Science AMA Series: I'm Derek Lowe - I've been doing drug discovery research in Pharma since 1989, and I'm the author of the oldest science blog on the internet, "In the Pipeline". Ask Me Anything!

dblowe [1] and r/Science AMAs[1]

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April 17, 2023

Abstract

Hi Reddit, I'm back again, ask me anything about drug discovery or blogging about science. You can read my blog here: In the Pipeline I will be back at 1 pm ET to answer your questions, ask me anything! Edit (5:30 PM EST): Keep the questions coming, if you have them - I'll be back later this evening (EST) to check for new ones, and thanks!

the WINNOWER

REDDIT

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DBLOWE R/SCIENCE

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Hi Derek and thank you for doing this AMA.

Even though we are just a quarter in, 2017 is already shaping up to be quite interesting from a translational medicine perspective. We've already had a number of high profile drug approvals (Dupixent, Ocrevus and Zejula, for example). We've seen two companies submit applications to the FDA for the approval of CAR-T cell medicines. And we've also seen setbacks, such as the failure of multiple Alzheimer's disease drug trials. My questions for you are looking forward to the rest of the year:

- what drug, recently approved or likely to be approved, do you think will have the biggest clinical impact? (my vote is for Dupixent).
- is there a data-driven event that you have your eye on going forward that you think will add clarity to a disease or drug class? (I'm looking forward to seeing more data from IDO inhibitors - a company like INCY is seeing their IDO drug valued by the market at tens of billions of dollars, but I'm not sure the drug class is any better than any of the other checkpoint inhibitors being trialed in conjunction with PD1/PDL1 agents)

- what do you see as the future of the abeta hypothesis in AD? (My hunch is that the drugs will fail in prodromal AD but still the hypothesis will find a way to live on)

SirT6

I was hoping that the recent outcomes trial in PCSK9 would help that area out, but I don't think it really did. I agree with you on the IDO inhibitors - oncology in general is a "show me the data" area, of course, as the recent PARP inhibitor data made clear yet again.

It's not a huge area, but I'm interested to see if Alnylam's amyloidosis Phase III trial works. But the biggest one that I can think of is Kite's CAR-T data - I'm interested in both the response rate and the safety profile, and so is everyone else! The Novartis JULIET trial data are going to be a big piece of news in this area, too.

As for the amyloid hypothesis, I'm getting more and more pessimistic. The problem is that everything

takes so agonizingly long to prove in Alzheimer's!

Could you give us a very brief description of "the pipeline" from drug discovery to clinical usage, including roughly how much time and how much money each step takes? I think most readers would find it edifying and possibly shocking.

With that in mind, what do you think of the presumptive next FDA commissioner Scott Gottlieb's ideas about bringing drugs to market faster by reducing the standard of evidence that a drug is effective? (described in this 2012 essay, but then here's an opposing view)

Epistaxis

In general, I'd say it works like this:**First**, have a good idea for a therapy. No way to put a timeline on that one! **Second**, start making proteins, developing assays, screening compounds, in order to get some kind of chemical matter to work on. That's a matter of months, if you have a good-sized team of competent people. **Third**, clear out the false positives from the hit list and decide which series of compounds look like they have "legs" for a med-chem team to work on. That's also in the months range, but varies a lot. **Fourth**, set a team of medicinal chemists and biologists to work making and evaluating better compounds, iteratively. This can take anywhere from a year and a half on up to four years or more, depending on the issues that have to be dealt with. **Fifth**, get the compound ready for the clinic (scale-up chemistry, toxicology assays, formulations work) - this generally gets done in the last part of the earlier step, but can easily take a year by itself. **Sixth**, into Phase I clinical trials. You have do a lot of FDA paperwork before that can happen (filing an IND), but you've been working on that for a while by this point. Phase I trials generally don't take too long or involve too many people; you can get one done within a year. **Seventh**, into Phase II. This is harder, and how hard depends a lot on the disease area in question. Some patient populations are easy to reach, others are a lot harder to enroll. Things thus are really variable here, and the same goes, and how, for the **eighth** step, which is Phase III trials. Together, those two parts can take you anywhere from two to who-knows-how-many years (if you're working on a slow disease like Alzheimer's or osteoporosis). Then stage **nine** is going to the FDA with a New Drug Application, which will also have been in the works the whole time you're in the clinic. Stage **ten** is FDA approval, and they're probably going to take 18 months or so from the time of your submission (depending on PDUFA requirements, priority review, and such).

So from a standing start, it's hard to see how you can do all this in less that (maybe) six or seven years. Ten to twelve is more like it, and it could take more.

As for cost, there's where the arguing starts. The cheapest therapeutic areas would probably be anti-infectives and some parts of oncology, and you're going to want to have as much as a hundred million to do a pretty cheap job of it, and hope that everything works. From there it just goes up, and up. A huge cardiovascular or Alzheimer's effort is going to send you way up into the hundreds of millions or even into the one or two billion range.

