WEBVTT

NOTE duration:"00:32:27.8230000"

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NOTE Confidence: 0.826016485691071

00:00:00.880 --> 00:00:03.100 Yale podcast network.

NOTE Confidence: 0.915459394454956

00:00:05.290 --> 00:00:17.380 Hello and Welcome to another episode of the Yale Journal of biology and Medicine podcast. YJBM is a pubMed index quarterly Journal edited by Yale medical graduate and professional students and peer reviewed by experts in the fields of biology and medicine.

NOTE Confidence: 0.911289870738983

00:00:18.080 --> 00:00:25.380 Each issue of the Journal is devoted to a focus topic and in this series. We're taking you through the past, present, and future of the clocks and cycles.

NOTE Confidence: 0.856154680252075

00:00:25.960 --> 00:00:44.070 Or July episode is devoted to YJBM's issues on Clocks and Cycles, which was just published last June and you can find this issue on why YJBM's website or and pub med. I'm Amelia Hallworth a second year graduate student in Microbiology and I'm Lisa Ogawa McLean and I am a fifth year student in molecular biophysics and biochemistry.

NOTE Confidence: 0.924982309341431

00:00:45.360 --> 00:00:57.540 Today we're interviewing doctor Adam Silver, an associate professor of biology at the University of Hartford. In addition to his work on the immune system and the circadian Clock that we will talk about today? He also works on the gut microbiome.

NOTE Confidence: 0.929601967334747

00:00:58.680 --> 00:01:15.580 So doctor Silver can you please give a brief introduction of the circadian Clock and the immune system as they pertain to your research? I'd be happy to. Thank you for having me today. Thank you for coming so the master circadian Clock is located in the Super chiasmatic nucleus of the hypothalamus in the brain.

NOTE Confidence: 0.931861102581024

00:01:16.170 --> 00:01:26.650 Regulates nearly all aspects of our Physiology, and behavior, which oscillate over the course of a 24 hour period. Now the Clock regulates activities that the Organism.

NOTE Confidence: 0.91137421131134

00:01:27.480 --> 00:01:35.140 So, like the sleep wake cycle this cellular so for example, the recruitment of cells in at the molecular levels like gene expression.

NOTE Confidence: 0.92389589548111

00:01:35.910 --> 00:01:47.330 So since we're more likely to encounter pathogens during the day when we are active. We initially were interested in determining if certain aspects of our immune system fluctuated over the daily cycle.

NOTE Confidence: 0.903452038764954

00:01:47.890 --> 00:02:14.490 So is our immune system at its peak. When were active and potentially more likely to encounter pathogens so in theory, we don't need our immune response at its peak. When were sleeping. So this would be kind of a waste of energy and could potentially inhibit tissue repair so currently I've been interested in the other end of the spectrum so how do pathogens or even microbes in general alter our Clock so This is why we feel tired? When were sick?

NOTE Confidence: 0.929235637187958

00:02:14.990 --> 00:02:20.510 So just the recognition of pathogens impact the Clock, which is closely tide to the sleep Wake Cycle.

NOTE Confidence: 0.908469557762146

00:02:21.660 --> 00:02:54.820 So Is it true then that the light is the main driver of the circadian Clock. That's what regulates the circadian rhythm. The Clock cycle. So it is so the master Clock isn't trained by exogenous cues and like you said light is the biggest one. However, other environmental stimuli can align the Clock such as temperature food, even exercise so the master Clock, then regulates peripheral oscillators throughout the body, so that can be found in various organs tissues as well as cells.

NOTE Confidence: 0.933290779590607

00:02:54.820 --> 00:03:03.650 And then this synchronization or you could think of it like talk to the periphery is mediated through various neural and hormonal signals.

NOTE Confidence: 0.913496673107147

00:03:05.570 --> 00:03:32.930 So if if those external signals like light and temperature aren't changing but then, when you get sick. The pathogens are altering the Clock. Even though those signals aren't changing I guess possibly the pathogens may be acting further downstream is that what you're finding that's a great question and I would say right now, we don't know so that would be something that I'd be interested in would be to determine those molecular mechanisms of how that is actually happening.

NOTE Confidence: 0.926511347293854

00:03:33.990 --> 00:03:55.080 So other than that? What are currently some of the bigger intriguing questions in your field kind of like I mentioned just now would be looking at some of those molecular mechanisms. So we know that various immune parameters fluctuate over the 24 hour period, however, really more work needs to be done to determine those molecular mechanisms.

