

We're Nicholas Heintz, Brian Cunniff, and Kim Nelson, and we recently published a PLOS ONE study showing that selective targeting of two related antioxidant enzymes causes mesothelioma cancer cells to choke on their own oxidative exhaust.

PLOScienceWednesday <sup>1</sup> and r/Science AMAs<sup>1</sup>

<sup>1</sup>Affiliation not available

April 17, 2023

[REDDIT](#)

**We're Nicholas Heintz, Brian Cunniff, and Kim Nelson,  
and we recently published a PLOS ONE study showing  
that selective targeting of two related antioxidant  
enzymes causes mesothelioma cancer cells to choke on  
their own oxidative exhaust.**

[R/SCIENCE](#) PLOSSCIENCEWEDNESDAY

[removed]

[READ REVIEWS](#)

[WRITE A REVIEW](#)

**CORRESPONDENCE:**

**DATE RECEIVED:**  
January 21, 2016

**DOI:**  
10.15200/winn.145329.93393

**ARCHIVED:**  
January 20, 2016

**KEYWORDS:**  
reddit, cancer, plos

**CITATION:**  
r/Science ,  
PLOSscienceWednesday ,  
We're Nicholas Heintz, Brian  
Cunniff, and Kim Nelson, and  
we recently published a PLOS  
ONE study showing that  
selective targeting of two  
related antioxidant enzymes  
causes mesothelioma cancer  
cells to choke on their own  
oxidative exhaust. , *The  
Winnower* 3:e145329.93393 ,  
2016 , DOI:  
[10.15200/winn.145329.93393](https://doi.org/10.15200/winn.145329.93393)

© et al. This article is  
distributed under the terms of  
the [Creative Commons  
Attribution 4.0 International  
License](#), which permits  
unrestricted use, distribution,  
and redistribution in any  
medium, provided that the

First, thanks for your work. I'm sure many on this sub (myself included) have been touched by cancer in some way, so this is huge.

What kinds of effects do you expect this therapy to have on other cancers? Could this be a more "universal" silver bullet? Have you noticed any non-benign side effects?

Thanks again!

[magicdragonfly](#)

Nick: Many aggressive human tumors have properties similar to mesothelioma, so we think this approach may be useful in other tumor types. Gentian violet (GV) has been used in humans as an antibiotic without toxic effects, and you can read papers by Jack Arbiser at Emory University for more information about GV. Thiostrepton (TS) is remarkably non-toxic in mice, as the lethal dose 50 (LD50) is 2,000 mg/kg, an amazingly high concentration. But we have not done enough studies to rule out all side effects. To my knowledge thiostrepton has not been used in any clinical trials for cancer in the US. Of course we would love to have the resources to test the GV/TS combination in human patients.

First, thanks for your work. I'm sure many on this sub (myself included) have been touched by cancer in some way, so this is huge.

What kinds of effects do you expect this therapy to have on other cancers? Could this be a more "universal" silver bullet? Have you noticed any non-benign side effects?

Thanks again!

[magicdragonfly](#)

Brian: To add onto Nick's response, understanding what drives cancer initiation, growth, metastasis

original author and source are credited.



and response (or failed response) to therapies is going to be very important in discovering drugs and probably more realistic, combinations of drugs to treat cancer. In the end getting as far away from invasive surgeries and therapies that come with massive side effects is a realistic goal. No two cancers are identical and therefore we need a diverse arsenal and not just a single bullet. That being said, metabolic alterations are a universal phenotype of cancer cells that has incredible promise as a therapeutic target!

Thanks for your work and for doing an AMA! A few questions:

Why did you use mesothelioma as a model, given that it has a relatively low incidence (at least in the US). Is it especially ROS producing relative to other cancer types? Did you look at Fox3 expression across tumor types/ tissue types? Is it higher in MM? You even noted that Fox3 expression in primary cancer cells wasn't high - are you worried that elevated Fox3 is a tissue culture artifact?

Given that these are non-targeted approaches, do you envision that these enzymes will be selective enough to cancer cells? Do you expect any off target effects? It seems that reducing normal cells' ability to regulate ROS levels by this mechanism may predispose them to other ROS-induced genetic alterations/ mutations.

