird Al or something less likely to send us into a post-prandial stupor
Rajasekaran NamakkalSoorappan	Hi Paul, we must have some dance to go with the music..
Paul Brookes	Hi Raj - Looking forward to your talk.
Ivor Benjamin	Hi Raj, I'm looking forward, too. IJB
Rajasekaran NamakkalSoorappan	Thanks Paul
Rajasekaran NamakkalSoorappan	Thank you Sir (Dr. Benjamin)
Sakthivel Sadayappan	Excellent start, Raj!
Rajarajan AmirthalingamThanda	Raj-looking forward your talk
Snekha Rajasekaran	Hi Dr. Raj- can't wait to hear your talk!
Huabo Su	Raj, look forward to your story
Rajasekaran NamakkalSoorappan	Thanks Su
Venkatesh Sundararajan	Great to see you Dr. Raj, one of my favorite topics!!! metabolism and Redox.
Rajasekaran NamakkalSoorappan	Thanks Venkat
Zhaokang Cheng	Raj, excellent background info!
Rajasekaran NamakkalSoorappan	Thanks Cheng
Rongxue Wu	Good job, Raja
Rajasekaran NamakkalSoorappan	Thanks Rosy..
Hind Lal	Great going Raj !!
Rajasekaran NamakkalSoorappan	Nice to see you Hind
Rajesh Kumari	Hello Dr. Raj, Is drecreasing age of heart failure related to changes in reductive stress signaling?
Rajasekaran NamakkalSoorappan	Thanks Kumari
Rajasekaran NamakkalSoorappan	Thanks Sakthi
Farhan Rizvi	Excellent talk Raj

sini sunny	Is there any statistics available in CAD patients or in healthy subjects for the prevalence of reductive stress?
Venkatesh Sundararajan	Raj, is this whole cell redox status right, not cytosol or mitochondria?
Rajasekaran NamakkalSoorappan	It is restricted to cardiomyocytes - the transgene is driven by alpha-MHC promoter
Rajasekaran NamakkalSoorappan	Yes, Sini We recently found that about 15% of the HF patients seems to have a hyper-reductive state!
Rajasekaran NamakkalSoorappan	Thanks Rizvi
Yajing Wang	Raj, i have the similar question with sini sunny.... is it shown in heat failure patients, or any other chronic disease?
Yajing Wang	Raj, thank you
Joseph Goldman	Hello Dr. Raj,
Rajasekaran NamakkalSoorappan	This group of HF patients had an EF of below 30 and down to 15%, they do not have any other major co-morbidities suchs as diabetes or cancer etc.
sini sunny	The concept will be a very useful marker in clinical aspect as a routine blood marker for 'reductive stress'
Rajasekaran NamakkalSoorappan	Dr. Yibin Nice seeing you and thank you for the interesting question. we need to expand this to a larger group
Zhaokang Cheng	Interesting data! Does overexpression of NRF2 induce myocyte hypertrophy, increase contractility in vitro?
Joseph Wu	Raj, great talk and great body of work!
Rajasekaran NamakkalSoorappan	Yes, initially hyper-contractility and over time there is a diastolic issues
Rajasekaran NamakkalSoorappan	Thanks Dr. Wu
Rajarajan AmirthalingamThanda	Raj, great talk, is there any stable technique to measure the ROS in live animals
Rajasekaran NamakkalSoorappan	Thanks Rajan
Rajasekaran NamakkalSoorappan	DMPO -adduct would be much realiable than any other techniques using the DCFDA or DHE etc.
Venkatesh Sundararajan	@ Rajarajan. MitoB is one you can use to measure in vivo ROS as well
Farhan Rizvi	did you seen the level ros scavengers enzymes?
Farhan Rizvi	in blood of HF
Helen Collins	Good job Raj. Hope all is well at UAB
Rajasekaran NamakkalSoorappan	Yes, we did all of them are dose-dependently increasing and I have another bifg story coming soon connecting the RS with impaired PQC as a mechanis
Daniel Turner	Never considered reductive stress, thank you for your talk!
Asa Gustafsson	Great talk Raj!

Yajing Wang	very interesting conclusion! nice work!
Luke Potter	great talk, thank you
Rajarajan AmirthalingamThanda	Thanks Raj and Venkatesh
Rajasekaran NamakkalSoorappan	Thanks Luke
Gopal Babu	Nice presentation Raj
Rajasekaran NamakkalSoorappan	Thanks Daniel
Paul Brookes	Raj - Do the global mice have any renal problems (given importance of GSH redox system in the kidney)>
Dennis Wang	Dear Raj. Do you think the HFiEF animals may ultimately develop into HFrEF?
Ivor Benjamin	Delighted to learn about this innovative line of investigations, Raj. Congratulations
Arul Veerappan	Raj, excellent work and great talk, Congrats!
Sakthivel Sadayappan	Dr. Mahesh Gupta, Thank you moderating this session!
Rajasekaran NamakkalSoorappan	Rizvi, we measured in our animal models.
Bradley Morgan	Great talk. do patients with high redox scores have hyper contractility?
Rajesh Kumari	Great Talk Dr. Raj!
Snekha Rajasekaran	Dr. Raj, nicely done!
Sakthivel Sadayappan	Sruti, Greta start!! Thank you for your presentation!
Venkatesh Sundararajan	Excellent, New avenue of work, Dr. Raj
Rajasekaran NamakkalSoorappan	Currently we are measuring in blood plasma of the patients as well.
Rajasekaran NamakkalSoorappan	Thanks Asa
Suresh Palaniyandi	Nice line of work Rajasekar
Rajasekaran NamakkalSoorappan	Thanks Wang
Sruti Shiva	great to be here!
Rajasekaran NamakkalSoorappan	Thanks Helen for joining
Farhan Rizvi	@Raj will catch you later for some discussion
Rajasekaran NamakkalSoorappan	Thanks Babu, I enjoyed your DMD story - very impressive!
Rajasekaran NamakkalSoorappan	Paul you're hittin the nail on the head- FYI- we did not look at in the Kidney, but in the brain there is a clear impact in the brain???

Rajasekaran NamakkalSoorappan	Morgan - in patients our findings are very limited and now began looking at the detailes of systolic vs. duiastolic functions. Hopefully, some answers anticipated in the near future
Sherin Saheera	Great talk, Dr.Raj!
Rajasekaran NamakkalSoorappan	Thanks Suresh
Rajasekaran NamakkalSoorappan	Sure, Rizvi, happy to talk with you sometime soon
Rajasekaran NamakkalSoorappan	Thanks Sherin..
Rajasekaran NamakkalSoorappan	Dr. Arul nice to see you! Thank you for helping us with the Right Ventricle measurements
Venkatesh Sundararajan	@Sruti. Very interesting topic. I guess Mb was transcriptionally induced during proliferation. After cardiac injury the decreased expression was transcriptional or translational?
Hind Lal	Surti -dose and number of injections of Tamoxifen
Sruti Shiva	Appears to be predominantly transcriptionally regulated after injury
Sruti Shiva	@Hind - 3 injections of tamoxifen, 1mg/ml
Hind Lal	Thanks
Paul Brookes	Thinking about this in the context of Hossein Ardehali's talk this morning, how much of the effect do you think is simply because w/o Mb there's more free iron (and that's working via JmJC HDMs)?
Rajasekaran NamakkalSoorappan	Dennis - A good question, yes, there is a progressive diastolic issue and we are trying to understand whether this could lead to reduced EF over time.
Rong Tian	cool data, Sruti
Santosh Maurya	Did you measure fatty acid oxidation in beating heart, ex vivo?
Sruti Shiva	Hi Paul, that's a great question and something we're wondering too. Haven't done free iron measurements yet (or looked at JmJC) but hoping to measure it soon.
Heinrich Taegtmeyer	Does knocking down myoglobin increase glycogen levels?
Sruti Shiva	Thanks Rong!
Sruti Shiva	@Santosh, no we haven't measured FAO in beating heart yet
Rajasekaran NamakkalSoorappan	Nice to see you Sruti
Venkatesh Sundararajan	@Sruti, thanks! was decreased Mb dependents on type of injury whether Ischemia, IR or drug induced. wondering what is the mechanism for the decrease in expression.
Rachel RothFlach	Hippo/yap are often considered mechanosensing pathways - does myoglobin affect cellular stiffness?