NOTE Confidence: 0.949756264686584

00:03:55.730 --> 00:04:02.890 I think it would be very important to determine the clocks influence on the adaptive immune response as well.

NOTE Confidence: 0.934264421463013

00:04:03.690 --> 00:04:15.700 And then if you take kind of both of these points and put them together. I think they'll enhance the field of Chrono Therapeutics. So time delivery of drugs and vaccines in order to develop maximum efficacy.

NOTE Confidence: 0.931645214557648

00:04:16.220 --> 00:04:48.830 And I think ultimately that's why I would like to see the research field. Go to kind of personalized. Medison, which takes into account and individuals circadian rhythm so really briefly on the topic of drugs targeting the circadian rhythm are there known diseases that are associated with I guess the Clock gene so interesting Lee in 2014. There was a paper that revealed that oscillating jeans or associated with nearly every major disease that was funded by the NIH.

NOTE Confidence: 0.936061203479767

00:04:49.400 --> 00:05:11.760 So diseases like cancer Alzheimer's disease, Schizophrenia Down syndrome, obesity, where most strongly associated with circadian jeans and they go on to reveal that 56 of the Top 100 best selling drugs in the US target the product of a circadian gene.

NOTE Confidence: 0.913543939590454

00:05:12.720 --> 00:05:25.940 Yeah, that's really interesting are there any drugs that currently target the Clock jeans specifically if it Clock chain not just once that oscillate that I'm not sure.

NOTE Confidence: 0.925866842269897

00:05:26.790 --> 00:05:44.040 OK, so how did you get to where you are and how did your research interests develop into studying the immune system in the circadian rhythm a long story. I'll try to keep it short, but I kind of consider myself a Jack of all trades master of nothing.

NOTE Confidence: 0.909246861934662

00:05:45.980 --> 00:06:13.140 So as a graduate student or I could say I consider myself a microbiologist at heart. Even though right now. I study circadian rhythms and the immune response so as a graduate student. I studied the beneficial symbiosis between Aeromonas Verrone and the medicinal. Leech so

really bacteria host interactions in the laboratory of doctor your graph the University of Connecticut.

NOTE Confidence: 0.936200797557831

00:06:14.220 --> 00:06:24.280 And after my PhD work I wanted to continue bacteria host interactions. But I thought it would be really cool living in Connecticut. I'm from Connecticut.

NOTE Confidence: 0.878672957420349

00:06:24.950 --> 00:06:32.940 To study tick bacteria interactions and then, who better to work with and Yale Zone Doctor Errol Vic rig.

NOTE Confidence: 0.917697846889496

00:06:33.520 --> 00:06:49.180 So actually started on a project in his lab for the first six months of my tenure, there looking at tix salivary gland proteins. That could help facilitate Borrelia. The causative agent of Lyme disease getting into the mammalian host.

NOTE Confidence: 0.913298368453979

00:06:50.160 --> 00:06:56.840 An and then during that time, another post doc in the lab who actually did his PhD work on circadian rhythms.

NOTE Confidence: 0.925334811210632

00:06:57.350 --> 00:07:14.630 He got some really cool. Preliminary data and then he actually took a job in Spain. He was from Spain. So he left an aerial approached me and said Hey. Adam do you do you want to take over this project and even though it was totally out of my comfort zone?

NOTE Confidence: 0.931997656822205

00:07:15.150 --> 00:07:20.800 I thought it was too great of an opportunity and just too cool of research to pass up.

NOTE Confidence: 0.923332631587982

00:07:21.620 --> 00:07:41.710 And for a while. I really struggled. Because imagine I was kind of on my own in the lab because I was surrounded by microbiologists or immunologists and no one really knew anything about circadian rhythms, so for awhile. I really felt like I was on an island on my my lab mates were great and trying to help me as most they couldn't help me with the immunology peace.

NOTE Confidence: 0.916469752788544

00:07:42.320 --> 00:07:47.820 But it wasn't until I found some collaborators and other labs here at Yale that were really able to.

NOTE Confidence: 0.72788393497467

00:07:48.340 --> 00:07:49.930 To help me?

NOTE Confidence: 0.945803761482239

00:07:52.440 --> 00:07:59.000 You know where I am now, I'm in a small really undergraduate institution that focuses on teaching.

