the WINNOWER

REDDIT

Hi, Reddit! I am Dr. Ian Blair, a professor of pharmacology at the University of Pennsylvania. Ask me anything about the use of stable isotopes in toxicology, mass spectrometry in drug development, or the role of mitochondria in diseases.

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CORRESPONDENCE:

DATE RECEIVED:
August 16, 2017

DOI:
10.15200/winn.150280.01510

ARCHIVED:
August 15, 2017

CITATION:
AmerChemSocietyAMA , r/Science , Hi, Reddit! I am Dr. Ian Blair, a professor of pharmacology at the University of Pennsylvania. Ask me anything about the use of stable isotopes in toxicology, mass spectrometry in drug development, or the role of mitochondria in diseases., *The Winnower* 4:e150280.01510 , 2017 , DOI: 10.15200/winn.150280.01510

Self-educated layman here. Chronic Fatigue Syndrome seems to have a high correlation with poor mitochondrial function. CFS is a disease that's not well understood, and as a result is surrounded by quackery and pseudoscience. That makes life for a layman very hard when trying to direct his learning - the signal to noise ratio is terrible! Do you think it's a reasonable hypothesis that the kind of generalised debilitating symptoms CFS presents is connected to poor mitochondrial function? Additionally and separately, are there any known or likely treatments for mitochondrial weakness?

russianmontage

Dear russianmontage

Unfortunately, I know very little about the potential role of mitochondria in CFS. It seems a reasonable hypothesis that there is mitochondrial dysfunction as this is where our energy comes form. We are desperately working to find therapeutic agents that can improve mitochondrial function in FA. Given the critical role of frataxin in regulating mitochondrial metabolism if we come up with something, it might find utility in other diseases. We certainly plan on analyzing frataxin levels to see if there is an association with other mitochondrial-based diseases. In view of your comments, I will explore the possibility of analyzing frataxin levels in patients diagnosed with CFS. In FA, we find a 75 % reduction in frataxin levels.

What role does mitochondria, to your knowledge, play in autoimmune disorders like multiple sclerosis? Would you say that there is credible evidence to support the idea of "eating for your mitochondria" as advanced by Dr. Wahls in her autoimmune paleo protocol?

clonedanmarinoplease

Dear clonedanmarinoplease:

There is recent evidence form the Cortopassi group at UC Davis that dimethylfumarate can induce

mitochondrial biogenesis (Hayashi G, Jasoliya M, Saccà F, Pane C, Filla A, Marsili A, Puorro G, Lanzillo R, Brescia Morra V, Cortopassi G. Hum Mol Genet. 2017 Apr 28 [Epub ahead of print]) suggesting a potential role for mitochondria in multiple sclerosis. However, I suspect that Nrf-2 activation also plays a role in regulating T cell activation.

What's the role of mitochondria in sepsis and what's your take on Paul Marik's metabolic resuscitation of sepsis?

cullywilliams

Dear cullywilliams:

This is a fascinating area for research. Evidence is accumulating that high mobility group box-1 (HMGB1) an important nuclear and mitochondrial protein is involved in sepsis. We have begun working with investigators at the Medical University of Carolina to try and understand what is going on. HMGB1 is transported into mitochondria by the receptor for advanced glycation products (RAGE) where it is involved in mitochondria DNA repair. How this is connected to sepsis is unclear but might have something to do with mitochondrial DNA repair. HMGB-1 is a fascinating protein with 43 lysine residues, many of which are acetylated. When this occurs on lysine residues in the nuclear localization sites (amino acids 28-44 to 179-185) , it prevents translocation of HMGB1 into the nucleus, although little is known about the effects of acetylation on mitochondrial function. I do not have any opinion on Paul Marik's metabolic resuscitation of sepsis.

I've read that large doses of heavy water (D2O) are toxic. However to reach such a dose, one would need to replace *ca.* 50% of their water with D2O. My question is then, what is the primary mechanism of the toxicity here? As a chemist, I understand that D^+ would significantly slow down many reactions where proton (H^+) transfer is a rate-limiting step. But is it a reaction being slowed down that causes the ultimate toxicity, or is it something else? What is your understanding, as an expert in mechanistic toxicology?