Sruti Shiva	We have not seen changes in glycogen levels acutely, but have not looked closely longer term yet
Mei Methawasin	@Raj, I have a naive naive question. Are the mitochondria in different organs (heart, brain,liver) different?
Sherin Saheera	Did you see any change in valve morphology in the knockout?
Farhan Rizvi	How aging affect Mb expression?
Oscar Bartulos	Nice talk Sruti! I was wondering, at what stage myoglobin expression appears during embryo development, and what is the hypothesis for lack of action in proliferation at early stages?
Sruti Shiva	@Venkatesh - the data I showed was aortic banding and pulmonary banding of wildtype animals. Those are the only two models we have data on right now. So not sure yet if it occurs in other models.
Rajarajan AmirthalingamThanda	Nice talk Sruti, Congratulations
Asa Gustafsson	Sruti- great talk. Hope all is well.
Sruti Shiva	@Rachel, we haven't looked at cellular stiffness yet, but a good question
Hind Lal	Excellent work @ Sruti
Venkatesh Sundararajan	@Sruti. Thank you!!
Sruti Shiva	@Sherin, we have not seen any change in valve morphology.
Mei Methawasin	@Sruti how does the myoglobin affect cardiomyocyte proliferation in patients with bllod disease such as hemoplobinopathy or Thalassemia?
Sherin Saheera	@Sruti. Thank you! Nice talk!
Sruti Shiva	@Farhan, it hasn't been extensively studied. We have looked at wildtype mice and there's no change in expression at 36 weeks. We're looking at much older now, but don't have results yet
Paul Brookes	Sruti, I guess another "low hanging fruit" issue is how much of the total protein content of a myocyte is made of myoglobin? (PeiPei Ping would probably know)... in other words, is this just an effect of knocking out the most (or one of the most) abundant protein in the cell, so it's affecting all kinds of things like autophagy, amino acid availability etc?
Joseph Wu	Great talk Sruti, thanks for presenting!
Sakthivel Sadayappan	Thanks to Patrick Hsieh, who is presenting from Taiwan.
Patrick Hsieh	Thanks. My pleasure and honor.
Rajasekaran NamakkalSoorappan	@Mei, I have a naive naive question. Are the mitochondria in different organs (heart, brain,liver) different?
Sakthivel Sadayappan	Thank you also for joining with us!!

Sruti Shiva	Yes, that's a good thought Paul. It doesn't seem to be a "non-specific" generalized effect. The cardiomyocytes look good under the microscope and there's no change in basal rate of respiration or in apoptosis. But it is a good question. We have also made a point mutation mouse that has the protein, but lacks functional heme. So we will compare to that soon.
Sruti Shiva	Thank you all for the questions and feedback!
Paul Brookes	Super-interesting data Patrick, because the tetracycline antibiotics (doxycycline etc) are actually cardioprotective, whereas here you see detrimental effects with other antibiotics.
Rajasekaran NamakkalSoorappan	@Mei - regarding mito in different organs - I am pretty sure that the redox status in the mito of different organs is different! But, I am not sure about the structure? May be there could be some size variations!!
Helen Collins	@dr hsieh what do you think underlies the sex differences in the MI survival? differences in gut micobiota? estrogenic effects?
Guo Huang	Very intriguing findings, Patrick! Congratulations!
Paul Brookes	Sruti - now that's gonna be an interesting mouse to see! Thanks for great talk - lots to think about.
Patrick Hsieh	@Paul. Good point. No, we only use combination of antibiotics.
Patrick Hsieh	@ Guo. Thanks.
Rajasekaran NamakkalSoorappan	Interesting observations Patrick
Joseph Wu	Patrick, good to see these new data on microbiota and cardiac repair. Hope you're doing well in Taiwan.
Patrick Hsieh	Thanks Joe and Raj.
Rajesh Kumari	great talk Dr. Patrick. which bacterial species are involved in cardio protection?
Patrick Hsieh	@ Rajesh, will be shown soon.
Rajesh Kumari	got it , thank you.
Rajasekaran NamakkalSoorappan	Eat more home-made YOGURT-lactobacilli
Zoltan Arany	These are striking and impressive data
Andrew Carley	Was the SCFA effect restricted to the gut or do you think there were any direct effects on the heart?
Adam Wende	Wow, exciting new findings.
Patrick Hsieh	@ Andrew. Likely some direct effects on the heart.
Rajarajan AmirthalingamThanda	Great talk, any specific method to measure the SCFA and did you get chance measure in the plasma
Zoltan Arany	so do probiotics, or SCFAs, improve post-MI outcomes in a naive (no abs, full germs) mouse?

Sean Wu	Great talk Patrick!
Patrick Hsieh	@ Raj, by HPLC.
Patrick Hsieh	Thanks Sean.
Andrew Carley	How did you administer the SCFA?
Rajarajan AmirthalingamThanda	Thanks
Heinrich Taegtmeyer	Interesting to see the difference between even and odd chain fatty acids (propionate). Any explanation? Anaplerosis?
Patrick Hsieh	@ Zoltan, yes.
Farhan Rizvi	Some time earlier a study showed the children born to c-section deprive some microbes of gut biota affect lungs physiology whether any heart related study in this context?
Patrick Hsieh	@ Andrea, iv injection.
Gabriele Schiattarella	Great data. Not sure if I missed. What is the "heart bacterial load" you measured? Did I see the same scale bar for the feces bacterial load?
Zoltan Arany	have you tried time course to determine when, postMI, is the key period that needs germs/SCFA?
Patrick Hsieh	@ Dr. Taegtmeyer, not sure.
Qutuba Karwi	Very nice talk Patrick! I am wondering if the same protection can be seen in aged mice?
Patrick Hsieh	@ Farhan, not to my knowledge.
Rajesh Kumari	Great Talk Dr. Patrick, I have another question, gut microbiome vaires geographically. Are there studies which show difference in gut microbiome vs occurrence of heart failure?
Heinrich Taegtmeyer	Just an idea to test. Great work. Impressive.
Rajesh Kumari	great Work!
Patrick Hsieh	@ Gabriele, no. Much low bacterial load in the heart. We are confirming it wit more experiments now.
Yibin Wang	Hi, Patrick, Great talk and really enjoy it. My question is how do we know the SCFA in circulation are directly produced by gutBiota not through other tissues such as liver and fat tissues?
Patrick Hsieh	@ Zoltan again, no time course studies yet, but it's likely the case.
Zoltan Arany	Really beautiful story -- congratulations !
Yibin Wang	And do we know the mechanism why these SCFA have immune modulatory function?
Patrick Hsieh	@ Qutuba, not sure, but interesting point. We are working on germ-free old mice now. Initial results show similar.
Zoltan Arany	@Yibin woudl be really interesting to do BMTs with GPR kos for exmaple
Yibin Wang	Yes
Patrick Hsieh	@ Rajesh, yes, similar observation to ours.

Qutuba Karwi	Very exciting findings! Congrats and waiting to see these data in a nice paper soon!
Rajesh Kumari	Thank you Dr. Patrick
Patrick Hsieh	@ Yibin. We did not measure all the sources of SCFAs. But our results suggest at least the gut is a major one.
Yibin Wang	Congratulations, Patrick, for such as an exciting story.

ACS ACRE: Critical Signaling Pathways in Heart Failure

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.
Adam Wende	For some reason I am seeing Session 9A here.
JohnHarry Caufield	Yes, also seeing the other session here.
Heinrich Taegtmeyer	I am in the wrong seen too.
Gopal Babu	Wrong session
Pamel Burrage	Once the other session has ended this session will be available to view.
Faqian Li	Welcome to the ACS ACRE session. . I am your moderator, Faqian Li from the University of Minnesota Medical Center. We have three exciting and interesting talks in this session. If you have any questions, please type them in the chat and they will be answered by the speakers. If they are not answered during the session we will have time at the end for questions. Enjoy these excellent talks!
Martin Young	Thanks for moderating this session Faqian!
Pamel Burrage	Just as a note the previous session is running a little over in time. The ACS ACRE session will begin after that session.
Xuejun Wang	Looking forward to this exciting ACS/ACRE session!
Rongxue Wu	Looking forward to listening to the talks. Thank you for moderating the session Faqian!
Sean Wu	Thanks Faqian for getting the ACS ACRE session ready.
Faqian Li	Thank you for your support, Dr. Young
Xuejun Wang	Nice to "see" you here, Faqian.
JohnHarry Caufield	Thank you for moderationg, Faqian. Looking forward to any discussion during or after the talks.
Jiang Chang	Go for ACS ACRE. Thanks Martin, Sean and John for supporting this program. Thanks Faqian for monitoring the section
Joseph Wu	Looking forward to an exciting ACS ACRE session!
Xinliang Ma	Hello Martin:
Faqian Li	Thank you for your contribution, Harry!
Xinliang Ma	Greatly appreciate your support! Looking forward to hearing from you.
Martin Young	Hi Xinliang
Yibin Wang	Looking forward to a great session!
Suresh Verma	Hello Martin, Looking forward for your talk!!!
Sakthivel Sadayappan	Congratulations ACRE.. you rock!
Martin Young	Thanks Suresh