NOTE Confidence: 0.925911903381348

00:07:59.600 --> 00:08:10.860 Anne I kind of took that route because as a graduate student. I really enjoyed my interactions with the undergraduates. When I was teaching labs and I was kind of kept in the back of my head and.

NOTE Confidence: 0.953500866889954

00:08:12.100 --> 00:08:14.210 I've been there 6 years now.

NOTE Confidence: 0.934394836425781

00:08:17.030 --> 00:08:20.260 How many students do you have in your lab currently?

NOTE Confidence: 0.909437716007233

00:08:21.010 --> 00:08:27.580 So because their undergraduates and I have quite a bit of turnover, it fluctuates.

NOTE Confidence: 0.930987417697906

00:08:28.140 --> 00:08:37.960 Anywhere from 2 to 5, so and I try to stagger them. So I can have more senior students training newer students on various projects.

NOTE Confidence: 0.901969909667969

00:08:39.270 --> 00:08:58.010 So I guess we're on the topic of your post doc while you're at your post. Doc you published a couple of very cool papers that came out in 2012, so in the first one, you showed that there were Clock jeans that were being expressed in a rhythmic way in various immune cells so which immune cells were you studying where there are reasons. You picked those and what do they do?

NOTE Confidence: 0.908452033996582

00:08:58.810 --> 00:09:07.610 So we looked at splenic macrophages, dendritic cells and B cells and these have various roles.

NOTE Confidence: 0.905533790588379

00:09:08.570 --> 00:09:21.030 For example, a macrophages are best known for regulating inflammation and whose defense dendritic cells for their work as integer presenting cells and B cells for antibody secretion.

NOTE Confidence: 0.914580762386322

00:09:21.590 --> 00:09:27.050 So really kind of cells that were involved in both the innate and adaptive immune responses.

NOTE Confidence: 0.853118300437927

00:09:27.650 --> 00:09:29.550 And you know why.

NOTE Confidence: 0.917966246604919

00:09:30.160 --> 00:09:33.870 Just some of the major major cell types that are found in the spleen.

NOTE Confidence: 0.907845139503479

00:09:35.430 --> 00:09:54.060 And I guess sort of looking back at this, it seems like you would expect every cell in your body would know what time it is, but at the time that seems like it was kind of a surprising result. So why was that so surprising and has something changed since then to make this seamless less surprising overtime.

NOTE Confidence: 0.910054922103882

00:09:54.800 --> 00:10:01.140 Yeah, I think that's you're exactly right the way you ask that question.

NOTE Confidence: 0.939302980899811

00:10:01.740 --> 00:10:10.010 Because I think 10 years ago, it was kind of surprising as we knew that some immune parameters fluctuated over the 24 hour period.

NOTE Confidence: 0.895979583263397

00:10:10.540 --> 00:10:20.250 And then at that point right about 10 years ago. We were uncovering more and more mean parameters fluctuating over over the daily cycle.

NOTE Confidence: 0.920077085494995

00:10:21.050 --> 00:10:26.550 But even look, but like you said. Looking back on that now I still think it's interesting that.

NOTE Confidence: 0.926636636257172

00:10:27.100 --> 00:10:34.420 We have those 3 different cell types. We looked at and if you look there on slightly different time so to speak.

NOTE Confidence: 0.901802778244019

00:10:35.000 --> 00:10:46.590 And what I think is so cool, you have different cell types in the spleen on slightly different time and also they?

NOTE Confidence: 0.957097470760345

00:10:47.560 --> 00:10:54.300 Their absolute numbers in relative cell numbers can also fluctuate throughout the day.

NOTE Confidence: 0.901043355464935

00:10:55.070 --> 00:11:01.820 And then so you have individual cells in the spleen on their own time and then the spleen as a whole site tissue.

NOTE Confidence: 0.916166365146637

00:11:02.940 --> 00:11:14.250 All those individual cells make up the timing of the spleen and do you know if that pertains to their functional role in the immune response?

NOTE Confidence: 0.929930984973907

00:11:16.030 --> 00:11:22.590 I think it. It definitely contributes but to what extent it's not quite known just yet.

NOTE Confidence: 0.917000949382782

00:11:23.560 --> 00:11:56.430 OK, well in in another paper, you showed that um toll like Receptor 9 expression is controlled by their circadian Clock. So you look specifically you found that this toll like Receptor had this circadian rhythm so first? What are the toll like receptors and what role do they play in our immune response so to like receptors are a class of pattern recognition receptor located in or on the surface is of certain immune cells that identify pathogen associated molecular patterns.