MurphysLab

Dear MurphysLabPhD

Normally, we think of replacing an endogenous isotope such as N-14 with a stable isotope such as N-15 here is little effect. In fact you can buy mice that have been almost completely labeled with N-15. However deuterium is different. Replacing hydrogen (H-1) deuterium with deuterium (H-2) results in endogenous molecules with different physicochemical characteristics than the H-1 (protium) form. Replacing as few fas our hydrogen atoms can make it possible to separate that two forms by liquid chromatography. Thus replacing large numbers of hydrogen atoms with deuterium would cause the inhibition of many important enzymatic reactions resulting in a general metabolic dysfunction and ultimately death.

What part of exercising causes an increase in mitochondrial proteins, and if possible, what medications can be given to simulate this

billyvnilly

Dear billyvnilly

I hope so! All we can do to improve our health is not smoke, to eat healthy and to get adequate exercise. I am a great believer in exercise and try to walk 14,000 steps/day, although I am not aware of

any specific science that shows mitochondrial function improves. Anecdotally, in the disease I work on called Friedreich's ataxia (FA, see my response to trianglelightening) there is evidence that exercise improves quantity of life. One of the patients with the disease that I work with (Kyle Bryant) is an avid cyclist and has started "ride for ataxia" and participated in the "Ride Across America" featured in the movie "the Ataxian." Unfortunately, I have no evidence that his mitochondrial function has improved, although he is a very dynamic individual doing his best to overcome FA by exercise. With our new frataxin assay, I plan on monitoring the effect of exercise on frataxin levels so perhaps my lab will be able to generate some positive data in the future.

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I have never thought about cannabinoids in terms of their effects on mitochondrial metabolism. From my general knowledge I have not seem any reports of an association between Parkinson's disease and cannabis use. I am struggling to think of a potential mechanism. Perhaps concerns come from the illegal street drug MPTP, which caused a devastating Parkinson-like syndrome. This was due to oxidation of MTPT to MPP+ by monoamine oxidase rather than mitochondrial function (see for example: Goetze O, Woitalla D.Exp Neurol. 2008;210(2):281).

Proton pump inibitors work at the mitochondrial level, as I recall (omeprazole). How does that work in with the recent report that their prolonged use might result in early dementia?

victalac

I have not examined the effect of protein pump inhibitors on mitochondrial function and I am not aware of any publications that describe negative effects. It seems unlikely that they could specifically cause dementia.

I have been hearing a lot lately about the role of mitochondria in MS, and the idea that if you eliminate certain foods from your diet and include others, that MS symptoms will improve or even disappear. The doctor Terry Wahls is a large advocate of this. What are your thoughts on the relationship between mitochondria and neurological diseases like MS?

Vital_Statistix

I am not an expert on MS - I would be very surprised if diet alone would cause MS symptoms to disappear

What techniques have you found to be most effective for characterizing lipid adducts?

milfpoop

This seems like a planted question! We have found that stable isotope dilution coupled with high resolution tandem mass spectrometry is the best. We published a method recently based on our 2000 discovery of electron capture atmospheric pressure chemical ionization mass spectrometry that allows the quantification of chiral serum lipids (Mazaleuskaya LL, Lawson JA, Li X, Grant G, Mesaros C, Grosser T, Blair IA, Ricciotti E, FitzGerald GA. JCI Insight. 2016;1(12). pii: e87031). We are currently working on using this technique for mitochondrial DNA-lipid adducts.

Hi, thanks for the AMA! You've been in research for quite a long time, as an aspiring research scientist I hope one day to have a track record as impressive! When you started research, did you have any expectations for what we might learn in the future? What development would you say is/was the most interesting or exciting for you? Any trends you see in the field that you're particularly excited for?

gorgeousaurus

I always loved science for some reason and was only interested in a scientific career. Of course working for a Nobel Laureate was a special privilege and he raised my expectations of what I could accomplish. When I left his lab Professor Barton said to me that "all I needed was one good idea!" Hopefully, it will come soon. The two amazing technologies of mass spectrometry and molecular biology are to me the exciting advances. We just identified a new protein with an N-terminal blocking group by high resolution tandem mass spectrometry on nanogram amounts of material. My lab then cloned and expressed the protein and we confirmed the structure within a week. This would have been a PhD thesis when I started out!