Paul Brookes	Wrong session! I'm not seeing Martin here bu the 11A one instead???
Walter Koch	my favorite society(stareyed)
Jiang Chang	wrong session
Hind Lal	Wrong session
Santosh Maurya	yes
Heinrich Taegtmeyer	Wrong session again!
Ganesh Halade	Need attention
Sumanth Prabhu	Yes, where is the ACS session
Guo Huang	I think it is mixed up with session 33.
Xinliang Ma	Wrong session....
Faqian Li	I think that it plays wrong. Everything is controlled centrally, sorry.
Rongxue Wu	It is not the right session
Hind Lal	Martin talk ??
Xuejun Wang	looks like wrong session is playing
Asa Gustafsson	definitely the wrong session
Zoltan Arany	hopefully it's an error swap and we can come back in 2 hours
Suresh Verma	Anyone can check it. Wrong session...
Li Qian	They mixed up with concurrent session 11A....
Wenbin Liang	This is session 33
Wenbin Liang	sorry; this is 33 - Concurrent Session 11A
Martin Young	Maybe my talk was not interesting enough :)
Venkatesh Sundararajan	I am chating with support agent
Faqian Li	Viola in AHA is talking to the vendor
Jeremy Little	We are aware of the issue and are currently working to fix it! Thanks you for your patience!
Venkatesh Sundararajan	they are aware and working on
Guo Huang	@Faqian, can you contact the organizer and IT support to change the program?
Suresh Verma	I can see your PDF slides Martin but no talk.
Jiang Chang	i have reported
Hind Lal	@ Martin..I am sure thats not the case..
Guo Huang	Thank you, @Jeremy.
Pamel Burrage	We are looking into this item. Thank you for your patience.
Li Qian	Yeah, back to the right one!
Jiang Chang	welcome come back
Wenbin Liang	(thumbsup)
Joseph Wu	I agree, technical glitch, looking forward to your martin Martin
Suresh Verma	Here you are Martin...
Sean Wu	Great! We're back.

JohnHarry Caufield	There we are! Looks right now.
Hind Lal	(thumbsup)
Pamel Burrage	Thank you all for your patience.
Walter Koch	here we go !!
Shyam Bansal	Finally!! Dr. Young is here...
Sumanth Prabhu	Welcome, Martin. Look forward to your talk!
Qutuba Karwi	(thumbsup)
Pamel Burrage	The correct session is now playing.
Joseph Wu	(thumbsup)
Xuejun Wang	(thumbsup)
Faqian Li	Sorry for the problem It is the IT contractor's error
Qutuba Karwi	it all good now thanks
Laihua Xie	(thumbsup)
Jie Xu	(thumbsup)
Adam Wende	(thumbsup)
Oscar Bartulos	Dr. Young, nice talk. Would be the ECs the main target cells of your NPs in the in vivo model?
Heinrich Taegtmeyer	Great concepts!!!
Martin Young	Hi Oscar, certainly, in vivo, multiple cell types will play a role in nutrient utilization. Not just the cardiomyocytes, but also EC. We've mainly used CM-specific genetic manipulation models. Would be great to manipulate EC too!
Jiang Chang	Hi Dr. Taegtmeyer, thank you for coming this section. Really enjoy your keynote talk yesterday
Zoltan Arany	Martin at what time of day do you do the cardiac studies? these are Langendorffs i presume? what time of day are animals harvested, and does that time of day harvest matter?
Detlef Obal	very interesting study, well done
Jiang Chang	@Martin HFD includes high carbons?
Martin Young	Hi Zolt, we perform ex vivo heart perfusions at multiple times of the day.
Faqian Li	Thanks for very interesting and exciting data, Martin. We need to modify our eating habit.
Zoltan Arany	all else equal, do you think doing heart perfusion in AM vs PM would change RPP? have you ever looked?
Martin Young	Hi Jiang, the high fat diet does have an increased caloric density compared to control diets. So there is also a difference in caloric intake.
Faqian Li	Any change in body fat distribution
Martin Young	Hi Faqian, Yes! Its better to consume calories in the morning. Not so good in the evening.
Jiang Chang	@Martin so it is not so called "Western diet"

Martin Young	Hi Zolt, great question. When we challenge hearts with an increased workload, they do better during the active phase ex vivo. But during baseline conditions, RPP is equal between day and night perfused hearts.
Zoltan Arany	that is very intersting...
Venkatesh Sundararajan	@Martin, any idea on fasting, whether intermittent or not, on cardiac function?
Martin Young	Hi Faqian, Yes, the ad lib high fat fed mice exhibit increased adiposity. However, the 2 weeks of active phase restricted feeding did not reverse this.
Qutuba Karwi	Exciting data Martin!
Martin Young	Hi Jiang, Yes, this is more like a Western diet..
Hind Lal	Seems like we should select the dinner menu very carefully !!
Faqian Li	Thanks very interesting. It will be great to have a human population study
Shyam Bansal	Dr. Young: Great work as always! Did you check if BCAA diet had any effect on systemic/cardiac inflammatory state?
Sean Wu	Interesting Martin. Since mice are nocturnal animals, activity-wise, should the timing of experiment be adjusted accordingly?
Gobinath Shanmugam	Very interesting Study Dr. Martin.
Margaret Chandler	Hi Martin! Glad they managed to get your talk up and running!! Excellent as always!!
Liming Pei	Nice work and nice talk, Martin!
Sumanth Prabhu	Outstanding talk, Martin!
Xinliang Ma	Unfortunately, we always have big, fat dinner...
Helen Collins	Very nice work, Martin. Hope all is well at UAB
Zoltan Arany	70% increase in CM size is incredible! but that means the heart weight itself should also increase by 70% since CMs make up most of the heart -- does it?
Li Qian	Thanks for sharing this interesting work, Martin!
Xinliang Ma	Hello Sean: Nice to see you!!
Detlef Obal	Hi Sean, looking forward to your talk
dongwook choe	Wonder what happens to VO2 and other factors.
Martin Young	Hi Sean, Yes, we were feeding mice only during the dark period, which is the mouse's active period.
Dominic DelRe	Martin, very interesting talk!
Sean Wu	Nice to "see" you Xinliang
Ajit Magadum	Exciting work Dr. Young.
Guo Huang	That's a crazy increase of CM size, Martin. Nice work!
Sean Wu	Great thanks Martin!
Qutuba Karwi	@Martin, I am wondering if all BCAA are equal when it comes to triggering mTOR activity?

JohnHarry Caufield	Great talk with substantial implications for diet!
Prabhat Ranjan	Excellent talk (thumbsup)
Gangjian Qin	Martin, So exciting data! Congrats on the wonderful talk as always!
Martin Young	Hi Dongwook, We placed the mice in metabolic cages, and found tat the time of day at which lipid and BCAAs are consumed does affect oxygen consumption and RER.
Hind Lal	Great talk Dr. Martin, as always.
Tariq Altamimi	A great presentation by Dr. Young. I enjoyed it. Thanks
dongwook choe	Thanks!
Faqian Li	Thanks Sean for the great talk!
Sean Wu	Thanks Faqian!
Emmanouil Tampakakis	Great work and presentation Dr. Young. Always fascinated by the circadian heart cycle
Suresh Verma	Great data Martin...
Shyam Bansal	Great Talk, Dr. Young!
Martin Young	Hi Zolt, I didn't have time to show the data, but we also have heart weight, dry heart weight, and protein synthesis data. Heart weight increases by approax 15-20% in 4-hrs. Protein synthesis also increases dramatically - but only when BCAAs are consumed at the end of the active period.
Faqian Li	Can these treatments be continued after patching or grafting
Joseph Wu	Great talk Martin!
Zoltan Arany	fascinating... beautiful story, Martin!
dongwook choe	Does this mean other muscle structures increase in size other than the heart given late BCAA consumption?
Martin Young	Thanks to everyone for the positive feedback :)
Guochang Fan	Great work, Dr. Young. Congrats!
Martin Young	Hi Dongwook, Wonderful question! This is something that Mary Latimer, an excellent postdoc in the lab, wishes to find out.
dongwook choe	Thank you!
Martin Young	Hi Shyam,
Raj Kishore	great story Martin. Greetings
Martin Young	Hi Shyam, Thanks for asking about inflammation and systemic effects. So far, we don't know if the timing of BCAA intake affects inflammation. Great idea!
Martin Young	Hi Venkatesh, Intermittent fasting is certainly a hot topic. This strategy of eating does indeed have cardiovascular benefits. One thing we would like to know is whether the timing of breaking the fasting period should be considered. Is it better to break the fast early or late in the day?
Li Qian	"Development-neering" Cool idea, Sean! Congrats on the work!