NOTE Confidence: 0.893003523349762

00:11:56.430 --> 00:12:04.170 Also refer to his pants and some researchers in the field refer to those as Maps microbial associated molecular patterns.

NOTE Confidence: 0.913832724094391

00:12:05.000 --> 00:12:16.160 So these are conserved microbial components that are exclusive to micro organisms, so as an example things like bacterial DNA or viral DNA.

NOTE Confidence: 0.885918021202087

00:12:16.690 --> 00:12:44.260 Bacterial LPS or flagella and so things that are unique to micro organisms and to date, 10 human TL. Rs have been identified 12 mouse. TL Rs have been identified and imagine each of these TL Rs recognizes and binds to a specific microbial login and then there's some binding. We usually induce proinflammatory cytokines. Some kind of a stab Lish in Anti Microbial State.

NOTE Confidence: 0.847275495529175

00:12:44.840 --> 00:12:49.060 In addition to this, it'll initiate.

NOTE Confidence: 0.894033074378967

00:12:49.580 --> 00:12:53.270 Or help direct the adaptive immune response as well.

NOTE Confidence: 0.88001549243927

00:12:53.820 --> 00:13:25.670 So what is recognized by toll like receptor 9? What is the leg in DNA so specifically materialen viral or do what are called. CPG DNA motives so to stimulate synthetic to stimulate TLR 9. Muse they think like a synthetic nucleotide. So what would I guess. We talked about this a little bit earlier, but what is the functional relevance for the circadian rhythm and TLR receptor expression you mentioned you probably wouldn't want to have your immune response activated too much at night.

NOTE Confidence: 0.897825121879578

00:13:25.670 --> 00:13:27.640 How much of a role with this business play?

NOTE Confidence: 0.903538942337036

00:13:28.250 --> 00:13:30.030 So we're looking at.

NOTE Confidence: 0.878652036190033

00:13:30.980 --> 00:13:34.930 Like TLR expression itself.

NOTE Confidence: 0.211825996637344

00:13:35.730 --> 00:13:36.410 Uh.

NOTE Confidence: 0.938300669193268

00:13:38.250 --> 00:14:08.370 So imagine if MRNA levels fluctuate over the 24 hour period. It would write suggests that save responsiveness of these toll like receptors also fluctuates over a 24 hour period, making them more likely to pick up those microbes have heightened responsiveness at certain times of day compared to others when we are more likely to encounter those pathogens and.

NOTE Confidence: 0.922904849052429

00:14:08.370 --> 00:14:15.010 Just sort of give People a sense of the scale. How much is this punctuating is it like nothing to 100 or somewhere in the middle of that.

NOTE Confidence: 0.883113980293274

00:14:15.630 --> 00:14:18.680 Oh, that's a That's a great question.

NOTE Confidence: 0.95028281211853

00:14:20.640 --> 00:14:29.260 So a friend of mine who helped develop a statistical program that detects the cycling of jeans.

NOTE Confidence: 0.896244466304779

00:14:30.350 --> 00:14:48.810 You know, Essentia Lee told me one time over coffee that you can set this so low that you can detect cycling and very minimal amounts of gene expression very small differences and you could almost argue that maybe every gene is cycling if.

NOTE Confidence: 0.909998655319214

00:14:49.760 --> 00:14:52.250 If looking at right those small differences.

NOTE Confidence: 0.914292097091675

00:14:53.180 --> 00:15:00.610 But honestly it's going to depend on say which TLR which team we're looking at.

NOTE Confidence: 0.861686527729034

00:15:01.670 --> 00:15:03.140 There will be.

NOTE Confidence: 0.878913760185242

00:15:03.870 --> 00:15:08.660 Larger differences in amplitude during the cycling we could say.

NOTE Confidence: 0.894917547702789

00:15:09.160 --> 00:15:20.010 So then do all the toll like receptors cycle or are there. Some that aren't oscillating at all, even when you're looking at small changes so?

NOTE Confidence: 0.924634754657745

00:15:21.160 --> 00:15:25.280 It's going to depend in this cell type or looking at.

NOTE Confidence: 0.911776006221771

00:15:25.890 --> 00:15:30.350 And then so a lot of the work I've done recently so again I work at A.