Hi there doc, sorry to put you in an awkward position but could you go into a bit of detail on the Charlie Gard case, both treatment and disease and whether or not GOSH made the right decision in the end?

Silverbackus

I am not sure that there is any evidence that it would have worked and I believe the decision was absolutely correct.

I'm interested in studying pharmacology what advice would you give me as a second year undergraduate student?

Adders090

That is great! I trained originally as a chemist and had to teach myself pharmacology. Pharmacology is very much a hybrid science, which can be though of as the effect of xenobiotics and drugs on the body as well as the effect of the body on drugs and xenobiotics. This allows us to study almost anything! A strong grounding in chemistry, biochemistry, cell biology, and genetics would be very helpful.

How does mass spec help elucidate the structure of a protein responsible for synthesis of iron-sulfur clusters, which would seemingly extensive require tertiary folding? Additionally, why does the subsequent excess Fe concentration specifically cause oxidative damage to neuronal mitochondria? Thank you for your time, feel free to just drop a doi.

TheDeaknessss

Actually, it is the primary structure that has been the biggest problem. For some reasons the proteins run on PAGE in an unusual way, which, has caused tremendous confusion over the years. Frataxin is formed as a 210 amino acid protein with a mitochondrial targeting sequence. When expressed normally it all translocates to mitochondria and its prices by mitochondrial processing peptidase. There are three sites of potential cleavage but ist is clear that the initial cleavage is at G41 and to an intermediate form (42-210) ad that this undergoes a second cleavage at a K-80 to give the mature form frataxin (81-210). There are no cysteine residues in the mature form and so tertiary structure is not so important. Confusingly, four additional transcripts of the FXN gene have been reported. A minor alternative transcript containing exon 5B in place of exon 5A (Figure 1A) encodes a 196-amino acid

form of frataxin (1-196), which is also known as isoform B or FXN-2 (Q16595-2, Uniprot). An in-frame stop codon in exon 5b encodes a shorter protein of 171-amino acids known as isoform A1 or FXN-3 (Q16595-2, Uniprot). These two proteins have identical N-terminal amino acid sequences from M1 to K171 when compared with full length frataxin (1-210). Two additional transcripts give rise to frataxin isoforms II and III, which have quite different N-terminal sequences. Isoform II is a 135-amino acid form of frataxin (176-210) found primarily in cerebellum, whereas isoform III is a 164-amino acid form of frataxin (1-5, 53-210) found primarily in the heart. We are working to determine the relevance of these other isoforms.

Hi Dr Blair! I'm currently doing an undergraduate in pharmacology and preparing to to my post graduate. I'm wondering what is the best way to be set apart from the other hundred graduates when it comes to applying for jobs?

ashy262

Research, research research! This is the best predictor for success in the future

Does a strict ketogenic diet improve mitochondrial function? There is emerging science to support a ketogenic diet in overall health, control of blood glucose levels and blood pressure, reduction of oxidative stress, improvement of autophagy and neuroprotective properties with regard to ALS and Parkinson's and Alzheimer's but is the mechanism of this improvement a reliance on ketone bodies rather than glucose for ATP production?

Adagio3691

This its a fascinating area. For example, triolein has been used to treat seizure disorders that are refractory to drugs. Our own work has shown that inhibition of complex 1 causes rapid depletion of medium chain fatty acids so I think it is reasonable that dietary manipulations could be useful. In the UK, a drug is being tested [(R)-3-hydroxybutyl (R)-3-hydroxybutyrate] in various metabolic diseases with the idea that it can increase ketone body levels. Therein also some evidence that ketone bodies can improve left ventricular function in heart failure.

I hear a lot about foods you can eat or things you can do to "eliminate the toxins in your body."