I've written several times on the blog about the idea of lower standards of evidence at the FDA. I think it's a bad idea that could lead to a bunch of borderline frauds taking advantage of the system. And even without that, I don't see how we're saving anyone any money by making them (and their insurance companies) pay for things that we're not sure are efficacious.

Hi Derek,

I've been following your blog since High School I think (your "Things I won't Work With" series initially got my attention), and it's been interesting to watch how as I progressed through school I have been able to understand more and more of your technical posts.

My question for you is, what is the biggest publicly held misconception about the pharmaceutical industry that you would like to see corrected?

kerovon

I think that the biggest one is that people don't realize how hard it is to find a drug that works. People think that we know a lot more about biochemistry and disease than we really do. But in general, the public doesn't have much of an idea where drugs come from. It sounds like we're making excuses when we keep going on about how hard it is, but it's the flat honest truth.

I have been following your blog for many years, and love reading about your thoughts on many current issues in chemistry research. Notably, you were bringing to light the behavior of firms like Turing and Catalyst well before the popular press caught onto them.

- If you were made commissioner of the FDA, what sorts of changes and policies would you pursue?
- The FDA has policies to incentivize drug companies to develop therapies for diseases that affect small populations (orphan drugs). While this is important to allow drug companies to recoup R&D costs for treating patient populations that would otherwise be unprofitable to serve, many have charged various drug companies with abusing orphan drug rules to extend the lifetimes of many of their patents without creating much value added. Do you think current orphan drug policies are working well and if not, are there any changes to these policies that could solve some of the abuses?
- If you were starting graduate school today, what topic would you pursue for your thesis?

catalysts_cradle

Geez, I do *not* want to be FDA Commissioner. That's a thankless job if ever there was one! I think that orphan drug laws, priority review vouchers, and so on are good ideas in principle, but I think that there should be (as there is) occasional review to see if they're working in the way that was intended, or if they've gone off the rails a bit. I'm not sure how I'd change them, though, although I've thought about the problem some. It's very, very hard to devise a reward system that can't be gamed somehow.

One thing I would do, if I were in charge, is to adjust the agency's rewards to companies that bring old drugs up to current regulatory standards. I think that process has been badly abused. And I would also watch out for the various regulatory games that people like to play (as with T*ring et al) to turn generic drugs into scarce, expensive moneymakers.

As for the last one, good question! Probably some sort of chemical biology, is my guess.

"Things I Won't Work With: The Book" Yes, no, maybe? With a side order of "How Not To Do It"?

Torvaun

I'm actually working on that again, targeting an ebook release. I know that I've said that before, but I think I really mean it this time (!)

If you could change one thing about the pharmaceutical industry, what would it be?

Also, any thoughts on the March for Science?

-Metacelsus-

One thing. . .honestly, I'd ask for more knowledge about what the heck we're doing. But that's an early research guy talking. The hope is that that would cut down our failure rates in the clinic, which should make everyone happier. And it wouldn't take all that much. Right now, we fail nine out of ten times. If we only bombed eight out of ten, we'd double the number of drugs that get through!

As for the March for Science, I'm not a big march-and-protest guy. I think it's important to let people know your opinions and be counted, sure, but in this case, I think the purposes of the march are a bit fuzzy, at least from what I've seen.

Hey Derek! What is your take on the future of psychedelics in pharmacology? With all the new research into psilocybin therapy to treat end of life depression, I'm very interested in what you think will happen with this field in the years to come.

kocopelly

That's an interesting field. I've never experimented with anything like that myself (never felt much like messing with my brain chemistry), but I'm intrigued by the reports of sudden changes in major depression and the like. I hope that controlled trials can obtain some solid data in this - any opportunity in that field is worth following up.

Drug discovery vs. Pharma marketing - How do you feel about the lopsided amount of resources that Pharma companies spend on "branding" and marketing drugs vs R&D? Do you feel that the current Pharma business model is assembled in a way that promotes the most beneficial results for society (humankind) as a whole?

mudsak

I've written about this several times on the blog as well. Long story short, I don't think it's all that lopsided. Have a look at these for more details, and come back around for follow-up if you want:

http://blogs.sciencemag.org/pipeline/archives/2013/05/20/but_dont_drug_companies_spend_more_on_marketing

http://blogs.sciencemag.org/pipeline/archives/2013/05/23/another_look_at_marketing_vs_rd_in_pharma

What's your opinion on medical marijuana?

dabdaddy6969

I think it has some real use in preventing nausea/increasing appetite in chemotherapy and the like, but the field is full of wild-eyed claims that make no sense. I see people claiming effects in cancer, Alzheimer's, MS and other diseases, and I think that the evidence for those is slim to nonexistent.

Do you think flow chemistry will be a realistic medichem option? Process guys love it, but things that start as batch processes tend to stay that way.

nate

I think so, but only as the equipment becomes cheaper, more easily available, and more "plug and play". No one wants to turn setting up a reaction into a project all its own. Batch mode is hard to beat for convenience, and flow will always be a bit more complicated (and there will always be clogged lines!).