NOTE Confidence: 0.923326551914215

00:15:30.950 --> 00:16:01.680 Smaller predominantly undergraduate institution and I don't have a tremendous amount of funding funding. So the questions. I can ask are going to be smaller scale, so recently. I've looked at M. RNA expression levels. But in an ideal scenario. I look at M. RNA expression followed up by protein levels to see if protein levels also oscillate in circadian fashion and then follow that up with looking at responsiveness.

NOTE Confidence: 0.913928806781769

00:16:01.680 --> 00:16:09.090 Over the course of a 24 even 48 hour period and then do we see cycling because imagine?

NOTE Confidence: 0.938169836997986

00:16:09.870 --> 00:16:30.050 Just because we don't see circadian variations at the M, RNA level doesn't mean we won't see them at the protein level or responsiveness because sometimes your post transcriptional regulation could be done in a Sir Cadian fashion, so there are multiple levels of complexity at play here.

NOTE Confidence: 0.916431784629822

00:16:30.850 --> 00:16:36.060 And so there are known proteins that have sort of that post transcriptional regulation.

NOTE Confidence: 0.885104477405548

00:16:36.750 --> 00:16:38.130 But so the big thing is.

NOTE Confidence: 0.90837174654007

00:16:38.830 --> 00:16:52.420 At least you know what I can show is do we see at least daily variations in responsiveness. So we see daily variations in M RNA expression and then couple that with.

NOTE Confidence: 0.908246874809265

00:16:53.000 --> 00:17:08.160 Daily changes or variations and responsiveness, then we can say OK. This gene is most likely under controlled by the circadian Clock and then you could really dive into the molecular mechanisms. There, like we did in the TLR 9 paper.

NOTE Confidence: 0.904629468917847

00:17:08.950 --> 00:17:41.040 So I guess if you're looking at the TLR is that seemed to be like the most circuiting controlled in the ones that seem to be the least circadian controlled are there any functional differences that jump out at you in terms of I guess what? They're doing in the immune system and what they might be recognizing like you said. We had the paper on TLR 9:00. We went into a good amount of detail on that some of my recent work is looking at the TL Rs as a whole, but kind of dialing it back several years now. Some of the preliminary data that my colleague came up with.

NOTE Confidence: 0.914394617080688

00:17:41.150 --> 00:17:44.410 Was actually dealing with TLR 3?

NOTE Confidence: 0.946886003017426

00:17:45.300 --> 00:17:48.270 And its role in West Nile virus.

NOTE Confidence: 0.919846177101135

00:17:48.820 --> 00:18:08.580 And he actually had some really cool data that shows that in mice. Mice are more susceptible to West Nile virus infection at certain times of day compared to another an really had some initial data. That kind of link that with TLR 3's TLR 3 does play a role in West Nile recognition.

NOTE Confidence: 0.912168502807617

00:18:09.650 --> 00:18:14.670 So, like big picture big scale TLR work I think that would be.

NOTE Confidence: 0.916671633720398

00:18:15.870 --> 00:18:18.640 Kind of the next cool thing that's out there.

NOTE Confidence: 0.914633512496948

00:18:19.500 --> 00:18:37.400 And so I guess then even bigger picture are any of these receptors potential drug targets for sort of stimulating the immune response. So are there any drugs that currently target them or is there any like the field sort of looking at that at this point?

NOTE Confidence: 0.906095802783966

00:18:38.130 --> 00:18:58.890 He is so researchers are always trying to find new adjutants out there, so things that are going to boost vaccine efficacy. Ann I know. Some studies out there that have used TLR agonists to try to enhance vaccine efficacy for example.

NOTE Confidence: 0.847226977348328

00:18:59.700 --> 00:19:01.030 I know.

NOTE Confidence: 0.89116495847702

00:19:01.700 --> 00:19:32.890 They've used TLR 9 logins in an anti tumor vaccine and a vaccine against Melanoma actually so are any of these in clinical trapped in the clinical trial stage or is I believe I believe so cool. That's very cool like this has potential to do all kinds of stuff just as you mentioned the circadian Clock is impacting basically all the diseases. So as we mentioned earlier. We talked about the pathogen molecules feeding back in regulating the circadian Clock.

NOTE Confidence: 0.905678868293762

00:19:33.100 --> 00:20:03.180 So just sort of evolutionarily big picture why might it be important for the circadian Clock to be affected by the presence or absence of microbes so really to be quite honest that I think this is just right speculation almost anecdotal. But, perhaps from the pathogen's point of view. If you disturb the Clock. It will essentially weak in the host, which might confirm survival advantage for the Organism or flipping that.