What is a toxin? What does it do, and why does it respond to certain foods or practices?

hunterglenn

Biological toxins are hazardous substances that can be harmful when inhaled, ingested, injected, or absorbed. All I can suggest is eating a healthy diet with plenty of fruits and vegetables and to not smoke. This will make it unlikely that you are exposed to any toxins

1) What is your preferred instrumental setup for stable-labelled fluxomics experiments in animals?

2) What is the role of mitochondria/peroxisomes in influenza infection and what are the metabolites that would play a role in possible dysregulation of these organelles?

mudbot

1. I am a big fan of high resolution mass spectrometry. We conduct metabolic labeling experts in human platelets and analyze the metabolites using ultra-high performance liquid chromatography-

high resolution mass spectrometry using a Thermo Q-Exactive HF.

2. I have not done any research on influenza so I cannot comment.

Should advertisement for prescriptive drugs be legal? I feel far too many people watch the commericals and fake symptoms to their doctors because of commericals they have seen.

jimmyolsenblues

I am not a big fan of commercials for drugs. Unfortunately, I cannot imagine that it would be possible to make them illegal.

How limited are you by instrumentation in analysis? Namely, do you believe that with the resolution that orbitraps afford us we are limited only by the heterogeneity of the sample?

Also, what role do you think ion mobility plays in pharmacology?

1l1l1l1

Mass spectrometry is a wonderful aide but has to be used in conjunction with many other techniques. For example, Gary Patti at Wash U has shown that up to 150 signals can come from a single analyze in a complex biological matrix. There, you need to use sophisticated stable isotope methodology coupled with the best chromatography you can get your hands on. For low level samples we now routinely use 2D nano-liquid chromatography. I am impressed with ion mobility but it is just a technique and if I could afford to use it with high resolution mass spectrometry I would probably find it useful. However, we have not run into a problem that needs this technology yet.

There is a fair amount of research showing mitochondrial dysfunction in Alzheimer's Disease. While much of this seems to be a result of tau and A-beta aggregates impairing cellular trafficking, there is also some research that suggests mitochondrial dysfunction may occur even before aggregates appear. Do you think mitochondrial dysfunction in AD is causative or compensatory? Could this be a viable therapeutic target?

crazyladyscientist

Good question! My bias would be that improving mitochondrial function would be good.

Hi Dr. Blair!

I'm in medical school, 2nd year, and I worked with one of your colleagues at Penn as an undergrad. Do I need a PhD to succeed in pharmacology research?

Phil_Pennster

Wow! Small world

One MD student and one MD fellow worked in my lab who have gone on to very successful careers in research - one at Harvard and one at Memorial Sloan Kettering. All you need is passion for research - nobody can give that to you. It has to come from you!

I don't know what those things are, but thank you for your work!

The world needs more scientists and less celebrities.

aasteveo

Of course I agree!

I want to study pharmacology when I get to college(I'm still in high school). What's your favorite part of your job? Also was your education very expensive? Thanks!

fairlylights

I love research, I live for research, and research is my hobby. I received scholarships for all of my training.

Excuse me for being not too educated in anything about what you do, all while being generally dim. I understand that each disease is different, yada yada yada, but why can't we cure all diseases?

Do we not know how? Do we know how but don't know how to do it? Do we know how and know how to do it but we can't physically do it now or ever? Do we know how, know how to do it, and we can physically do it, but can't do it for some other reason?

And, finally, do you feel we're less advanced in fighting disease than we should be?

e-tough

Every time I think I understand biochemistry I realize that my knowledge is inadequate! Progress can only cone from good science and often you have to fail miserably before making any advances. I have certainly had my share of failure! The only way forward is funding good science.

My father has a mitochondrial mutation, Mitochondrial Myopathy. He has quite the grocery list of health problems and usually gets sick very easily, especially if someone else in the house has caught a bug. How does this mutation affect his likelihood for other diseases, like heart disease and diabetes?

nellen291

I think his physician would be much better at telling him than me. Hopefully, research is advancing at a pace that will be helpful to him in the future.

Has there been any work done in differential analysis of expression at the mitochondria level (i.e. chrmM), in relation to drug development?

phosphodiester_bond

I am not award of any - but I not an expert on drug development.