Sean Wu	Thanks Li!
Xiongwen Chen	Hi Sean: in your cultured cell study, except for the direct contact, were there any paracrine or autocrine factors playing roles?
Rene Packard	Exciting work Sean, and kudos on the CSC paper!
Patrick Hsieh	Sean, wonderful talk and study.
Raj Kishore	beautiful work, Sean. Congrats
Yi Hong	Great talk. Sean.
David Paik	Great talk Sean
Emmanouil Tampakakis	Sean excellent work and presentation as usual.
Katherine Yutzey	Does the Wnt pathway intersect with hippo signaling in cell-cell contact effects on proliferation?
Matthew Wolf	Great talk!
Brian Orourke	Sean, Wonderful talk. How do you separate out effects due to Wnt versus other pathways affected by GSK3B inhibition?
Carolina Gonzalez	Wonderful talk, amazing work. Thank you
Qutuba Karwi	Fascinating work Sean! Congrats (thumbsup)
Detlef Obal	Sean, great work !
DaoFu Dai	Great talk Martin and Sean
Jiang Chang	Exciting work! Thank you Sean!
JohnHarry Caufield	Great talk!
Venkatesh Sundararajan	@Martin, Thanks!!! Excellent work and it is readily translational. Thank you for presenting.!!
Mingfu Wu	Great work, Sean! Sarcomere dis-organization promotes adult CM proliferation, can I interpret this way? Thanks
Gangjian Qin	Sean, congrats on the beautiful Cell Stem Cell paper. Fascinating story!
Sean Wu	@Xiongwen : We did a conditioned media study but did not see any effect from the media alone. Thanks for asking
Faqian Li	Thanks, Harry. Great power of bioinformatics.
Martin Young	Great talk Sean!
Chulan Kwon	Excellent talk, Sean!
Sean Wu	Thanks Rene, Patrick, Raj, Yi, David, Emmanouil
JohnHarry Caufield	Thank you, Faqian
Suresh Verma	Great work Sean. Congratulations for your upcoming Cell paper...
Sean Wu	@katherine - good question. We showed that when Wnt is fully activated, the hippo effect is no longer active. When we inhibit Yap nuclear translocation, there was no decrease in proliferation
Ying Ge	Excellent talk Sean! Congrats!
Zoltan Arany	beautiful stuff, Sean!

Oscar Bartulos	Very interesting data Dr. Wu. Did you see cardiomyocyte trans-differentiation upon Wnt stimulation in any condition?
Sean Wu	Thanks Matt, Brian, Carolina
Guo Huang	Great talk, Sean. I like your idea and the golden gate bridge image. Again, congrats on your recent Cell Stem Cell paper!
Katherine Yutzey	Sean, nice work. Congrats on the paper!
Sean Wu	@Brian - excellent point. In the paper we show that GSK3b inhibition activated two separate effects - one directed at LEF/TCF which regulated maturation, the other is AKT phosphorylation. These two effects were separable with small molecule inhibitors
Sean Wu	Thanks Qutuba, Detlef, DaoFu, JC, JohnHarry.
Madhumita Basu	Great talk, Dr. Wu! Congratulations on the paper as well.
Venkatesh Sundararajan	Incredible work!! Dr. Wu. Congratulations!!!!
Sean Wu	@Mingfu - thanks! We are exploring specifically whether inducing sarcomer dis-organization able to induce hiPSC-CM proliferation. Not sure if adult CMs can also be induced to proliferate this way but possible, I think.
Sean Wu	Thanks GQ!
Sean Wu	Thanks Martin, Chulan, Suresh!
Sean Wu	Thanks Ying, Zolt! Can't to be able catch up in person.
Joseph Wu	Great talk Sean!!
Detlef Obal	Harry, very nice tool
JohnHarry Caufield	Thank you, Detlef
Yun Huang	Excellent talk, Dr. Wu! Have you tried pressure stress or mechanic stress on hiPSC-CM proliferation?
Sean Wu	@oscar : we did not see a trans-differentiation effect away from cardiomyodytes. In fact, we actually saw some enrichment of CMs over fibroblasts from iPSC differentiated cells due to selective proliferation of CMs.
Sean Wu	Thanks Guo, Katherine, Madhumita!
Mohsin Khan	Development-neering..cool term..Congrats Sean
Sean Wu	Thanks Joe, Yun! We have not tried pressure/mechanical stress but my guess is they are likely to reduce proliferation.
HeeCheol Cho	Great story, Sean! Wonderful to see how you advanced your previous work by combining cell signaling and concepts of cell-cell contact!
Sean Wu	Thanks Mohsin, Hee Cheol!
Ying Ge	Great work Harry (and Peipei)! An excellent session! Congrats to all the speakers, Martin, Sean and Harry!
JohnHarry Caufield	Thank you very much Ying!
Sean Wu	Great presentation Harry!
Joseph Wu	Great talk Harry!

JohnHarry Caufield	Thank you Sean
Gangjian Qin	A great talk, Harry (and Peipei)! Congrats!!
Li Qian	Great talk, and useful tool, Harry!
Martin Young	I really enjoyed your presentation Harry. Great work!
JohnHarry Caufield	Thank you Gangjian, Li and Martin!
Ricardo Frausto	Harry, how do your literature tools exclude retracted studies, if at all?
Gangjian Qin	Thank you for creating these valuable tools for the science community!
Xuejun Wang	Thank you all three speakers, I enjoyed all of them!
Faqian Li	It will be interesting to use informatics compare and correlate basic research with clinical data. What a great tool you have, Harry!
JohnHarry Caufield	That's an excellent question, Ricardo - I've been looking into how to use the Retraction Watch database to filter those out.
Gangjian Qin	Such an exciting session!! Congrats, Martin, Sean, and Harry!!
Rongxue Wu	Great talks!
Faqian Li	We thank Martin, Sean and Harry for sharing their new exciting research findings.
JohnHarry Caufield	Yes, thank you Faqian - we're hoping to assemble all of this into tools the community can use without much need for bioinformatics experience.
Sean Wu	Yes, an open source tool for the biomedical community would be really great. Thanks Harry for working on this!

Concurrent Session 11A: Molecular and Cellular Therapy for Heart Failure

name	message
Kohta Ikegami	anybody here?
He Wang	◦ ◦
Michelle Tallquist	Yes
Li Qian	Hi everyone and welcome to this session. I am your moderator, Li Qian from University of North Carolina at Chapel Hill. We have three excellent talks lined up for you. If you have any question, please post them in the chat and if they are not answered during the session, we will have time at the end for questions. Enjoy the Session!
Rajasekaran NamakkalSoorappan	Hi
Claudia Preston	I'm here
Qutuba Karwi	Yes :)
Wuqiang Zhu	I am here
Maria Cimini	yes
Jiayi Yao	hi
Qutuba Karwi	Hi
Michael Czubryt	Here
Jianyi Zhang	(thumbsup)
Sakthivel Sadayappan	Good...
Guochang Fan	Hi, Li, greetings to all
Amadeus Zhu	The system was down for a few minutes but it looks like we're back
Rongxue Wu	It works
Yun Huang	Hello Li!
Claudia Preston	Thank you!
Ronglih Liao	yeah there is some sign in problem. hope all fixed now
Li Qian	Hello everyone! Welcome to this session!
Joseph Wu	Looking forward to talks by Wuqiang, Karen, and Guo!
Jianyi Zhang	(thumbsup)
Karen Christman	(thumbsup)
Liming Pei	Thanks for moderating, Li.
Li Qian	Nice to "see" you all here. Thanks for joining the session!
Raj Kishore	good work, Wuqiang
Rongxue Wu	Thanks for your moderating ,Dr. Li. Great session
Wuqiang Zhu	Thank you, Raj.
Karen Christman	Wuqiang, how and when did you inject the NPs?
Maria Cimini	Dr. Zhu, what is the dose of nanoparticles?
Yi Hong	Karen, nice to see you here.

Karen Christman	Hi Yi!
Yi Hong	Wuqiang, same question as Karen
Wuqiang Zhu	Hi Karen, We injected nanoparticles 45 min after MI induction.
Guochang Fan	IV injection? wuqiang.
Wuqiang Zhu	Thank you Karen and Yi!
Yi Hong	Wuqiang, inject into the infarction area or vein?
Dominic DelRe	Wuqiang, beautiful work. Maybe I missed this, are the NPs engineered to confer any cell type specificity?
Ke Cheng	Nice work Wuqiang. Pig study rocks...
Wuqiang Zhu	Hi Guochang, it was intramyocardial injection
Wuqiang Zhu	same answer to Yi
Yi Hong	thanks. Wuqiang
Wuqiang Zhu	Hi Dominic, Excellent question. The nanoparticles promote cell cycle in hiPSC-CMs, but not adult mouse and pig cardiomyocytes
Wuqiang Zhu	the nanoparticles promote angiogenesis in adult hearts
Wuqiang Zhu	Thanks, Ke.
Ronglih Liao	(thumbsup)
Rongxue Wu	Wuqiang, interesting, and novel findings. Can the nanoparticle be delivered on tissue- specifically to CM
Aijun Qiao	Beautiful work! Wuk.(thumbsup)
Eric Olson	Do a lot of nanoparticles end up in the liver? If so, what happens to the liver?
Wuqiang Zhu	Not myocyte specific. The nanoparticles were taken up by endothelial cells and other cell types
Khanh Ha	Can you design the NPs in a way it selectively go to myocyte?
Wuqiang Zhu	Hi Dr. Olson, Thank you for asking. In this study, we didn't check the liver. We will check it in our ongoing studies. Thank you for nice suggestions.
Rongxue Wu	Can it go through BBB ?
Eric Olson	Thanks. Very nice work.
Joseph Wu	Great talk Wuqiang!
Wuqiang Zhu	Hi Khan, We are collaborating with chemical engineers for cell type specific delivery. Thank you
Wuqiang Zhu	Hi Rosie, I am sorry we didn't check the brain. Very good suggestion. Thank you!
Mingfu Wu	Great job, Wuqiang!
Wuqiang Zhu	Thank you, Dr. Wu! We used your luciferase construct.
Matthew Wolf	Do you observe an increase in arrhythmia in the model?
Li Qian	Nice work and great talk, Wuqiang!
Wuqiang Zhu	It works well
Guochang Fan	Great work, Congrats. Wuk.