Finally, are you worried that your therapy is inducing ROS-dependent senescence and not killing the tumor cells? Alternatively, if the therapy does kill tumor cells, are you worried that you are treating only one population of the tumor cells that are especially sensitive (like those further from blood vessels) and that tumor initiating cells are still there? It seems that you showed reduced tumor burden at the time point of controls succumbing to disease, but if the therapy is continued is the decreased tumor size maintained? Do tumors shrink further over time? Do they recur?

Sorry if some of these were answered in the paper. I didn't have time to read super closely! Thanks again!

[serenesquid](#)

Nick: Our department has had a focus on environmental pathology for many years, and one substance we have studied for decades is asbestos. So we use mesothelioma as a model for environmental cancers, but these tumors share certain properties with other highly aggressive human tumors. We think the GV/TS combination may be effective for other tumor types, but we have not formally investigated this possibility.

Many other cancer types produce ROS. We stained mesotheliomas for Foxo3a - it was all nuclear. We don't know if this is significant or not. We know that TS attacks a specific catalytic intermediate in the PRX3 reaction cycle, and we suspect this intermediate is generated at much higher levels in cancer cells due to the high levels of mitochondrial ROS, so we believe this is the reason the compounds preferentially kill tumor cells. We do not know the nature of any off target effects. And we have not looked at senescence or cancer stem cells - this would be an interesting avenue to pursue. And we don't know much about long term treatments since we have to sacrifice the treated mice when the tumors in the control mice get large. We will try these experiments if we get funding.

Thank you for your work!

A few questions:

- You state that mesothelioma cells produce large amounts of ROS and that your combination treatment inhibits their metabolism. Do you think this therapy could therefore be used in combination with radiotherapy as a radiosensitizer?

- Are there any adverse effects known about thioestrepton or gentian violet? Could the inhibition of ROS metabolism have effects on other fast-proliferating cells like those in the gut, hair follicles, ...?
- Did you look at the immunogenicity of the treatment? Since it induces mitochondrial stress, I presume there will be quite some ATP-release upon cell death. Would it be interesting to also look at other markers for ICD like calreticulin, HMGB1, ...?
- Are you planning on further exploring this treatment in other tumour models? To follow up on my previous question: are you planning to test the treatment in immunocompetent mice?

#### Dries

Nick: Published work has shown TS enhances the effects of other redox-active compounds, like arsenic trioxide. I don't know if would work as a radiosensitizer - good idea. Gentian violet (GV) has been used in humans as an antibiotic without toxic effects, and you can read papers by Jack Arbiser at Emory University for more information about GV. Thioestrepton (TS) is remarkably non-toxic in mice, as the lethal dose 50 (LD50) is 2,000 mg/kg, an amazingly high concentration. But we do not know about side effects in rapidly growing tissues - we have yet to observe these. Since the tumor model was human tumor cells in immunocompromised mice, we don't know about the immunogenicity of the treatment, but we planning to look at this with Arti Shukla using mouse mesothelioma in congenic immunocompetent mice.

Hi, fellow scientist here. Just wondering about the choice of journals. Colleagues of mine told me that publishing my work in PLoS One would be a bad choice because of perceived low standards. I like a lot of the articles I've seen in PLoS One (a few strange ones though that didn't make too much sense). What are your thoughts on the journal and sending one's work there?

#### True Stock Canadian

Brian: Being a junior scientist I will give my take on this but also interested to see what my older more experienced colleagues have to say. The pressure is still on, especially to acquire money and land a big job, to publish in the top journals. Most of these journals have a more rigorous review and editorial process, which is very important as there is a ton of garbage research out there that can convolve and confuse even the most experienced scientists. A few points though, just because a paper is published in a big journal doesn't mean it is better or more influential than a paper published in a smaller journal. In the days of the Internet we have access to anything we want, including almost every scientific paper published! This can be good and this can be bad – see my point about the garbage. As scientists we are trained to conduct experiments in a controlled manner so that our findings can be repeated and interpreted by other scientists. No matter where the paper is published a trained scientist can recognize if the research was conducted properly or not.