What are your thoughts on the impact of ai-machine learning in drug discovery?

schorschico

I think it has a huge amount of potential, but I think the hype is way ahead at the moment. One big problem is that the medical literature (and all the databases) have some stuff in them that's just plain wrong, so using that as a basis for machine learning is likely to lead to grief. It's going to be a strenuous process, getting things into shape for the machines to really have at it.

Dr. Lowe,

Thank you so much for your contributions to the scientific community as well as this AMA. We have learned a lot from your work and love your blog.

I represent a group of Master's Students, at USF's Morsani College of Medicine, who recently began research in drug discovery (and love it!). We are hoping to ask you a couple questions regarding your overall approach to drug discovery so that we may learn from you and improve our process and understanding of the field.

1). Do you have any resources (aside from your blog) you would suggest relating to either Discovery or Design? Additionally, do you have a specific protein-protein interaction software you would suggest?

2). Is there an overall strategy you employ when you are researching a novel drug therapeutic? Can you please elaborate on your process? How do you get from identifying a target to post-development of a therapeutic?

3). We would also like to know about the transition from academics to industrial research, as we are interested in forming a pharmaceutical company based upon our research. Are there any tips or suggestions you can share with us?

Thank you so much for doing this AMA and for all of your work in Drug Discovery. I am sure that we will find this very enlightening.

Best wishes from USF Morsani College of Medicine

EjaculatingFish

Thanks! Taking these in order:

1 I have book recommendations every December on the site, but in general, I'd say that keeping up with the current literature is the only prescription. Journals like Nature Reviews Drug Discovery can be particularly helpful in getting up to speed. Wish I had something more for you, but it's such a big field that it's hard to get a handle on sometimes.

As for software, I'm not at all a computational guy, so I don't have much to offer there. I would take all software predictions for PPI results with a generous helping of salt, though.

2 Thank God, it's not just me doing that sort of thing. All kinds of considerations come in - does the target look tractable, given current technology? Could it come within reach somehow, if not? Is the disease one that has a solid clinical path forward, in identifying patients and getting a good readout on efficacy? Have others tried this target out, and if so, what happened to them and why? How would one go about setting up a screen for chemical matter, and what kind of false-positive and false-negative rates might you hae to deal with? And so on.

3 The best place I can send you is a recent book called "A Practical Guide to Drug Development in Academia". I thought a lot of the advice in there was very worthwhile. Good luck! I would also strongly suggest bringing on one or more people who have done that sort of thing before.

How accurate is the movie 'medicine man'? Do you think there are still plant and insect species that might one day assist us with currently difficult/incurable conditions?

Sexymcsexalot

“Medicine Man” was wildly, hilariously inaccurate in its depiction of natural products research, unfortunately. But natural products research itself is no joke - a lot of extremely interesting, useful, and active compounds have come out of it over the years. Problem is that it’s been suffering from diminishing returns over time, as we’ve learned more and more. It’s hard to keep from finding stuff that’s been found before, unless you’re looking at increasingly exotic samples.

Any tips on landing a med chem job these days for someone with a PhD + postdoc experience?

Also, what's the typical career progression for someone ending up in a chief science officer/division head/head of chemistry type role?

organiker

It's not easy out there, but it can be done. Your odds are probably better with smaller companies, and there are two ways to play that. One is to head to where the smaller companies (and many of the bigger ones) are, that is, Boston/Cambridge or the SF Bay area. That's not a bad idea, but another strategy might be to try outfits that aren't in such a rich labor environment and would be happier to get you. The downside of that is, when the small company wipes out, as many do, you're left without as many options. That factor alone is a big reason for the popularity of the big clusters.

I don't know if there's a typical progression, as to the second question. A lot of larger companies have two tracks (managerial and scientific), so if you want one of those jobs, you'll want to be on the first one. I never inclined that way, so I may not be a good person to ask!

Morning and thanks for joining us.

What your thoughts on the 21st Century Cures Act? Pros/cons?

Thoughts on the current administration proposals to strip NIH funding and the ramifications that would be felt?

PHealthy

It's a mixed bag. I wrote on it a couple of times at the blog:

http://blogs.sciencemag.org/pipeline/archives/2016/12/05/the-21st-century-cures-act-a-giant-pinata

http://blogs.sciencemag.org/pipeline/archives/2016/12/09/the-politics-of-the-21st-century-cures-act

In general, I think we're going to have to wait to see how much of an impact it makes, because I think that some of the provisions of the bill are just political grandstanding. Which is a common problem!

The NIH funding proposals are extremely shortsighted. It's not that every dollar spent there is a golden example of perfection, but this isn't the answer. The good part is that I think that the Trump administration's budget proposal, like every other presidential budget proposal, is a nonstarter in the House. And if Trump's approval ratings continue at their current levels, House members will be even less inclined to take his plans as written.