Timothy Aballo	Nice talk, thanks Wuk.
Rebecca Levit	Hi Wuqiang - impressive mature morphology. Can you tell if they electrically couple with the native heart?
Elaheh Karbassi	Dr. Zhu, very interesting. Is the maturation state of the hiPSC-CMs affected with respect to function (contractility)?
Yajing Wang	wuqiang, nice work, what is nano particles half life?
Wuqiang Zhu	Hi Matthew, Thank you for asking. Two pigs died after nanoparticle injection due to arrhythmia. We are not sure if it because of acute MI or nanoparticles. Will do more pig study to investigate this. No arrhythmias in mice
Wuqiang Zhu	Thanks, Li
Yun Huang	Dr. Zhu, great talk! Have you observed toxicity of nanoparitcles?
Wuqiang Zhu	Thank you, Tim and Guochang.
Matthew Wolf	Thank you. Great talk!
Rong Tian	excellent work, Wuqiang!
Jianyi Zhang	(wave)
Guo Huang	Nice talk, Wuqiang!
Wuqiang Zhu	Hi Rebecca, In our recent JMCC paper, the CCND2 expressing hiPSC-CMs electrically coupled with host mouse heart six months after implantation. Thank you!
Jianyi Zhang	(thumbsup)
Wuqiang Zhu	Hi Yajing, The PLGA nanoparticle half life in the heart has not been reported. We need to study that. Thank you for excellent question
Wuqiang Zhu	Hi Yun, We didn't observe an increased cell death or fibrosis in the nanoparticle without chemicals in vitro and in vivo. Thank you for asking
Yajing Wang	Wuqiang, thank you!
Wuqiang Zhu	Thank you, Rong for publishing our data.
Wuqiang Zhu	Thank you to ALL! please feel free to email me if you have further questions (Zhu.Wuqiang@mayo.edu). Many thanks to Jay for support!
Joseph Wu	Great talk Karen!
Li Qian	Karen, it is exciting to see Phase I Trial! I wonder if you guys have followed long-term beneficial effects and/or potential side effects in animal models.
Jamie Francisco	Dr. Christman, what did the immune profiles look like with the hydrogels?
Karen Christman	Thanks Joe
Karen Christman	In the pigs, we went out to 3 months, but that's the longest.
Rongxue Wu	Great talk Karen!
Jiang Chang	Great talk Wuqiang!

Karen Christman	We see pro remodeling immune cell polarization (M2, Th2, and also a proremodeling mast cells phenotype)
Oscar Bartulos	Nice talk Dr Christman! Did you have a chance to test the effect of the hydrogels in the local stiffness of the heart?
Li Qian	Thanks for the answer, Karen. Great talk and beautiful work!
Jamie Francisco	That's amazing! congratulations! and thank you for your answer
Maria Cimini	Dr. Christman, can you load the gel with monoclonal Abs?
Karen Christman	The hydrogels are very weak (only ~10Pa G') so we don't anticipate them to increase local stiffness. We haven't directly testing post tissue injection though.
Karen Christman	Can load the gel with many types of therapeutics. We've done small molecules, growth factors, miRNAs, exosomes, and showed increased retention and delivery. Haven't tried Abs though but wouldn't anticipate any issues.
Maria Cimini	Awesome! Thank you!
Amadeus Zhu	Dr. Christman - very exciting results! Do you anticipate significant barriers to commercialization (regulatory, IP, etc.) for your Ventrix product due to the fact that it's a naturally-derived decellularized ECM product?
Yi Hong	nice talk, Karen. Great progresses on ECM material
Jason Gardner	Great talk
Guo Huang	Nice talk, Karen.
Ke Cheng	Great talk Karen! Impressive data from the clinical trial. Wondering whether IC-delivered SolMM only stay in the lumen to have the effects or do they eventually go to the myo?
Patrick Hsieh	Hi Karen, great talk. Congrats.
Jamie Francisco	Excellent talk Dr. Christman!
Karen Christman	Amadeus, No issues related to being naturally derived. FDA is used to seeing a lot of naturally derived materials. So they had no issues.
Amadeus Zhu	Thanks!
Karen Christman	Ke, so far we've only seen it in the blood vessels/gaps between endothelium. We checked multiple timepoints and didn't see it gelling in the infarct. But likely as it degrades, some degradation products will go in.
Ke Cheng	(thumbsup)
Karen Christman	Thanks all. Glad you could join the session.
Guochang Fan	Thanks Karen for sharing us such great work. Congrats.
Fuli Xiang	Excellent work, Karen! Thanks a lot.
Ronald Vagnozzi	Hi Karen, really exciting data, thank you for sharing! Do you think having the hydrogel lining the vasculature might be

	preventing influx of certain immune cells (inflammatory monocytes, ie.) and changing the immune milieu that way?
Karen Christman	Yes, we are looking at that now.
David Paik	Very interesting and cool work Guo!
Eric Olson	Hi Guo. Fascinating work. I assume people with hypothyroidism can't regenerate their hearts post MI. If not, why not?
Guo Huang	Thanks, David.
Rongxue Wu	It is very interesting findings, Dr. Guo
Guo Huang	@Eric, we think the hypothyroidism has to start from birth. When we treat adult mice with drugs to cause hypothyroidism, the heart can not regenerate.
Yun Huang	Dr. Huang, interesting talk! The thyroid hormone regulation are gender specific. Its level is also changed during aging. Have you observed the gender difference and age effect in your experiment setting?
Joseph Wu	Great talk and beautiful work Guo.
Eric Olson	Do bats regenerate their hearts. Be careful with those bats!
Guo Huang	@Eric There are two people with dominant negative mutations in Thra. I suspect that they retain significant cardiac regenerative potential.
Guo Huang	Thank you, Yun and Joe.
Yi Hong	Guo, very interesting work.
Guo Huang	@Eric, we actually tried to study bat regeneration.
Fuli Xiang	(thumbsup)
Jamie Francisco	Dr. Huang, could this have to with immune systems/environment? Generally aquatic animals don't have a well developed adaptive immune system due to their low exposure to pathogens with the constant movement of water. Additionally, wound healing is improved in aquatic environments (even with people!) resulting in smaller scars, although it takes longer
Guo Huang	@Eric ...together with the group which published this paper "Cardiac adaptation in prolonged inverted bats (Eidolon helvum)" in which there was a sign of CM proliferation after inversion-induced cardiac injury. He did experiments but could not ship the bat hearts out of Nigeria.
Guo Huang	Thank you, Yi.
Tianfang Yang	Hi Guo, do you think the loss of regenerative potential and endothermal acquisition is a historical coincidence, or a functional limitation of relavant molecular machinaries?
Tamer Mohamed	Great talk Guo! How do you think thyroid hormone influence cardiomyocyte proliferation mechanistically? does it shift the metabolism or are there other possibilities