NOTE Confidence: 0.90971702337265

00:20:03.750 --> 00:20:11.500 It could be our body's way of forcing us to rest repair tissue damage. When we're sick right. Maybe This is why we feel tired? When were sick.

NOTE Confidence: 0.906532526016235

00:20:12.040 --> 00:20:27.700 Our body recognizes a pathogen that triggers are molecular Clock is kind of telling us to slow down so like I said kind of repair that tissue damage. But to really understand this and to get it. This I think we really need to workout those molecular mechanisms.

NOTE Confidence: 0.926837384700775

00:20:28.920 --> 00:20:59.750 OK so this has been nagging at me a little bit so if the immune system is controlled by the circadian rhythm. We know that there are some areas that see more or less light during a 24 hour period so like in Alaska in Canada. They have some really long days during part of the air and then in other parts of the year. They're really short do. We know and can you speculate maybe on how this effects the immune system or is because the?

NOTE Confidence: 0.933734178543091

00:20:59.810 --> 00:21:10.560 Circadian rhythm is regulated by the light, maybe they see no ill effects from having the shorter or longer days.

NOTE Confidence: 0.947027087211609

00:21:11.230 --> 00:21:16.770 So right circadian rhythms influence nearly all aspects of Physiology and behavior.

NOTE Confidence: 0.915702641010284

00:21:17.280 --> 00:21:34.380 So did it so to disrupt those rhythms or alter those rhythms can lead to serious short-term and long-term pathologies, such as depression or impaired immune function both of those have been shown but with That being said.

NOTE Confidence: 0.90419727563858

00:21:34.850 --> 00:21:52.550 Circadian rhythms will still exist in the absence of an external Q. However, the rhythms will slowly start to get out of sync. So we really rely on sunlight to kind of reset our Clock everyday thing to keep a sometime so to speak.

NOTE Confidence: 0.8899866938591

00:21:53.110 --> 00:22:11.450 So there are measures actually they can be taken by individuals, living in Alaska or say Canada like you mentioned by using artificial light like lightboxes early in the morning can help kind of reset your Clock and keep it on time.

NOTE Confidence: 0.918129324913025

00:22:12.260 --> 00:22:25.380 I always think it's I think back to this, but I was studying this when both my kids were born and you know imagine. I'm in the hospital with my wife and we're like OK. We need to get at least 1 decent night sleep when we're here.

NOTE Confidence: 0.914220452308655

00:22:25.890 --> 00:22:28.140 And we send the kids off to the nursery.

NOTE Confidence: 0.912792325019836

00:22:28.970 --> 00:22:43.120 In the nurseries in constant light so we're kind of getting their circadian rhythms off to a terrible start. You know, and I could even think native New Englander you know in late January, February.

NOTE Confidence: 0.927123129367828

00:22:43.650 --> 00:22:46.830 It feels like weeks where you just don't see the sun.

NOTE Confidence: 0.893730938434601

00:22:47.340 --> 00:23:14.580 An it starts to be a drag you know, so seasonal depression is a thing and it's Tide into the sun. It's tight into our circadian rhythms also I notice then like phones now have sort of the blue light filter. So I think that's wonderful so that helps us. Maybe not trigger the wake period. When were maybe like scrolling through our phones at night. It's it's so funny but that's what they say is that?

NOTE Confidence: 0.919934511184692

00:23:15.360 --> 00:23:32.170 How we live nowadays with TV and working late and constant light in your computer being on it really screws up our rhythms. You know in me like all even think if I go into the refrigerator in the middle of the night like Oh my goodness? What did I just do but our body has mechanisms in place to.

NOTE Confidence: 0.935544848442078

00:23:32.750 --> 00:23:44.200 Make it so we're not that sensitive but I always laugh how when I was studying these things I would perform 24 hours straight experiments or 36 hours.

NOTE Confidence: 0.91392183303833

00:23:44.770 --> 00:23:51.940 An thinking Oh wow. I'm showing how important our circadian rhythms are and I'm destroying my own.

NOTE Confidence: 0.917304039001465

00:23:52.470 --> 00:24:00.860 Yeah, exactly I feel like we've also been seeing in the news. A lot more about how night shift work and have a negative effect on our health and so, yeah, so it's really.