Hi Derek,

I work in antibacterials, and I feel that cancer is way too overplayed. Outside of profits, why is cancer such a huge focus in both industry and academia (especially in the western world)? Is the extension of someone's life by 3 months that much better than curing an ailment?

Thanks for doing these. I've really enjoyed your blog for many years.

gremlinstatus

I know what you're saying, but the hope is that we're going to eventually do a lot better than three months, and the progress is incremental. As the developed world ages, cancer is going to be (and already is) a constant concern - live long enough, and you're going to get it in some form, I'd say.

But that's not to say that anti-infectives aren't important - and if the resistance problem keeps going, we're going to start cutting into those developed-world lifespans (!)

Hi Derek, second question:

Do you think Theranos has sufficiently smartened up investors, or should they still be on the lookout for biotech that overpromises technologies that aren't truly feasible yet?

superhelical

Investors should never let down their guard. Highly technical fields are especially prone to this kind of thing, because too many people don't understand the details and the potential can be so huge. You'd have a lot harder time putting a disaster like Theranos over if it were (say) grocery cart technology.

Hi Derek!

No question, simply saying hi. We worked together briefly in Kendall Square. I was in the hood across from DDD, but you and i were never on a project together or anything.

I do process chemistry now. I miss the excitement and unexplored territory atmosphere of med chem, but this is very rewarding for different reasons. I've been on 3 projects now that have gone to commercial manufacturing, so finally i get to see the final results of drug discovery.

Just saying hello and i hope all is well :)

Khayeth

Thanks! Triple-D is still hanging in there, as you probably know. I do envy you seeing so many things that you've worked on going into the clinic. . .

Hi Derek!

As a postdoc interested on doing some writing and outreach on the side of my research, how would you recommend doing so? Do you have standard advice for aspiring writers?

superhelical

Sounds good! The best advice I can give someone who wants to write is to write. That maybe sounds odd, but it’s the key; just sit down and do it. A blog is a good place to start, because the barriers to entry are zero: there’s the screen and there’s the keyboard. It can be tricky to write about technical subjects in a way that anyone else will want to read, so if you can do it, you’ve got a skill that’s not very common. But the only way you’ll know is to sit down and write something and see how it looks and reads, and then improve it as necessary.

One old piece of advice has always helped me out: read your stuff out loud. It really improves the flow of sentences.

In your opinion, to what extent is drug discovery research driven by profit motive?

I think there is a popular narrative that the for-profit incentive structure of the pharmaceutical industry encourages them to fund ideas for drugs which will result in long-term treatment instead of a cure. From a behavioral economics perspective, this is pretty solid reasoning.

From a researcher's perspective, do you ever feel as though you are doing the "wrong work" when a better alternative would be possible, just not as profitable?

Sprizzlez

Ah, but cures would be even more profitable, if we could only find them. I've worked on a number of

cancer programs over the years, for example, and they've all been "Well, this is what we think we may be able to do, so let's try it". Never has it been "Hey, here's a possible cure, but we're not going to work on that". We simply don't know how to cure things, in general. That may seem odd, given how much medical knowledge there is, but compared to what we need, we still don't know that much.

For instance, we don't know what causes Alzheimer's, so it's kind of hard to cure it. And "cancer" isn't one disease, it's several thousand, all of which are different, because there are so many ways that a cell can end up in that unregulated-growth zone. So how can there be a single "cure for cancer"? And so on.

What are your thoughts on the March for Science this weekend? What's your opinion on how we can best communicate science to the public?

polygalchem

I answered a similar question above. In short, I'm not 100% sure what the march is trying to accomplish, and I'm not a big march-and-protest sort of person myself. I sometimes wonder what these things accomplish, outside of lifting the spirits of the participants, not that that's nothing in itself.

Hi Derek, thank you for doing the AMA.

Two quick questions. First, what is your stance on drug pricing in the US, and whether sharp increases are justified for R&D and profit margins? Do you think there has been a justified backlash from the general public against such moves from the likes of Mylen?

Also, how effective is the drug Cetuximab at treating certain types of cancer, and should there still be intense cost/regulatory restrictions in its application in markets?

ArtificialExistannce

Pricing is going to get us all in trouble eventually. Even justified price increases aren't popular, and not all of them are justified. The best take I've ever seen, though, on drug pricing in general is Jack Scannell's article: https://www.forbes.com/sites/matthewherper/2015/10/13/four-reasons-drugs-are-expensive-of-which-two-are-false/#15ddea024c3b

I think that Erbitux/Cetuximab has its place (depending on a patient's KRAS mutant status), but it's no magic bullet, for sure. I'm not sure what you mean about intense restrictions, though - it seems like it's in the same position as other oncology drugs in that respect.