Jie Xu	Great talk Guo! Super interesting. Good to see you again!
Guo Huang	@Jamie, a good question. This is one of the topic that many labs have been exploring.
Li Qian	Impressive work, Guo! Particularly enjoy your unique views and angles to explore loss or gain of heart regenerative capacity. Look forward to the next piece of your exciting work!
Eric Olson	alpha and beta myosin are two of the most thyroid hormone sensitive genes in the heart. Are they involved?
Yi Hong	Guo, an curios question. Does the ECM component affect such regeneration?
Mingfu Wu	Guo, great work! Congratulations on the paper in Science!
Chuanxi Cai	Very nice work!
Rong Tian	fascinating work!
Jamie Francisco	Thank you Dr. Huang! excellent talk! I know this is of particular interest with amphibians, as they go from aquatic to land based environments and have shifts in their immune systems
Li Qian	Applause to all speakers, thanks for delivering such a wonderful session!
Li Qian	Also big thanks to all participants, for listening, supporting and active discussion!
Ying Ge	A great session with three exciting talks! Congrats to Wuk, Karen and Guo for the fascinating work and stimulating presentations! Thanks Li for moderating! Hope to meet you in person next year :-)
Yi Hong	thanks. Li
Karen Christman	Nice work Guo. I had the same question as Yi.
Jiang Chang	@Guo fantastic discovery! a question: how could some organs like liver can keep regenerate capacity? because lack of TR?
Rong Tian	a terrific session, thx to Li for chairing
Hanqing Zhao	Nice work!
Li Qian	Hope to see you all in person in the near future!
Keith Jones	Dr. Huang, have you looked at non coding RNAs that might target relevant genes are TH regulated in this system?
Dominic DelRe	Incredible session! Thanks to speakers and Li for moderating!
Emmanouil Tampakakis	Great work Guo. I really enjoyed this
Keith Jones	nice session everyone!
Liming Pei	@Guo, very nice work! Any insights into the specific thyroid hormone receptor (alpha or beta) or isoforms that mediate the regeneration effect

Guo Huang	@Tianfang, this is exactly what we try to find out. It seems that becoming endothermy requires the increase of cardiac output by ~10 fold, which seems to substantially change the heart design. Now we are actively looking for the exact molecular link and causality.
Jijun Huang	Great story, @Guo! As thyroid hormone was supposed to regulate CM maturation, does that means a species differences in CM maturation status or timing?
Guo Huang	Thank you, Tamer and Jie. @Tamer, we found one of the thyroid hormone target genes Cpt partially contribute to the phenotype. It is in our supplemental figures. Cpt encoding the rate limiting step for fatty acid import into the mitochondria. So in this sense, metabolism may be involved. We are testing the functions of many target genes right now.
Rong Tian	@guo, do you see a correlation between cardiac work and regeneration capacity?
Jie Xu	@Guo, follow up on @tianfang's question, does the 10x more work for the heart reflected in a drastic increase in mechanical load? In other words does more mechanical load decrease regeneration abilitity?
Guo Huang	@Eric, Yes, both are excellent targets. We are using Crispr to test their functional contributions. Stay tuned.
Guo Huang	@Yi, we did notice expressional changes of many ECM proteins. Now we are testing some of them.

Concurrent Session 11B: Diastolic and Contractile Dysfunction in Heart Failure

name	message
Kohta Ikegami	anybody?
Rajasekaran NamakkalSoorappan	Hi
Alicia Mattiazzi	yes, waiting
Snekha Rajasekaran	Hi :)
Sakthivel Sadayappan	It is working
Willem DeLange	seems like there were technical problems!
Liya Yin	yes, it is working now
Rene Packard	Was unable to log on earlier - getting an error (service unavailable) message...
John Ralphe	Welcome everyone! Sorry for delay- technical issues it seems? I'm the session moderator- Carter Ralphe, from the University of Wisconsin. Please dont hesitate to piost questions on the chat line...if we are able to hear the talks, that is!
Heinrich Taegtmeyer	Are we late?
John Ralphe	Just started!
Sakthivel Sadayappan	Thank you John for moderating this another exciting session!!
Joseph Wu	Looking forward to an exciting session by Drs. Kloner, Stelzer, and Westfall!
Jil Tardiff	Yes!
Liya Yin	@Kloner, Did you check the shorter time of occlusion, like 5-10 minutes? Great talk! Thank you
Robert Kloner	we did not, but others have shown stunning after only 5-10 min of ischemia
Sakthivel Sadayappan	@ Dr. Kloner, Thank you for presenting at #BCVS20
Mei Methawasin	@DR Kloner, what is the mechanism that explains the slower recovery of diastolic function compare to systolic function?
Robert Kloner	Not entirely clear. Possibly related to alterations in calcium flux?
Rajasekaran NamakkalSoorappan	Very interesting observation Dr. Kloner! Spasm...
Robert Kloner	Certainly coronary spasm, if it occurs for more than 5 minutes or so could result in stunning.
Willard Sharp	Do you think cardiac dysfunction following short sudden cardiac arrest also represents stunned myocardium?
Liya Yin	@Kloner, what do you think about an animal model of repetitive ischemia model with 5 minutes of occlusion and

	repeat 4 times a day ? The myocardium stunned , recovery, stunned, recovery? Thank you
Robert Kloner	Yes, most likely.
Venkatesh Sundararajan	Dr. Kloner, can hibernating myocardium be viable and restored fully functional upon reperfusion similar to non-hibernating one?
Robert Kloner	Repetitive episodes of ischemia and reperfusion can cause stunning that may take longer to recover; but paradoxically can precondition the myocardium against necrosis due to a longer more severe episode of ischemia
Robert Kloner	Hibernating myocardium can recover function after revascularization, but it can take a long time to rebuild up the de-differentiated tissue.
Willard Sharp	Do you think molecular changes occurring in my-filaments in stunning contribute to eventual necrosis when ischemia continued
Robert Kloner	Ischemia refers to ongoing decrease in blood flow. In stunning the blood flow is restored so it is no longer ischemic. By definition, stunned myocardium is not dead tissue, but viable.
Nicole Purcell	Great talk Dr. Kloner..good to see you!
Liya Yin	@Dr. Kloner, thank you. The precondition model will stimulations revascularization, but myocardium might be injured?
Margaret Westfall	Appreciate your integration of stunning and associated dysfunction Dr Kloner! Thanks to the organizers for this session & John Ralphe for moderating.
John Ralphe	Dr. Kloner- excellent talk! I greatly admire your work and all the contributions you have made to the field. Thank you!
Willard Sharp	thank you Dr. Kloner!
Joseph Wu	That was a great talk Dr. Kloner! Joe
Jil Tardiff	Julian! Looking forward to this !
Sakthivel Sadayappan	Hello Professor Stelzer!!!
Christopher Solis	Great talk Dr. Kloner
John Ralphe	Hi Julian-- thanks for presenting! And good- a cpro talk!
Venkatesh Sundararajan	@ Dr. Kloner, thanks! that is interesting. I believe hibernating does not occur in all patients and it depends on the duration and severity of the coronary blockage, if I am right.
Charles Chung	Dr. Kloner, thank you for this talk. The de-differentiation is interesting. Is there any quantification of the time course of protein expression/post-translational modifications? (especially if there are differences between stunned and takasobu)

Robert Kloner	Most preconditioning protocols do not cause irreversible damage to the mycoardium.
Liya Yin	Thank you very much. Great talks!
Heinrich Taegtmeyer	Thank you for the memories, Bob. Still a lot to be learned about reverse remodeling after revascularisation of hibernating
Heinrich Taegtmeyer	heart muscle.
Robert Kloner	Dr. Chung, you ask a good question. We have not looked at the issue of protein expression in hibernating. Dr. John Canty at U of Buffalo may have looked at this. He has a terrific model of hibernating myocardium.
Charles Chung	Thank you, Dr. Kloner!
Jil Tardiff	Dr. Kloner beautifully discussed a subject that "torments" fellows to this day.
Robert Kloner	Thank you. Also in answer to one of the questions above, hibernating myocardium does not occur in all patients with coronary narrowings. It may be dependent on a number of factors including the amount of collateral flow available.
Venkatesh Sundararajan	Thank you Dr. Kloner!! great information
Hind Lal	What was the route of AAVs injection
Liya Yin	@Dr. Kloner, if the microvascular dysfunction is part of the cause for Takasobu , the stunned /hypernating myocardium is caused by microischemia? Does the stunned or hibernating myocardium happen INOCA? Thank you
Christopher Solis	Dr. Kloner, would increased caspase activity during the ischemic event (which leads to reduced myofibrillar sensitivity to Ca2+) be of significance in the context of patients experiencing myocardial stunning?
Sakthivel Sadayappan	What was the half of C0-C2 protein in the cardiomyocytes, compared to FL cMyBP-C?
Robert Kloner	Good question,. We have not looked at caspase activity in our models. Open emoticons window
Sakthivel Sadayappan	half life
Walter Koch	this is really nice
Willem DeLange	Great Talk Julian - Did you try this same experiments at a later time-point?
Joseph Wu	Great talk and beautiful work Julian.
Willem DeLange	I.e. at weaning or adult mice?
Jil Tardiff	Such a pleasure to see some xb kinetics - beautifully done.
Rene Packard	Dr. Stelzer - great lecture, thank you. 1. Have you looked at gene expression of other proteins involved in the contractile apparatus following AAV-9 delivery? 2. Have you assessed this approach in another CMP model?