That being said, I firmly believe journals like PLoS One are great places to publish as well as specialized smaller journals specific to your field. Science moves forward because of the free exchange of ideas and publishing results in a timely manner. If you have a complete story get some advice from your colleagues, make sure people inside and outside your specialty read it and give you feedback on the science and journal suggestions, then submit!

Hi, fellow scientist here. Just wondering about the choice of journals. Colleagues of mine told me that publishing my work in PLoS One would be a bad choice because of perceived low standards. I like a lot of the articles I've seen in PLoS One (a few strange ones though that didn't make too much sense). What are your thoughts on the journal and sending one's work there?

#### True Stock Canadian

Nick: I've been publishing papers in scientific journals since 1975, and have papers in Nature, Cell, JCB, MCB, etc. We originally sent this work to a top cancer journal, and they agreed to review it if we addressed about 10 issues that would have taken 2 years and hundreds of thousands of dollars to resolve. Frankly, I just got tired of being jerked around - PLOS provides a very fair review process, and open access means everyone can read your work world over. And the internet allows everyone to find the work. Publishing in top journals is still really important, especially early on, but that desire has to be balanced with how much money and time you have to do new experiments in response to the reviews. I think Brian has it about right.

just yesterday my dad was diagnosed with mesothelioma and estimated 12 months to live, and now this is here. Is there anything practical someone like me can use from this study at all?

[seshna](#)

Brian: Sorry to hear about your father. During my PhD and after people close to me were diagnosed and some have since passed away from mesothelioma, its a sad diagnosis to receive.

When it comes to finding cures for a disease, whether its cancer or alzheimer's, we need to understand the system, do rigorous experiments and report our findings. Only by sharing our research with colleagues and the world we make progress. The research being shared is not always easily interpretable nor going to have a direct effect on someone like your father. But we are moving forward and making some amazing discoveries that will influence the way we detect and treat cancer in the future.

Stay positive

Thank you guys so much for all your work, and for doing this AMA! I am deciding on colleges, and college majors soon. (I'm considering University of Vermont) If I were interested in doing more research on cancer, what would be the best field to go into? What field would you say has the highest probability of finding the "Cure for cancer"?

[Luke\\_Skytrodder](#)

Brian: Cancer research is very diverse; biologist, chemists, geneticist, physicists, computer scientists, nutritionists, physicians etc.. are all using their skills to better understand the disease and how to treat it. At any given time there are certainly "hot" areas of research that draw attention and greatly influence how we think about cancer but predicting whats going to be "hot" in the future is very difficult (at least for me).

My advice, figure out what you are really passionate about. This can take some trial and error. I was a philosophy/music major before jumping into science and never looking back! Once you find your passion, master the skills, start thinking outside the box and ask questions.

Also surround yourself with people from diverse backgrounds that are much smarter than you ;)

Thank you guys so much for all your work, and for doing this AMA! I am deciding on colleges, and college majors soon. (I'm considering University of Vermont) If I were interested in doing more research on cancer, what would be the best field to go into? What field would you say has the highest probability of finding the "Cure for cancer"?

[Luke\\_Skytrodder](#)

Nick: Any major in the biosciences will serve you well. And treatments for cancer involve chemists, pharmacologists, immunologists, biochemists, cell biologists clinicians, and people from many other disciplines. Just take as many science courses as possible and then go to graduate or medical school!

So, for the layman (me) reading above, does this mean that consumption of antioxidants is good or bad for humans?

#### [Positive Enforcement](#)

Brian: Just like everything else there needs to be a balance. We referred to the Goldilocks scenario quite a bit in lab as Nick mentioned.

My PhD project actually started out trying to find the source of ROS in mesothelioma cells and quench it with a multitude of antioxidants. What we learned from these studies is that these compounds were actually acting as pro-oxidants, increasing ROS and killing cancer cells, which helped us open our minds a bit and put some thought into other ways cancer cells might be susceptible to metabolic alterations.