Hi Derek,

I know you've talked briefly on your blog about being employed and writing during your lunch break or on the train but what is your typical day like (synthesis, characterization?) and how did blogging play into that? Also good luck finding a new job!

tylerking311

One train ride does pretty much equal one blog post (I compose on the fly and type quickly!) During a working day, it varies a lot. Some days I'm in the lab most of the time, working up reactions, clogging up the LC/MS, checking NMRs, the usual stuff, while other times I'll go days while hardly setting foot in front of the hood. At my point in my career, a company is not going to get their best value out of me as a full-time bench guy, although I do like to keep my hand in.

Hi Derek. Over the past few months I have noticed an increasing number of drugs for psoriasis. From what I have looked into, psoriasis has been around since the 90s. Why has there been such a sudden

growth of prescription psoriasis medication so recently?

ahwider

The answer from u/tansit is correct - it's an immunology play. A lot of other approaches have been taken over the years against the disease, but that's the one that's borne the most results, and the resulting compounds tend to get used for a lot of other things as well (arthritis, etc.)

Hi Derek, pharmaceutical companies are routinely blamed for high drug prices and high medical costs in general. To what extent do you believe this to be accurate?

kochikame

They're not blameless, but they're not the only actors. The Pharmacy Benefit Manager outfits (PBMs) are starting to come under more scrutiny, for example. The big problem is that pricing in the industry, and in health care in general, is relentlessly opaque. Everyone pays a different price, and no one knows what anyone else is paying. Not exactly a great situation for Econ 101 price discovery to work!

Hi Derek,

Where do you see the future of small molecule going? Is it diversify towards biologics etc or die, or do you think there a future for low volume, high potency small molecules?

bonedriven

I think that there will always be a place for small-molecule drugs. But it's true that when you look at the tables of best-selling compounds, there are more and more biologics (antibodies, mostly). So we small-molecule people have to be aware of that, and keep our eyes open for opportunities to use our expertise in wider fields than we're used to (which to me is where the whole field of chemical biology comes in).

Why isn't marijuana researched and studied more thoroughly?

Dave_10

Because it's not that interesting, and medicinally, not that useful compared to a lot of other fields. I know that sounds odd, and there are a lot of enthusiasts who see it as a wonder plant that does everything. But from a natural products/medicinal chemistry standpoint, it's not as big a deal.

Any luck finding a new job? As an 'older' chemist, do you find it harder or easier to get calls when out of a job? I imagine the popularity of your blog helps quite a lot, but thats my biggest fear: as I get older the more concerned I become at the prospect of being "overqualified" if I ever get laid off.

FleshlightModel

I have several things going now, and I feel very fortunate to be in that position. I do think I'll line something up. In general, I think it's harder, the older and more experienced you are, but the blog has been a tremendous help, both in terms of making contacts and in showing what I might be able to offer.

Hi Derek, I've been following your blog very closely for about two years now and I enjoy it very much. I'm doing a PhD in drug discovery myself (molecular cell biology/cell signaling) and I was wondering: What do you think are critical skills or knowledge that I can invest my time in to increase my chances of having a successful career in this field?

Second question: which blogs/websites do you read on a daily/weekly basis?

Greetings from Belgium!

thenumber42

I'd say that you should make sure that you know your own field well, of course, but also be ready and able to pick up knowledge "across the aisle". If you're a chemist, learn more biology than the typical chemist knows, and vice versa. The number of people who can bridge that gap is much lower, and you have a better chance of standing out, and of coming up with useful ideas that might not occur to someone else.

I have an RSS feed for the current literature, but as for blogs and web sites, I like to keep up with the industry news via Adam Feuerstein at Thestreet.com, Endpts.com, FiercePharma, and BioCentury. I also get a lot of use out of the news sections at Nature and Science.

Hi Derek,

As a current student, I'm so excited to see such a successful Hendrix alum posting here!

I was wondering - do you feel that attending Hendrix helped or harmed your pathway to success? I'm trying to get into the pharmaceutical industry after getting my PhD but I sometimes feel that a liberal arts education wasn't the right start. What do you think?

Also one more if you don't mind - how did you learn to write with such a fabulous narrative style in your scientific posts?

Thank you so much!

lexnerd

Well, it was quite a while ago by now, but I think that where you go to graduate school is a much bigger factor than undergrad. Of course, there's the undergrad effect on which grad schools let you in, but I don't think that a solid liberal arts education is a handicap, as long as you stay solid in your area of specialization.

As for the writing style, you got me. I've always had a fairly vivid style, and in fact, it was the realization that I wasn't really getting much out of my writing ability that led me to start the blog (!)

Hi, I've been following a company called Organovo which supplies 3d bioprinted liver and kidney tissue to pharma which has been shown to detect toxicity in potential drugs that current models, including animal models have failed to detect. The uptake of this technology has been much slower than I expected, and I am wondering why pharma companies are being slow to utilise new technologies to speed up development of new drugs and detect toxicity more reliably? Thanks

jayeluk1983

This is certainly interesting stuff, but there's a high regulatory barrier when you start talking about predicting human tox. There will always be a period where both the old way and the new way have to be run simultaneously, because no regulatory agency is going to throw away the methods that we know without a huge amount of data. That said, using this inside a company to inform FDA-targeted studies is certainly something that's feasible, but I don't know if that's going to make Organovo enough money to keep them going or not (which I think is the issue they're facing).