Hi Doctor, I have a friend who has Fredrick's Ataxia, she's incredible in both her ability to live a full life while bound to her wheelchair, while also fervent in her belief there will one day be a cure. What has it been like to work on such a disease, and what do you hope will happen in the future in this sphere?

Razortalons

Working with FA patients has been an inspiration. I rarely complain about anything any more! I am determined to find a cure for the disease - we have made huge progress over the last four years thanks to FARA. We now have three boarders to monitor treatment efficacy and we are understanding more about the basic biochemistry of iron-sulfur cluster formation. Most recently, I have become interested in extra-mitocnondual frataxin and the role it cil play in DNA repair. Kyle Bryant who started the ride for ataxia and is featured in movie "the Ataxian" has been a particular inspiration. I will be giving a talk at the next meeting in King of Prussia about our work on FA biomarkers. If your friend is there please ask he to come and chat with me

If someone were moving into the field of Toxicology, what could you expect for job saturation of that specialty? Had it been beneficial to your career versus studying another concentration?

burritoassbag

There are so many different types of toxicology that is difficult to see the field becoming saturated. The annual meeting of the Society of Toxicology would be a great place to explore career options - San Antonio in 2018. I think it has been very beneficial for me to work in this field because learning about toxic pathways has also provided an understanding of the normal pathways. My work on asbestos exposure has revealed pathways that are important in diseases such as Friedrich's ataxia.

Hello Dr. Blair. My questions are,

1) How good is the Ph.D path for someone with a Pharm.D degree. Do you think Pharm.Ds can succeed in this field?

2) What challenges did you face while doing your Ph.d or in your long career?

3) Are you only concentrated on the GSH for now or are you in a look out for other proteins as well?

4) How did you come across this GSH?

Thanks a lot for doing this AMA.

floyd007

1. You need a passion for research - unless you have it do not do it. In fact if you have to ask I doubt if you have it! A PharmD can be successful the time takes is rather intimidating but if you have a passion for research it is well worth the effort. I graduated with my PhD in 1971 (46-years ago!) and I am still going strong.
2. The biggest challenge I faced was my disastrous time in Uganda when Idi Amin destroyed Makerere University where I was a lecturer in Organic Chemistry. I was 27 years old, no job, no possessions, no money, and two young children. However, overcoming those challenges has made me very determined. The biggest challenge I face on a daily basis is to keep my lab funded. I am only as good as the wonderful people who work in my lab.
3. We are working on ApoA-I, frataxin, HMGB1, and fibulin-3 with particular emphasis is on post-translational modifications.
4. These proteins are all related to my interest in oxidative stress, Friedrich's ataxia, and mesothelioma';

Many of these questions confuse me, so I presume they're smart questions. Kudos to the people asking them.

My question may be... less smart. I generally disregard "expiration dates" on medication (both prescription and over the counter) thinking that the active ingredients don't become harmful, but perhaps become a little less effective. Is it potentially dangerous for me to do this? Are there any specific drugs or types of drugs that should definitely not be used past their expiration date?

straightline3

More likely that the active ingredients are no longer active. I would get rid of them through your pharmacy and remove an temptation to use them.

How accurate is Mass Spectrometry? Can't multiple proteins produce the same readings?

higgsparticles

Depends who is doing it. We always use a heavy isotope labeled protein as an internal standard, choose peptides that do not appear in the proteins, use high resolution mass spectrometry with 3 ppm accuracy, and monitor the retention time of all the peptides. For low abundance proteins we use immunopurification to remove potential interfering proteins. Validation is performed under FDA guidelines.

What's the most surprising thing you've learned or discovered through the use of mass-spectrometry? I ask because I know a professor who did a lot of mass-spec research for her PHD and would always talk about the interesting and surprising things she found that she didn't expect to see.

jrainer234

The discovery of an alternatively spliced cytosolic protein with important biological activity that was present in high abundance and had been previously unrecognized because it had a blocked N-terminus

How do pharmaceutical companies produce natural body hormones (like melatonin)?

Also, do you (and your peers) ever use the Chemical Abstract Societies CAS Registry? My father works at CAS and I'm wondering how their service is used in the real world.