NOTE Confidence: 0.898837506771088

00:24:01.360 --> 00:24:31.950 That's funny but you are noticing it as you were working through the night and there are measured with night shift work. There are measures. You can do, but it's very challenging. You essentially have to train your body like it's a complete flip cycle like draw your shades and pretend like it's it's Day when it's really night so today. We've mostly been talking about human and mouse circadian clocks, So what other organisms have circadian clocks and what differences are there.

NOTE Confidence: 0.863325119018555

00:24:32.210 --> 00:24:39.560 Between these kind of clocks do ticks have a circadian Clock that might affect whether or not you get Lyme disease.

NOTE Confidence: 0.926360547542572

00:24:40.060 --> 00:25:10.640 So I'll answer the first part of the question to start so virtually all forms of life, including bacteria. Fungi plants drosophila. The fruit flies. Fish mice and obviously humans exhibit circadian rhythms. I think it's pretty wild that even single. Celled organisms right like bacteria, which reproduce many times over the course of a 24 hour period experience circadian rhythms for example, sign on.

NOTE Confidence: 0.9112908244133

00:25:10.640 --> 00:25:23.380 Bacteria express' daily rhythms and photosynthesis, but imagine like their entire life span is like 20 minutes right. So why would they experience circadian rhythms.

NOTE Confidence: 0.929069042205811

00:25:24.180 --> 00:25:36.470 So I think it fits into the notion of bacteria being treated like a multi cellular Organism? Do the quorum sensing so cell communication. That's probably a topic for another podcast.

NOTE Confidence: 0.890597581863403

00:25:37.340 --> 00:25:44.580 Invite you back if we ever get around to talking about that, but but actually that's so that's actually one of the things I'm interested in in.

NOTE Confidence: 0.907454550266266

00:25:45.130 --> 00:25:49.510 You know now that I have tenure at a smaller institution. I feel like I can.

NOTE Confidence: 0.904640257358551

00:25:50.580 --> 00:26:18.760 Tackle some of the questions that I'm interested in and can wander off a little bit so like I said my PhD work was looking at the beneficial symbiosis between microorganism in the medicinal each and I'd love to take that system and bring in my circadian rhythm work. So how does the Leech undergoes circadian rhythms I have some?

NOTE Confidence: 0.931841433048248

00:26:19.580 --> 00:26:25.030 Anecdotal evidence that it does from some of my former labmates that notice things.

NOTE Confidence: 0.910540163516998

00:26:25.650 --> 00:26:32.250 Like higher bacterial numbers present in the digestive tract of the Leech at one time of day compared to another.

NOTE Confidence: 0.885030090808868

00:26:34.280 --> 00:26:47.380 But then going back and seeing how bacteria could impact the leeches circadian rhythms how the leeches circadian rhythms impact

the bacteria and the digestive tract. A Leech and then we could apply that to our own gut microbes.

NOTE Confidence: 0.942475199699402

00:26:48.030 --> 00:26:49.070 That would be very cool.

NOTE Confidence: 0.912862777709961

00:26:49.640 --> 00:27:04.470 And I know it's it's been a couple years since I've been following the circadian Clock literature. Other than cyanobacteria do you know if they found circadian clocks and other bacteria, particularly pathogens. It would make a lot of sense for them to be able to tell the immune system going to be ready for me or not.

NOTE Confidence: 0.938009440898895

00:27:05.100 --> 00:27:17.890 So that was something that really was our initial hypothesis was especially being an arrow's lab in all the vector borne diseases that we worked with.

NOTE Confidence: 0.920392394065857

00:27:20.490 --> 00:27:40.020 You know was there a manipulation between the microorganism in the vector where it would manipulate the vector to bite us at the time when our immune system was at its lowest in order to enhance infection or Conversely did our immune system evolved to peak when those the counters might occur.

NOTE Confidence: 0.925051867961884

00:27:42.800 --> 00:27:56.900 I'm trying to think of I feel like that. I know of some pro does Ella that experience. Some type SUV of rhythms, but examples of bacteria off the Top of my head. I can't think of any.

NOTE Confidence: 0.925097644329071

00:27:57.400 --> 00:28:18.550 Well, one of the arguably maybe one of the most important bacteria to humans and other animals is the mitochondria and our endosymbiotic relationship with our mitochondria has anyone looked at whether the mitochondria show or mitochondrial gene expression shows any sort of circadian rhythm.

NOTE Confidence: 0.893449485301971

00:28:19.190 --> 00:28:24.020 Or in immune cells or other cells of the body. I don't know off hand.