Derek,

My question is a small change of pace- I'm a non-traditional, working full-time student desperately

grasping onto the reins of the charging, rabid, and possibly on fire bronco that is Organic Chemistry I. With that in mind, what is your best advice for surviving Orgo I and II?

spinch

Look for the similarities in reactions and reaction mechanisms. If you approach it as a collection of unrelated Name Reactions, you're making it harder than it has to be. I can barely keep the various alphas-carbonyl-condensation name reactions straight, but they all do similar things, and I can work with them as if they're all variations on the same thing. Same with carbocation-driven mechanisms (like Friedel-Crafts), and then the pericyclic reactions are yet another category. Try to get a feel for "pushing electrons" in mechanisms, if you can, and that'll serve you well.

Hi Derek, I love reading your blog and especially your posts giving context about how the pharmaceutical industry does what it does, and I frequently link to your posts in online discussions. Its particularly disheartening to hear people *still* argue that drugs would be enormously cheaper if companies simply stopped marketing them, a point you have so simply and convincingly refuted. Can you think of any new way to spread your view on this point to simply nullify this argument?

quantum-mechanic

I wish I could. And I wonder if there really is something that can be done about this view, given human nature and all. I mean, people believe a lot of things that just aren't true, and it's always been that way. I do what I can to spread what I think is better information, but I also try not to have too many illusions about what can be done on the large scale.

I'm a huge fan of your blog!

How did your employer find out about your blog (did you tell them in advance, ask permission, etc.), and how did they feel about it? I've noticed that you're pretty careful not to mention them by name and your personal opinions seem to be pretty carefully phrased.

Have they ever asked you to change or take down anything you've written?

spinur1848

My most recent employer was well aware of the blog when I came in - in fact, it helped bring me to their attention, so that was good. I've never had any situations like the ones you describe, probably because I do try to be careful not to ever been seen as a spokesman for where I work.

I'm fascinated by tellurium compounds, due to their acute stinkiness. Why aren't people trying harder to work with them? They could possibly have enormous benefits if they could be studied with some way of shielding researchers from the smell.

I really want to know what they smell like. As a person who doesn't find H2S and other foul smelling compounds particularly nasty in terms of smell, they must be something else. Have you ever smelled them?

NiceAnusYouHaveThere

The problem isn't just the smell - they tend to be toxic as well. Anyone proposing an organotellurium drug will have to deal with several issues. One is the smell, of course. That's going to reduce patient compliance, and it's also going to make it next to impossible to run a double-blinded trial. And the bigger one is potential tox. Te compounds are going to presumably have effects wherever there are free SH groups, and that's an awful lot of active sites and active protein surfaces.

What about the lack of studies considering the potency of cannabidiol (and other cannabinoids) for many diseases including Cancer (have dug pubmed back to 1981, recent papers show value [1]) ?

Dr LeChevalier blasted the idea out of the room the second I mentionned the molecule's name.

Has it been proven mostly useless by serious pharma labs since or is it lack of interest disguised inefficacy ?

[1] mcallister and desprez 2007, 2010

- https://www.ncbi.nlm.nih.gov/pubmed/18025276
- https://www.ncbi.nlm.nih.gov/pubmed/27087608
- https://www.ncbi.nlm.nih.gov/pubmed/20859676
- https://www.ncbi.nlm.nih.gov/pubmed/27364596
- https://www.ncbi.nlm.nih.gov/pubmed/28378188

ps: I should have added that these are mice models using human cancer lines, so far I only found 2 human studies (thanks to Cristina Sanchez) using CBD (breast and brain) and couldn't find the last report. Funding is needed by these researchers to do more and reach phase I and II.

pps: not affiliated with them, just very curious on the pharma viewpoint on this topic

agumonkey

I know that this is going to sound weird, but the cannabinoids really don't have exceptionally interesting activity against cancer and other diseases. People who've worked in these fields aren't excited by them because for the most part they've seen plenty of other things that have the same sort of behavior.

What do you think of the current popular belief that opiates don't work for chronic pain?

By their logic, are there any drugs that work well for chronic pain?

Pinkmongoose

A big problem with pain is that there are so many different kinds - acute, chronic, neuropathic, and the mechanisms for each one are somewhat different. So it's true that what works on some of them aren't so effective on others, and I'm really not sure if there are any good choices for chronic pain. A lot of people have taken cracks at it, and are currently, but there have been a lot of failed clinical programs there over the years.

How do you suggest one address anti-vaxers. They seem to be immune to facts? They often dismiss the sources as tainted because they are "in the pocket" of big pharma. Waist of time?

foundbypat

It's hard, and it's a slow process. A direct attack almost never works. I've tried working up to it, with Socratic-type questions along the way. But only a certain percentage of these people with these views are willing to change their minds, in my own experience.