CakeKanri

Melatonin that his sold in the US is synthesized (this includes the melatonin in health food stores that is labeled "all natural"). Apparently, it was to buy megaton isolated from cows, but that has been banned in most countries because of the risk of viral infection

Ok, here is my question, what are you talking about? Haha. I'm interested in these things, but I have no clue what that all meant! :)

AeroUp

There is an article about my research in the Advocate that you might find useful.

http://www.curefa.org/news/the-advocate-winter-2014-2015

Dr. Blair my girlfriend has battled with Lyme Disease for some time as it went untreated for many years in her childhood.

Recent blood tests have shown increased clumping of mitochondria and disrupted membranes, and an overall reduction in ATP production leading to heavy fatigue.

Since "Chronic Lyme" is essentially not considered existant by insurance companies she has been forced to see many integrative doctors and specialists almost always out of pocket. Based on this do you have any recommendations for what we could present to more mainstream doctors to help treat this mitochondrial disfunction? What do doctors consider a mitochondrial disease or disfunction other than those that are genetic based, and are there tests available?

I realize this question is somewhat more medical in nature but perhaps with your experience you will have insight :) thank you!

Thesource674

Unfortunately, I cannot be of much help. Mitochondrial diseases not recognized as a medical discipline. Many Universities have Centers that study mitochondrial function. This would be good place to start looking for an MD with interest in mitochondrial disease.

Hi Dr Ian Blair!

What is the point of measuring serum biomarkers? Is it just to identify whether the individual in question has mesothelioma or not?

What is the process and equipment used in measuring biomarker levels, such as soluble mesothelin, in the blood?

Thomas_Wales

Early detection - much greater chance of survival

We are using mass spectrometry-based approaches

Hi Dr Blair! Cheers for doing this AMA. I'm an 18 year old just about to get my A-Level results which decide my University, my first choice being Imperial College where I hope to study Chemistry! I'm just curious about your experience at Imperial College, how did you find lectures, the opportunities it offered you and what links it gave you when you left university! I understand you studied there a while back, but anything you have to say about the place would be great! Thank you!

jakeyguitarist

Wow - congratulations. It was an amazing experience because my PhD mentor (Derek Barton) won the Nobel prize just when I started (1969). I am here today because of what I learned during that time. The biggest challenge if being surrounded by people who are smarter than you! My passion for being a researcher saved me. Therefore, I think the most important thing for you is to decide what you want and then go for it.

Hello Dr. Blair! Thank you for taking the time to do this. I have a family member with Cyclic Vomiting Syndrome, and in reading we have seen it described as a mitochondrial disorder, but this doesn't really help us understand it at all. What exactly is a mitochondrial disorder, can it be passed on genetically, and it there any hope of fighting it?

ArdQuadberry

Sounds terrible, I have no experience with this syndrome. I will check it out after the session.

Good Morning!

I'm a recent geology graduate (B.S.) who is moving on to grad school in the fall. Having studied geochemistry, I have learned there how stable isotopes, particularly those of hydrogen, carbon, and oxygen, are used to study geological processes. I am curious about which isotope systems you use in your work, and in how isotope fractionation in biological systems differs from that in non-biological systems.

Sekkanar

We use stable isotopes in tow main ways:

1. Internal standards.
2. Metabolic labeling

3. Internal standards: N-15 and C-13 labeled molecules are essentially identical to the corresponding N-14 and C-13 forms. This means that they have identical chromatographic properties but can distinguished by mass spectrometry by their difference in mass. A labeled internal standard can be added to a biofluid immediately after it is collects so the ratio of endogenous compound too internal standard is set and any losses are identical. By measuring the ratio we can calculate how much of the endogenous analyte is is present. No other analytical method can provide this level of specificity.