Quenching ROS, aka antioxidants (especially in multicellular organisms), has been something very difficult to do especially as you need high concentrations of localized antioxidants to actually make a difference. Most ROS act locally and therefore they hit their target long before they can interact with an exogenous antioxidant. Our colleague and co-author on this paper Mike Murphy (along with other groups across the country) is developing strategies to both measure and quench ROS at localized sites and have shown promising results in the fields of cardiac ischemia reperfusion, cancer, neurodegenerative disorders and so on.

Side note: In my personal opinion the box of Pop Tarts labeled to contain antioxidants isn't going to do much for you ;)

So, for the layman (me) reading above, does this mean that consumption of antioxidants is good or bad for humans?

#### [Positive Enforcement](#)

Nick: The \$10,00 question. It's all about balance, so taking large amounts of antioxidants has not proven effective in most contexts. Vitamin E, for example, is not useful for treating lung cancer, and the RDA has been reduced over the past few years. In my opinion supplements cannot replace a good diet and exercise - our bodies generally know what they're doing! It's like Goldilocks - too much or too little impairs the system, and most people err on the side of too much.

Thank you all for taking the time to answer questions. Is your work investigating an established avenue for fighting cancer or are you exploring entirely new territory?

Side note: "go choke on your own oxidative exhaust" is a fantastic insult.

#### [talanton](#)

Nick: I'm not much into clever insults but yours caused me to chuckle. I'd love to say this is entirely new territory, and some of our work is quite novel, but every scientist builds on the ideas and work of others. After years and years in the lab you begin to trust your hunches a bit more, and can recognize the significance of an unexpected result. The early stages of this work were heavily dependent on the creativity and hard work of two graduate students, first Kheng Newick and then Brian Cuniff, who

were unafraid to challenge conventional wisdom and test new hypotheses based on unexpected findings.

Thank you all for taking the time to answer questions. Is your work investigating an established avenue for fighting cancer or are you exploring entirely new territory?

Side note: "go choke on your own oxidative exhaust" is a fantastic insult.

[talanton](#)

Brian:As more research is done and we better understand drug mechanisms in relevant experimental models we and numerous labs across the world are establishing this approach for the treatment of cancers. New drugs are being identified as pro-oxidant therapies while older compounds with "known" mechanisms are being re-evaluated after uncovering their pro-oxidant potential.

Thiostrepton and Gentian Violet (drugs used in this study) were not developed as cancer drugs decades ago and now have shown great promise in a variety of cancers. Drug repurposing, especially compounds already deemed safe for human consumption, can cut down on costs of getting a drug to the people who need it most.

Side note: I am not sure if it influenced the cancer cells response to these drugs but I often found myself insulting the flasks of cells in the incubator ;)

I know that this is fantastic and a huge step forward, but I am wondering what the possible side-effects are for other cells in the body. Could this effect cells on a longer term due to a change in their outer layer?

[AzagabanianPost](#)

Nick: Cancer evolves as it develops, gaining an overall advantage over surrounding normal tissue. We believe that at the right concentrations these compounds eliminate the growth advantage of tumor cells without unacceptable levels of toxicity to normal tissues. But we have not tested this in human patients, which of course is the ultimate aim.

Do you guys realistically think we can find a cure for cancer?

[peaceasy](#)

Nick: I think the thread of these answers is pretty much right on. Cancer is a collection of over 100 distinct malignancies, and much progress has been made on certain types of cancers, and on others not so much. There will never be a single cure - there will be effective treatments based on the individual properties of each person's disease. There has been tremendous progress, but what has happened to date will pale in comparison to what will be available even 10 years from now.

Initially, thank you for your research! I'm an attorney who has represented mesothelioma victims. Cancer is of course a terrible disease, but the speed and mortality of mesothelioma is something else.

Two questions:

1) You mention, "given their role in regulating redox signaling, and the pro-oxidative state of tumor cells, it is not unexpected that the expression of PRXs is up-regulated as an adaptive response in

many tumor types [54,55]. We have focused on this adaptive response due to its almost universal existence in tumor cells [16]." Has this sort of targeting been done on other types of tumors? Do you think this will become a new general direction for inhibiting other types of cancer?