Thanks for doing this sAMA.

I'm developing a cell-based approach to reveal genetics of drug responses/actions (among other biological processes). What would be your drug of choice to investigate that has a therapeutic response but is poorly understood in terms of targets or mechanisms of action? My current choice is lithium.

Echo_are_one

Lithium's a pretty good one. You might also consider metformin - people have a fairly good idea of how it might be working, but it's far from settled. Another one might be gemfibrozil; there have been a lot of arguments about that one over the years, too.

How did you get into drug discovery and what level of degree did you need to start? I'm interested in pursuing this as a career.

Icyalex

I'd recommend going all the way to the PhD for your best shot. It's possible to work with a Master's as well, but you're always going to have a ceiling over your head, in almost every company. I think that the long-term trend, between outsourcing and automation, is for the medicinal chemistry that's done in high-wage countries like the US to be the high-value stuff. The grunt work is done offshore or by machines, more and more, which means that the chemistry that remains here tends to be at a higher level (or had better be).

I got into it myself back in the late 1980s, so my own experience is increasingly less relevant (!)

Hello, Derek.

How was blogging in the early internet?

Shawnj2

You found yourself explaining what the heck a "blog" was a lot of the time, that's for sure! And it was such a smaller community of people - I mean, I was one of the first, perhaps the first person to have a science-focused blog at all. Seems strange now!

I've heard of companies like Organovo that uses 3D tissue to evaluate things like efficacy, metabolism, and toxicity and supposedly has better evaluation because of the 3D tissue. Is this technique used very much? If not, why?

Also, how far along are things like synthetic biology or gene drives for drugs (synthetic biology where you're doing reprogramming or building machinery in the target cell, rather than, say, using yeast to make drugs which I know we've been doing for a while)

Humes-Bread

More complex tissue culture techniques are really interesting, because it's for sure that the easier ones don't give you "real" tissues that recapitulate the functions you want. But there are so many variables and things to try, that it's very hard to make progress in the field. I think we'll get there, but there are an awful lot of blind alleys to go down.

The gene-drive stuff is a good way off, I'd say. The problem with doing it that way it that it's harder to adjust dosages or turn things off entirely, compared to dosing something externally. The first applications will surely be correcting inborn errors of metabolism, so you could consider that an application of making a drug in situ, I suppose.

Love your blog. Wish I could say I read it as religiously as I like. It provides a very interesting perspective on pharma. Also love the articles in things that go boom.

One subject I haven't noticed you tackle is that of excipients. Any thoughts on that as a topic?

Edit: grammar

thatguy314z

That's a really good subject, and it's one that I could use to know more about. I'll educate myself first, and then do a post!

Have you read the book PhIKAL? And has it influenced you in your research?

MC_Kloppedie

I've read some of it over the years. Shulgin was a very interesting guy, no doubt about it, but his worldview was very, very different from mine. I don't even drink alcohol, because I don't want to mess with my brain chemistry, and messing with his was such a big part of his life!

Do you think it is acceptable to price people out of life saving medication? Poverty.com states that 3 million people die from curable disease a year.

Am I wrong to say the high reward/high risk about drug production that is regularly stated, is a way of justifying greed, as you have potentially life saving products that you KNOW people will always pay VAST amounts for?

What is your opinion on the development of superbugs? Resistant to all antibiotics.

'The arrogance of man is thinking nature is in our control and not the other way round.'

Flipmodesquid

No, I don't. But keep in mind that in many cases, the issue isn't necessarily availability of costly drugs. Many people die from lack of very low-cost things like rehydration therapy. I'd like to recommend Jack Scannell's take on drug pricing (https://www.forbes.com/sites/matthewherper/2015/10/13/four-reasons-drugs-are-expensive-of-which-two-are-false/#15ddea024c3b), and you might find this post of mine of interest, too (http://blogs.sciencemag.org/pipeline/archives/2008/01/10/drugs_and_money_and_how_it_feels).

I'm quite worried about the development of resistant bacteria. I have no desire to move back to the pre-antibiotic world. But I've done antibacterial projects, and finding new useful antibiotics is really, really hard, so I'm not sure who's going to win that race.

Dr. Lowe, I have one or two questions. Firstly, Apple pie, pumpkin pie, or cherry pie? Do you happen to enjoy video games, and if so which ones? Dogs or cats or neither? What sort of music might you listen to while working? Do you believe college *as it is today* is still a good investment?

darkstar1031

I'll take blackberry cobbler over any of those, and if we're strictly in pie territory, pecan over any of them, either. Don't have much time for gaming - I have no objections, but it's been many years since I've done much, and certainly nothing "long-form". Music's a good question - I generally don't have much on in the lab, honestly, because the fume hood background doesn't make it that enjoyable.

And as for college, I think that it's not as good an investment as it was, but it's still worthwhile, if you choose carefully. "Any generic college" is not a good choice. This has been very much on my mind recently, since both my kids are of late-high-school age.