John Ralphe	Agree- this is beautiful work!
John Ralphe	Did you detect any undesired effects on the cells/hearts?
Darshini Desai	Interesting talk Dr Stelzer! Did you happen to look at the phosphorylation of SR proteins, calcium dynamics etc.
Farid Moussaviharami	Hi Julian, great talk. Did you guys look at calcium dynamics in isolated cardiomyocytes?
Sakthivel Sadayappan	Hi Margaret, Excellent start! Thank you for your presentation!
Jil Tardiff	As I commented yesterday - cTnI is a bit of a devil in the thin filament. The questions she is addressing in this work have flummoxed us for years and are very translationally relevant.
Jil Tardiff	Pretty quick - interesting
Andrew Carley	Does this residue exist in ssTnI?
Margaret Westfall	There is an equivalent Thr and Ser but the amount of phosphorylation seems to be much less
Farid Moussaviharami	Beautiful work Dr. Westfall. Do you think there will be similar results if an inducible promoter is used to turn on the transgene in adulthood?
Margaret Westfall	Good question - would like to look at this but it will take longer to get this model up and going.
Farid Moussaviharami	Are there changes in other phosphorylation sites or phosphorylation of other myofilament proteins?
Sakthivel Sadayappan	@MW, Did you use fibers to measure pCa-force of contraction and rate of force redevelopment (ktr)? I guess HE-SD myocytes have faster kinetics, leading to hypertrophy at later stage!
Margaret Westfall	Not yet but it is in the que!
Farid Moussaviharami	(thumbsup)
Joseph Wu	Good to see you Margaret and thanks for a great talk! Joe
Margaret Westfall	Ditto!
Grace Muller	Dr. Westfall, fascinating! Have you noted any gender-specific differences?
Darshini Desai	excellent talk! Have you looked at the mitochondrial membrane potential?
Charles Chung	Dr. Westfall, interesting data. Does resting sarcomere length differ in the ME-SD or HE-SD mice?
Sakthivel Sadayappan	I am curious to see myosin kinetics in the HE-SD myocytes!
Grace Muller	And could there be changes in mitochondrial morphology or the mPTP/mitochondrial membrane potential change
Jil Tardiff	Margaret - what's your bet on the identity of this sarcomeric stress, it is, as you know, the 64K question
Margaret Westfall	We are in the process of looking at mitochondrial size & number. Initial experiments in 3 mos old mice do show

	reduced membrane potential but these studies were interrupted by COVID so hope to get back to this soon.
Liya Yin	@Dr. Westfall, Great talk! Did you check the methylation of mitochondrial DNA?Thank you

Session 12: Genomic, Genetic and Epigenetic Mechanism of Heart Failure

name	message
Susan Cheng	Welcome!
Joe Trusso	Welcome! Thank you for joining us. You should be seeing a chat prompt slide as we wait for the session to begin. If you do not see this, please submit a support ticket by clicking on the Request Support button located at the bottom left of the player.
Sakthivel Sadayappan	Welcome everyone!!!
Susan Cheng	We have a fantatstic line-up of speakers and topics! please feel free to contribute thoughts and questions to the chat, and we can address them during the Q&A... thank you!
Jinqi Fan	great talk, Dr. Cheng. Nice to see you Here
Susan Cheng	great to see you also!
Ke Cheng	Thank you Susan for charing. Great to see you Jinqi.
Joseph Wu	Great talk Ke and a fantastic body of work. Joe
Ke Cheng	Thank you Joe!
Liya Yin	@Ke Great work!
Chuanxi Cai	Beautiful work!
Zhongjian Cheng	Fantastic work Ke!
Ronglih Liao	great talks! Thanks for sharing!
Rongxue Wu	It is a powerful method and interesting findings, Dr. Cheng
Detlef Obal	Impressive work
Mingfu Wu	Great work, Ke! I always have the question about how the patch sticks to the heart?
Yajing Wang	Ke, nice work, did you need to break epicardium when you did patch to the heart?
Ke Cheng	@Mingfu, for the STM paper work, we still need to use sutures
Mingfu Wu	OK. Thank you!
Yang Xiang	Ke, Beautiful work, are there specific cell surface markers can be used to stick patch on heart?
Karen Christman	Nice talk Ke.
Sakthivel Sadayappan	Ke Cheng, Thank you for your excellent presentation!!
Sakthivel Sadayappan	Hello Megan!!
Yi Hong	Nice talk. Ke
Ke Cheng	@Yang, sorry we have not yet looked into this possibility. Good suggestion!
Susan Cheng	Amazing work!
Fuli Xiang	Ke, very impressive work! Thank you:)
Megan Puckelwartz	Hi Sakthi!

Ke Cheng	Thank you all for attending and commenting.
Zhongjian Cheng	@Ke, impressive! how long the cells can be stay/survival in the nanogel/patch?
Ke Cheng	@Zhongjian, in the nano gel paper, we still see engraftment at 3 weeks
Yang Xiang	@ke. I remember you have identified a marker for intracardiac delivery of particles. is it integrin?
Zhongjian Cheng	@Ke, cool! Thank you!
Susan Cheng	the race/ethnicity predominance is intriguing
Susan Cheng	given the more diverse genetic architecture
Ke Cheng	@Yang, not by our lab, but YES one of my colleagues Dr. Yucai Xie published a nice Stem Cell paper indicating the beta 1 intern on cardiomyocytes is important
Ke Cheng	sorry for the typo, I mean integrin
Megan Puckelwartz	We were also intrigued and careful to correct for the expected number of variants (greater in ore diverse subjects).
Susan Cheng	nice
Susan Cheng	wondeirng if you saw any sex differences (if sex-stratified analyess were done)
Megan Puckelwartz	It really speaks to how necessary careful VUS adjudication is going to be as we sequence more diverse cohorts.
Susan Cheng	agree!
Megan Puckelwartz	We did not stratify by sex - but that would be very interesting to try!
Susan Cheng	cool... and btw, really love the longitudinal analysis approach -- very important!
Megan Puckelwartz	Thanks - a grad student in the lab, Tess Pottinger, spear-headed these studies. It really pulls ALL the data out and is useful for richly phenotyped, but small cohorts.
Susan Cheng	nice and great approach to leverage data from smaller cohorts.. also accounts for potential effects of aging (and accumulation of other exposure effects over time)
Megan Puckelwartz	Indeed! This is critical for cardiovascular phenotypes!
Susan Cheng	great talk!!!
Megan Puckelwartz	Thanks Susan.
Susan Cheng	looking forward to watching out for more pubs to come out of your lab on all this!
Sakthivel Sadayappan	Megan, Thank you for a beautiful and very informative presentation.
Megan Puckelwartz	Thanks - there are a few manuscripts in the pipeline!
Megan Puckelwartz	Thanks Sakthi!
Susan Cheng	great ;)
Susan Cheng	the brown fat story has been really seminal...

Sakthivel Sadayappan	All the best, Megan. Look forward to seeing those papers
Ippei Shimizu	Hi Susan, thanks for the comment!
Susan Cheng	i didn't know about the vegf connection or coag factor relations
Megan Puckelwartz	Thanks! I'm looking forward to seeing your next genetics paper too!
Sakthivel Sadayappan	Of course with your collaboration!!
Megan Puckelwartz	:)
Ippei Shimizu	Our coagulation factor project is now in revision (reviewers comment really tough to answer,,)
Susan Cheng	reviewers can be tough! feel free to reach out to any of us or bcvs folks on circ res ed board for curbside on appraoches, if helpful... sometimes brainstorming from outside colleages (without need for obligation) can be helpful
Susan Cheng	so cool... love the video of thermoscanned mice
Ippei Shimizu	Hi Susan, thank you for your great suggestion! ^^
Liya Yin	@Ippei, is the lower temp related to the low activity /less exercise /low metabolic rate? Thank you, interesting study
Ippei Shimizu	Hi Liya, that's important point, but we have not analyzed activity yet. Let this be our homework. BAT implantation increase thermogenesis, and cardiac function improves, so we consider BAT has causal role for maintaining cardiac function.
Oscar Bartulos	Hi Dr Shimizu. I guess there is correlation between beat rate, age and body temperature, right?
Joseph Wu	This is very interesting work, thanks for presenting Ippei. Joe
Ippei Shimizu	Hi Joseph, great to have your comment! Thank you.
Susan Cheng	love the aging theme
Susan Cheng	amazing work!
Ippei Shimizu	Thank you Susan, I really enjoyed this session! cheers,
Susan Cheng	senocules is a very compelling theme and great way to tie it all together
Liya Yin	@Ippei, is BAT is decreased in aged animals? Thank you
Susan Cheng	very in sync with network biology approaches
Santosh Maurya	how does ANP play as a crosstalk molecule between heart and BAT in heart failure?
Ippei Shimizu	Hi Liya, BAT function declines with aging.
Susan Cheng	very important, is this finding published?
Susan Cheng	given that fat vs lean muscle ratios change with aging...
Liya Yin	I meant the fat distribution? Thank you
Ippei Shimizu	Hi Santosh, yes ANP is important for activation of BAT. Together with SNS, we speculated this would increase BAT function. But the result was opposite. Heart failure reduces BAT function in our LV pressure overload model.