2) It's my layperson understanding that, in a normal cell, the dysregulation of mitochondrial metabolism generally leads to apoptosis. Cancer cells are, of course, resistant to apoptosis. Did you see any indication in your work that you were capable of 'restarting' apoptosis by interfering with the mitochondrial metabolism? Is there any research in that direction?

[maxkennerly](#)

Nick: 1) Mesothelioma is indeed in a special category when it comes to aggressive cancers, but meso shares properties of other highly aggressive malignancies. Pro-oxidant approaches to other tumor types have been reported, and there is a great deal of research being conducted in this area. We think our approach is applicable to any tumor type with high levels of PRX3, a signature of mitochondrial oxidative stress.

2) Andrei Gartel has shown thiostrepton induces apoptosis in other types of tumor cells, but have not investigated this in our work.

Thanks for the work, and thanks for taking the time to do this AMA. I suppose my biggest question is, what other cells besides the tumor cells will be subject to this high level of oxidation stress? Will it be the usual, fast dividing cells of mucous membranes, hair, and so on?

In any case, toxicity aside, it must be amazing to make headway with such a generally terminal condition. Amazing.

[Aelinsaar](#)

Brian: The redox state (how we refer to the balance between ROS and antioxidants) in cells varies and not all cells produce reactive oxygen species in the same manner nor metabolize it using the same antioxidants. There is still a lot we need to know about how other cells respond to increasing ROS levels by these compounds. From our work using primary mesothelial cells from human patients it is evident that the concentration of compounds used was well tolerated by normal cells but not the cancer cells. Also from our studies and others who used these compounds at much higher concentrations in animals indicate they are well tolerated.

In cancer cells peroxiredoxin 3 is enzymatically hyperactive trying to remove the cytotoxic levels of ROS produced. Thiostrepton preferentially attacks this hyperactive state of the enzyme. Whether or not other cells in the body with increased ROS levels are utilizing peroxiredoxin 3 like cancer cells would be interesting to know.

What would you say to a young person trying to gain a position working with yourselves?

[Princess In Panties](#)

Brian: Get good grades and gain experience, take a few years after college to work in a lab and expand your horizons. Make sure you love what you are doing or you will find yourself miserable ;)

So, basically, you did the equivalent of stuffing a potato in the tailpipe?

[BlueDrache](#)

Nick: You got it - that expression is our favorite analogy, and both nipedo and nearlydammit have hit the nail on the head.

Interesting work, a few questions:

- How were the GV and TS administered to the mice? Tail vein? - Not familiar with them, are GV and TS considered safe? What are their LD50's like?

Edit: Apparently IP injections were used, should have read closer

[QWERTY\\_licious](#)

Brian: We have done both IP (inject into the peritoneum aka body cavity) and subcutaneous (below the skin). Both results are reported in the paper.

GV has been used (and well tolerated) in humans and is still used in veterinarian medicine. I believe Nick commented above that TS has not been used in humans but not entirely sure.

We would love to see them in practice one day!

Hi Kim, under 2. Above you mention visualization. Can you share what we're actually able to see, how we're able to see them, and what we're looking at? Thanks!

[OregonOrBust](#)

Kim: Some of my collaborators (including Bruce King, Leslie Poole, and Cristina Furdui) have been creating chemical compounds that only react with oxidized cysteines in proteins and have fluorescent groups on them that "light up" a particular color when hit with a special light. We've been using confocal microscopy to visualize these labeled (oxidized) proteins in cell culture models. We are still very early in this process but some of the studies we would like to do include looking to see how cysteine oxidation changes when we treat cells with compounds like thiostrepton. We also have some compounds that label oxidized cysteines and the isolate the labeled proteins which will hopefully allow us to identify which proteins are getting oxidized.

Have you noticed any efficacy differences due to genetic differences in the tumor cells?

[shivasprogeny](#)

Nick: We have not explored this, but cells with higher levels of FOXM1 and PRX3 are more sensitive. Other genetic differences have not been investigated to date.

What does the current NIH funding situation look like from the trenches?

[LabKitty](#)

Brian: The recent \$2 billion increase is not going to cut it ;)

Does Thiostrepton affect other proteins - particularly those that also have cysteine residues?

the kinetic, biophysical, and structural analysis of features in the peroxiredoxin family of proteins that modulate their rapid reaction with peroxide

What are some of the structural features in them (and other peroxide-sensitive proteins) that makes them so prone to reacting with peroxide?