NOTE Confidence: 0.882032513618469

00:28:26.150 --> 00:28:30.750 I would I would think someone has in A.

NOTE Confidence: 0.911294281482697

00:28:31.410 --> 00:28:38.350 And it would be a friend of mine who is actually was a postdoc here who did transcriptome analysis.

NOTE Confidence: 0.178396865725517

00:28:38.870 --> 00:28:39.540 Of.

NOTE Confidence: 0.899283409118652

00:28:40.090 --> 00:28:42.590 Many different tissue types.

NOTE Confidence: 0.925575077533722

00:28:43.200 --> 00:28:46.700 I don't know I don't think they looked at mitochondria sorry China.

NOTE Confidence: 0.905545830726624

00:28:47.260 --> 00:29:01.890 Go through the rolodex in my head. I don't know, but yeah, that's really interesting. This push it right. Then you could write tight and I don't know if you flick chloroplasts in sino bacteria right exactly if listeners wanted to learn more about this topic. What resources might you recommend.

NOTE Confidence: 0.902230978012085

00:29:02.460 --> 00:29:33.260 So I don't know if it's OK to plug my own work, here, but they can start by reading the short review article. Let's set to be published in the June issue of the Yale Journal of biology and Medison so in that review was actually 3 undergraduates and I reviewed the field of the circadian immune connection really from the past 5 years, so really just a little snapshot, but really in that article. We cite some really excellent reviews from some huge names in the field.

NOTE Confidence: 0.917749345302582

00:29:33.660 --> 00:29:47.300 In biology in the immune response so they could start with our review and then look at some of those. I think more comprehensive kind of bigger picture reviews that we site. I think would be a great place to start.

NOTE Confidence: 0.890989780426025

00:29:47.970 --> 00:29:54.180 And we are Open Access, so anyone is free to access this review article.

NOTE Confidence: 0.926268517971039

00:29:54.760 --> 00:30:03.370 And then finally do you have any practical advice for listeners, especially potentially young aspiring researchers maybe are starting to think about joining a lab?

NOTE Confidence: 0.88472455739975

00:30:04.840 --> 00:30:08.560 I think in terms of joining a lab.

NOTE Confidence: 0.929699897766113

00:30:09.060 --> 00:30:13.230 I think try to get a few rotations under your Belt to see what you really like.

NOTE Confidence: 0.936457693576813

00:30:13.820 --> 00:30:16.570 And I think looking back on my time.

NOTE Confidence: 0.871421217918396

00:30:17.400 --> 00:30:21.950 When it came time to make a career decision I think.

NOTE Confidence: 0.920732915401459

00:30:23.370 --> 00:30:42.970 Or how should I say think about where you want to end up an if it's an industry. I would really try to learn as many techniques as possible so I did apply just some industry jobs and I feel like having experience doing many different types of techniques really got me those interviews.

NOTE Confidence: 0.915283203125

00:30:43.510 --> 00:30:56.530 At the end of the day I wanted to work at a smaller research institution, where teaching was also a focus and in hindsight. I wish I had more real teaching experience.

NOTE Confidence: 0.919317424297333

00:30:57.100 --> 00:31:18.830 So I know potentially go out to even a Community College and see if you can add junked at night to really see what it's like to be a professor and have your own class an that will help you tremendously in your first year as well as getting an interview because I've been on a few search committees and that really makes a difference.

NOTE Confidence: 0.941029727458954

00:31:19.340 --> 00:31:20.950 Thank you for that great advice.

NOTE Confidence: 0.888459324836731

00:31:21.450 --> 00:31:51.070 And thank you for being on our podcast today. You're very welcome. Thank you for having me it's been great listeners. Thank you for tuning into this episode of the Yale Journal of biology and medicine podcast join us next month for a second podcast on clocks and cycles, where we will be interviewing Doctor Shah Yang, who works on the interaction between the circuit in Clock in the metabolism and thank you to the school of Medicine for being a home for YJBM the podcast. Thank you to the Yale Broadcast Center for help with recording editing and publishing our podcast.

NOTE Confidence: 0.877894282341003

00:31:51.570 --> 00:32:23.080 Thank you to the YJBM editorial board, especially the deputy editors for this issue, Ian and Devon. and For more information on

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NOTE Confidence: 0.836652517318726

00:32:23.080 --> 00:32:27.830 And Spotify see you next month for the next installment of the YJBM podcast.