Santosh Maurya	Interesting. Did you notice reduced UCP1 expression?
Ippei Shimizu	Hi Susan, now we are in revision (Nature), hope we can survive this. Again reviwer's comments really tough,,,.
Susan Cheng	wow! ok those reviewers will defn be tough... but will be worth it if you can get through...
Ippei Shimizu	Hi Liya; we have not checked fat destribution yet. We can analyze this with CT (let this be our homework), thanks
Susan Cheng	feel free to pull in your collagues and collaborators to help... if substantial, they can be added to the manuscript (this has happend for other papers at nature and other journals as you probably know already)
Susan Cheng	sounds like this work really needs to get published!
Susan Cheng	thank you so much for sharing your work in this forum
Ippei Shimizu	Hi Santosh, as for UCP1, I remember this as comparable. because of two direction. Hyper activation of BAT, and cell death of BAT due to activation of SNS in BAT.
Susan Cheng	super exciting and will forward the field
Santosh Maurya	Was there any sex specific change in BAT in heart failure model?
Ippei Shimizu	Hi Susan, thanks indeed for your helpful comments!
Ippei Shimizu	As for gender difference, we have not checked yet.
Santosh Maurya	i mean BAT function was different in male vs. female in heart failure model
Liya Yin	For HF patients, did you check the lipid level or obese parameter? Thank you

Workshop 2: The Practice of Biomedical Research: Honesty, Transparency and Early Career Funding Opportunities

name	message
Ganesh Halade	I believe not current session, please check
Pamel Burrage	The previous session is running a little over in time. Once that session has ended Workshop 2 will start.
Ganesh Halade	Got you, thank you !
Leslie Leinwand	Yes, thank you!
Jane Freedman	Thanks!
Sakthivel Sadayappan	Welcome everyone..
Chen Gao	Waiting for workshop 2!
Leslie Leinwand	Thank you! Where will questions show up, Sakthi?
Jil Tardiff	They will show up in this chat sequence
Joseph Wu	Good to "see" you Leslie and thanks for moderating! Joe
Leslie Leinwand	You too, Joe!
Sakthivel Sadayappan	Hello Leslie! Thank you!!
Sakthivel Sadayappan	Here only
Sakthivel Sadayappan	Participants will post questions here
Jil Tardiff	What a terrible number
Jane Freedman	So true
Leslie Leinwand	Agreed
Joseph Wu	Jane, thanks for this very important talk to all the PIs and trainees. Joe
Alicia Mattiazzi	Excellent talk Jane!
Sakthivel Sadayappan	Nicely done, Jane!!
Charles Chung	As an early career investigator with a small lab, blinding would be difficult. I wonder if there is guidance anywhere on alternate methods for blinding or minimizing bias?
Jane Freedman	Thanks!
Jane Freedman	The need for blinding really depends on the study. If not done, just be open about this as a limitation.
Xinliang Ma	Hello Jane: Excellent talk! Great to see you here..
Jane Freedman	Thanks!
Ronglih Liao	Thanks Jane! great talk!
Jane Freedman	Thanks Ronglih!
Nicole Purcell	this is a great session and relevant to everyone. Nice talk Jane!
Rong Tian	Question for all: lots of misconduct investigation requires original records. How many years in general Is there a consensus for many years the records should be kept?
Heinrich Taegtmeyer	The nuts and bolts we all need to know. Thank you, Jane. Thank you, Dr. Garfinkel. What a session!

JoanHeller Brown	A faculty member had agents come in and confiscate their lab computers to look for possibly falsified data, without any prior notification from the university or NIH regarding any allegations. Is this standard operating procedure?
Susan Garfinkel	Most institutions have data retention policies, the NIH says keep data for 3 years after the close of a grant project. If a RM case occurred, data needs to be kept for 10+ years.
Jane Freedman	That's a great question. I always was told 10 years (some say 7) but I know we get claims of plagiarism from 20 year old papers. It is complicated, even for an editor trying to vet these issues.
Charles Chung	We try to re-write methods for each of our manuscripts, however, it is difficult to make substantive changes. Any suggestions on whether self-plagiarism is acceptable (e.g. copying most of the methods from our previous papers without citing every paragraph?)
Susan Garfinkel	Usually methodology, if it is standard, can only be written in so many ways and this would not be included as an issue of self plagiarism.
Charles Chung	Thank you
Chengxue Qin	Thansks great talks
Joseph Wu	Thanks Joe for touching on this topic.
Joseph Hill	Thanks, Joe. We'll see how it goes!
Jane Freedman	Great question. But, as Susan said, we do not consider re-stating your own methods as plagiarism
Jil Tardiff	Thanks a million for participating, Susan - sobering and very important for all of us
Susan Garfinkel	Thank you!
Yajing Wang	thanks all chief editors for such informative talks
Sakthivel Sadayappan	Dr. Hill, Thank you for your presentation in this exciting session!!
Joseph Hill	my pleasure
Poonam Rao	Very Informative. Thank you Jane
Chen Gao	Great topic!
Xinliang Ma	Hello Joe: Great to "see" you here. Excellent topic!!!
Joseph Hill	Thanks to you both!
Ganesh Halade	Excellent session to improve cardiovascular research quality !!
Jil Tardiff	Very important to de-mystify this process.
David Paik	Very informative session, Dr. Hill. Thank you
Rong Tian	very important points, Joe. Thank you for bringing them up!
Chengxue Qin	Very important. I had to say those practice are "eye opening" sadly.....Thank you

Farid Moussaviharami	Hi Joe, could you comments on some criteria used for not sending a paper out for review?
Ronglih Liao	These are very impotant topics, thanks to both Jane and Joe for doing this. (thumbsup)
Joseph Hill	If a paper has any chance of achieving priority for publication at Circulation, or in one of our subspecialty journals, -- any chance -- then we send it out for review. That said, our acceptance rate is 6% and yet we review 50%.
Meenakshi Madhur	I see lots of negative clinical trials get published in prominent journals but I feel like there is no good home for negative basic science studies. Yet I think it is important to publish negative basic studies so that other investigators know what doesn't work and won't waste time trying it again. What are good journals that will accept negative data?
Yajing Wang	nice to 'meet' you, Joe.
Rajasekaran NamakkalSoorappan	@Meenakshi- I agree this has to be discussed and find ways to pusblish the negative results! We struggle to convince about reductive stress with ton s of data as everyone believes that Oxidative Stress is driving the whole world!
Jiang Chang	Thank you so much Joe for bring this point! I personally know a victim hurt by these so called "knowledge"
Joseph Hill	Hi Yajing!
Jane Freedman	There's a difference between negative results and those that refute previous data
Danish Sayed	Thanks for covering predatory journal Dr. Hill, surprisingly, some of these journals are on Pubmed
Rajasekaran NamakkalSoorappan	Thanks Dr. Hill, wonderful talk!
Jil Tardiff	That's a great point, Jane.
Joseph Hill	Thanks, all!
Suresh Verma	Agree Jane
Farid Moussaviharami	Great talk!
Rene Packard	Thank you to the speakers and the BCVS for another great session with important implications.
Meenakshi Madhur	@Dr. Freedman. Yes there is a difference between negative results and those that refute previous data. I was referring more to the former - negative results. Do you think there is value in publishing that and where?
Suresh Verma	Great talk Prof. Hill.
Meenakshi Madhur	Thanks Dr. Hill.
Hind Lal	Very informative session, thanks to all speaker and the organizing committee.

Jane Freedman	I do think there is value but agree that they are harder to publish (I've been there many times). Reviewers often say "underpowered" or cite methodological reasons why the study was negative.
Suresh Verma	Excellent piece of information. Thanks Joe, Jane and Susan.
Rajasekaran NamakkalSoorappan	Thats true Dr. Freedman
Venkatesh Sundararajan	Great session! and information
Meenakshi Madhur	@Dr. Freedman. Thanks. Agree.
Charles Chung	Thank you to all of the speakers. Great Points. I do think that "honest" mistakes are quite easy- transposing data in Excel, etc. (A year ago, I did not submit a manuscript revision when I found transposed data for an essential result). Any guidance from experienced mentors on keeping data organized, accessible, etc to ensure that data can be quickly checked for errors (honest or not)?
Hanqing Zhao	Nice talk. Thank you all.
Poonam Rao	Thanks to organiser committee for this important session and a big thanks to the speakers too for sharing there expertise
Leslie Leinwand	Thanks to everyone!
Jijun Huang	Great sessions! Thanks to the speakers! One question: any comments on Pubpeer's role from a journal Editor's perspective.
Michael Czubryt	Great session - thank you
Jil Tardiff	Thanks for moderating , Leslie!