Can the combination of blocking both of these antioxidant enzymes result in increased levels of oxidative stress in other cells, particularly neurons? (that could maybe accelerate the rate at which they accumulate oxidative damage?)

[inquilinekea](#)

Kim: There is data indicating that thioestrepton binds to cysteine residue in a bacterial transcription factor (TipAS) using a similar type of reaction to what we see with Prx3.

The list of proteins have peroxide-sensitive cysteine residues is growing and there is still much that is not known about the extent this type of oxidation occurs in either normal or cancer cells. We do know that peroxidoreoxins are VERY good at reacting with peroxides with rates that are ~10,000,000 times faster than observed for a "typical" cysteine.

There are a lot of studies looking the structural features that allow peroxidoreoxins to react so rapidly with peroxide (Recent reviews include Poole et al 2015 Trends in Biochemical Science 40, 435-45 and Hall et al Antioxidants & redox signaling. 2011;15(3):795-815.) One contributing factor is a local environment around the important cysteine residue that lowers the pKa and stabilizes the deprotonated form (essentially "activating" the cysteine allowing it to react with the peroxide). However, more recent studies that indicated that peroxidoreoxins also specifically bind to and interact with hydrogen peroxide in a way that stabilizes the transition state and it is this interaction with peroxide that accounts for a significant portion of their ability to react with peroxide so rapidly.

Does Thioestrepton affect other proteins - particularly those that also have cysteine residues?

the kinetic, biophysical, and structural analysis of features in the peroxidoreoxin family of proteins that modulate their rapid reaction with peroxide

What are some of the structural features in them (and other peroxide-sensitive proteins) that makes them so prone to reacting with peroxide?

Can the combination of blocking both of these antioxidant enzymes result in increased levels of oxidative stress in other cells, particularly neurons? (that could maybe accelerate the rate at which they accumulate oxidative damage?)

[inquilinekea](#)

Brian: There is also evidence that thioestrepton can bind directly to the oncogenic transcription factor FOXM1, but it must be noted that derivatives of TS were used in this study and the actual intact compound bound poorly to FOXM1.

To expand on Kim's answer we believe (based on her work and other colleagues) that PRX3 has unique structural features that are exploited during its enzymatic reaction that provide some specificity for the cross-linking effect of thioestrepton to PRX3 dimers. Some experts are hopefully in the process of expanding our understanding of this mechanism ;)

Are there any clinical trials in the works based upon your research?

[sublimemongrel](#)

Nick: Not yet, but a company in Israel is now making TS suitable for use in humans, and GV is FDA approved for other uses. We're hoping to enlist clinical partners to move this forward.

Hello! Both articles are great! Just have a few questions. It seems TS activity is dependent on the oxidative state of the cell (amount of ROS) and will inhibit FOXM to thereby increase the amount to increase the amount of ROS, essentially creating a positive feedback loop. The mechanism you propose seems sound, just the question for me becomes is how specific is it to cancer cells, and not to other cells who might be in a similar oxidative state due to other diseases or other metabolic processes? Also, in a clinical setting, how would this drug be administered i.e. Pills, IV, with the current chemo regime? And finally, did you notice any AEs (adverse effects) when administering the drug and on follow up examination of the mice? Thanks again!

[Aakash1120](#)

Nick: We did not observe significant effects on peroxiredoxins located in the cytoplasm, and TS is known to accumulate in mitochondria, so the drug may only affect cells whose redox state is perturbed by mitochondrial hydrogen peroxide. We noticed no adverse effects on the architecture of the lungs or liver, no loss of weight, or any behavioral effects on the mice. We know TS and GV delivered IP can impede the growth of subcutaneous tumors, so the compounds can travel through the bloodstream. We dissolved the compounds in DMSO, which cannot be given to humans. We need a medicinal chemist to help us devise delivery strategies and formulations for use in human patients.