4. Metabolic labeling: We added labeled glucose or a labeled fatty acid to a cell and analyze the amount of label that ends up in a metabolite (eg acetyl-CoA). We can do this with human platelets and show differences between normal and disease platelets. This then serves as a biomarker to monitor if a drug is correcting the deficiency

Hello Dr. Blair, and thank you for doing this AMA. My questions for you are:

1. What is your opinion on the current state of gene therapy research in regards to intrinsic apoptosis?

2. Could we one day not only treat all cancer types, but also reverse, or at least stabilize, cystic growth in those with auto immune cystic diseases (eg. polycystic kidney disease)? Would this be possible?

bluemonetlily

1. I am working on gene therapy for Friedrich's ataxia but do not know anything about intrinsic apoptosis. Our preliminary work in mouse models look very promising. We have just embarked on a human trial with a group at the University of Florida.

2. My experience in pharmacology is that there is never a "magic bullet". I anticipate that it will require many different approaches to treat all these different diseases.

Can the levels of coenzyme Q10 effect the (side) effects of statins. Or can statins effect your coenzyme q10 levels, in turn, contributing to symptoms of myalgia and chronic fatigue? mitochondria and energy?

robbd07

Interesting! We treated Friedrich's patients with statins to increase the ApoA-I levels and ethically they had to be given coenzyme Q10. Several patients dropped out of the trial but not because of myalgia. The effect of statins is still not well understood because they inhibit HMG-CoA reductase in all cells not just liver and intestine (where ApoA-I is made). I believe there needs to be more research on this topic and so I cannot give you a definitive answer.

What do you make of claims that many cancers are mitochondria gone rogue and patient health can be significantly improved by starving body of sugars(ketogenic diet)?

keymone

I am rather skeptical

What's your take on bioinformatics & related interdisciplinary fields? And would your career have been any different had such information processing technology been available when you started out?

DukeAlegon

My research career woful have have always involved generating new knowledge rather than recycling or interrogating existing knowledge. Therefore, I would do exactly the same thing today. However, for our biomarker studies we rely heavily on bioinformatics. Fortunately , the group that I work with in Ann Arbor, MI (A2IDEA) has training in mass spectrometry si they can understand the nuances of the complex detests I provide. Therefor, I think it is important to have cross-disciplinary expertise.

Hi Dr. Blair-

Sounds like your current research isn't really geared towards animals, but I was wondering if you had any collaboration with similar research in veterinary medicine? I know Penn has a great vet school, so I'm curious if your work has any relevancy or application for that particular branch of medicine at Penn.

Thanks!

AhhhBROTHERS

For some reason, I do not have many collaborations with the Vet School. It is impossible to be good at everything so I leave the animal studies to my collaborators. Many of the methods developed in my laboratory are used by other researchers at Penn as you can see if you check out my bibliography on PubMed

I understand the degradation of mitochondria play a role in the release of ROS (the vicious cycle) during senescence. How big is this role and have any efforts been made to study the reversal of mitochondrial aging as a disease?

Coffee_Lattes

It is tricky to study the role of ROS in aging. There are papers appearing on the importance of oxidative

damage to mitochondrial DNA and its repair by glycosylases such as OGG1. The link to mitochondria is through mitochondrial aconitase (ACO2), which is protective against oxidative mitochondrial DNA damage. I anticipate some significant advances in this area over the next five years.

How do you feel about the 3-parent embryos/children being created to reduce/eliminate mitochondrial disorders?

Also how do MS methods for analyzing Friedreich's ataxia compare to analyzing the expansion of trinucleotide repeats? Is there an additional chemical or biomanufactured marker of this disease?

Thank you so much for your time!

bringingspicyback

1. Any approach that would allow somebody to become a parent without the risk of disease is worth testing.

2. We are mass spectrometry is used to monitor treatment of the disease not to diagnose it. When we began our work there was no way to monitor the efficacy of difference treatment options. Now we have three approaches all based on mass spectrometry including the ability to monitor the increase frataxin levels. The disease results from decreased expression of frataxin and we believe that it will be cured if frataxin levels can be returned to normal.

Will be finishing up my Masters in Pharm Sci this December. Any advice for someone looking into a career in Toxicology?

Jonnydrama2

Options:

1. Research Specialist in an academic lab specializing in toxicology
2. Research Scientist in a toxicology laboratory in pharmaceutical industry
3. Research scientist in a contract laboratory specializing in toxicology