In our lab we've seen that in reaction to Oxidative stress a small nuclear protein (Cyclin C) is released and helps promote mitochondrial fission and eventual apoptosis. By promoting its release (which is a main goal of our lab) we can sensitise cells to ROS, which as you know cancer cells have a lot of. So in short my question is, what consequences would raising ROS in normal cells be? Obviously you aren't raising them to levels to kill the cells, but surely it can't go without some consequence to the cells, such as DNA damage and the like.

[norml329](#)

Nick: Normal cells make ROS during cell division, with the highest levels derived from superoxide generated during mitosis. But ROS generated during the cycle is highly regulated in time and space, and normal cells have a significant antioxidant reserve capacity. In contrast, cancer cells constitutively produce high levels of ROS. To tolerate this, cancer cells rewire their redox signaling circuits, including up-regulation of the expression of some (but not all) antioxidant enzymes. Enhancing ROS production during a normal cell cycle causes cell cycle arrest, activation of stress responses or apoptosis. Cancer cells generally lack the appropriate checkpoints and stress responses (or have corrupted them to their advantage) and they don't care about DNA damage. It is one of these adaptive survival response we are trying to target.

As an 18 year old who's very interested in science, but doesn't know enough about it, could you put some of the information in to layman's terms? E.g. dysregulation of redox signalling?  
Thankyou for your time :)

[Mattybmate](#)

Nick: If you love puzzles you'll love science. All mammalian cells, as a consequence of using oxygen in aerobic metabolism, produce and metabolize reactive oxygen species (ROS), reactive derivatives of molecular oxygen. All cells have evolved systems for detecting ROS, detoxifying them, and responding to them. In a general sense this is like sticking your nose up the exhaust pipe of a car - you can tell what's going on in the engine from the exhaust. Redox signaling refers to those elements of a cell that control responses to ROS, and like most pathways that control cell fate decisions, redox signaling is

corrupted in many cancer cells.

I always wondered... Hypothetically I get mesothelioma. I already know I am going to die if I dont get some serious treatment. Can I actually apply somewhere, waive some stuff, and be part of the testing? Basically giving the scientists free reign, so I can be one of the first human trials?

[nut-sack](#)

Kim: First, I will say that cancer is a complex disease and many medical trails are approved for specific patient populations. You would need to apply for each trial individually and talk to a doctor who knows about YOUR diagnosis and medical history to see if you would be a good fit. But there are resources out there that help you look for ongoing clinical trials. If you are in the USA, a good place to start looking is at <http://www.nih.gov/health-information/nih-clinical-research-trials-you/finding-clinical-trial>

Who has access to this treatment now? When will this become a practical treatment?

[KasurCas](#)

Nick: There are no clinical trials as yet. We are in the process of developing a group of clinicians and other scientists with the expertise required to take this forward. The good news is that both compounds are now available in a form suitable for administration to humans. If all goes well testing should begin within 2-3 years, and maybe sooner.

Radiation oncologist here- fascinating stuff! Have you tried adding ionizing radiation to thiostrepton to increase tumor cell death rates? 80% of radiation damage to cancer cells comes from indirect attack of DNA by reactive oxygen species caused by formation of a hydroxyl radical from water by the radiation. I would imagine there could be significant synergy between your intervention and radiotherapy, as increasing the availability of ROS should in theory lead to more double-strand DNA breaks caused by radiation, and thus more tumor cell death.

[OTN](#)

Nick: No, we haven't tried that, but someone about mentioned this possibility and it's worth exploring.

Hi there guys, great to have the chance to interact with such distinguished scientists as yourselves. Two questions: What do you think of the new foldscope as a means for less affluent children to experience microscopy? And What would suggest as the first steps to take for a student of Biology that would like to publish a paper? Thank you for your time

[AllHailJesse](#)

Haven't heard of the foldscope, do tell?

Hi there guys, great to have the chance to interact with such distinguished scientists as yourselves. Two questions: What do you think of the new foldscope as a means for less affluent children to experience microscopy? And What would suggest as the first steps to take for a student of Biology that would like to publish a paper? Thank you for your time

[AllHailJesse](#)

Nick: I don't know anything about the foldscope - sounds intriguing. To get your name on a paper find a way to work or study in a research lab. Good luck!