Hi Derek - Love your blog, I initially started reading "Things I Won't Work With" and then it branched off from there. Lately in the news we have seen headlines about natural products being found as possible drug candidates. Two that come to mind are a compound made by bacteria in the Berkeley mine pit

which kills MRSA and a compound in frog mucus that shows promise in killing the flu. How do we decide to test these things out as drugs?

the_quassitworsh

I'm going to blog about at least one of those, actually. The way they get tested is just the way that any other drug candidate gets tested, but for natural products, that means first finding a way to make the stuff in quantity. That can be a hard step, and often involves engineering bacteria to make it (or as much of it as possible) for you. A good example would be Taxol - turns out that it's a fungus that lives with the yew tree that makes the compound, not the tree itself, so now it's made by industrial culture of the fungus.

How do you know you have the oldest science blog on the internet?

jumpmanjumpjumpman

It's a tough question to be sure about. When I started, I got linked to by other bloggers in terms of "Hey, here's even a science blog, imagine that", so it certainly wasn't something that people were used to. It gets down to one's definition of what a blog is, in the end, because I'm sure that there were computer science/IT people who were writing regular internet things in that line well before me.

Do you have a list of "Things I Won't Work With Again" for things you've tried, but decided weren't worth the potential cost?

IBreakCellPhones

I hadn't thought of it in those terms, but I probably do. "Worth the cost" is a sliding scale, though, depending on the expected reward. But there is no reward that I can think of that would make me want to work with some of the stuff I've written about (!)

Given your status of oldest science blog on the net, I'm curious about how many hits you get per day, if you don't mind sharing. You must have a pretty great ranking built up by now!

AmbivalentFanatic

Google stats show me as between 20k and 30k pageviews on an ordinary working day. If this were 1999 again, I'd probably be selling stock in InthePipeline.com (that's a joke, I'm fairly sure).

Got two questions for you: do you know of anyone who is working on horrible fluorine chemistry? Also, are there any "one ingenious idea plus a lot of work could make a huge difference" topics in drug discovery area?

ksr15

There are quite a few academic groups doing fluorine chemistry, which is horrible by definition. I keep seeing people (well, one group in particular) recommending dilute fluorine gas as a reagent in organic chemistry, and I keep thinking "You first".

As for the second, there are a lot of those - in fact, too many to count. There are so many outstanding problems in drug delivery, in (for example) getting things to work against protein-protein interactions, transcription factors, and other hard targets, in understanding disease mechanisms, that ingenious ideas have a lot of room to run. That's one of the appealing things about the field, actually.

This is a bit uninformed of a question, so please correct me if my assumptions are wrong, but as I

understand it, drugs only need to have statistical significance over a placebo to be passed through phase 3 trials.

Do you think this causes a lot of large pharm companies to release drugs to market that have little or no actual impact?

Yngstr

That's not quite right. You have to test versus "standard of care" in most cases, not just placebo. Now, when the first compound was approved for renal cell carcinoma (kidney cancer), it was tested against placebo, because (sad to say) placebo *was* the standard of care. But now any new kidney cancer drug has to be tested against the current treatments. Doctors, patients, and insurance companies all want to see head-to-head comparisons as well, which is another reason to run them.

Two questions for you:

1) What are you doing to lower prices of drugs in America, or if that's out of your wheelhouse what's the best way to get drug prices to drop in America?

2) How do you feel about America being one of two countries in the world that allows public advertisement of pharmaceuticals? Do you support this practice?

Thanks for your time!

squanchy-squanch

The best article I've ever read on drug pricing is this one, by Jack Scannell: https://www.forbes.com/sites/matthewherper/2015/10/13/four-reasons-drugs-are-expensive-of-which-two-are-false/#15ddea024c3b

It may or may not give you much hope. As for public advertising, I have no philosophical objections, but as a practical matter, I think it's hurt the reputation of drug companies in the US a great deal.

Got any drugs in the the pipeline for weight loss? They had one along time ago.... I think it was call MDMA. Anything around those lines? :)

nikefredo

Well, a few years ago, there was a lot of excitement about a drug called rimonabant. Since I always get a lot of cannibis-themed questions at these things, I should mention that that one was a cannabinoid antagonist, to basically give people the opposite of the munchies. It did do that, to an extent, but it also increased thoughts of suicide in test patients (to everyone's surprise and dismay), so that was that.

Weight loss in general is a very hard field, because there are so many overlapping, redundant systems involved in feeding. Evolutionarily, every organism that did not have very robust food-seeking behavior was outcompeted by the ones that did!

Hey Derek,

I know you're not able to talk about Orkambi, but my question is related to it's implementation in Canada and how to fix drug pricing. After gaining approval and going through the review process the CADTH review recommended not paying for it, and BC has folllowed that decision. https://www.cadth.ca/sites/default/files/cdr/complete/SR0471_complete_Orkambi-Oct-28-16.pdf Mostly because the QALY was only valued around $50000 a year not the price that the PMPRB recommended. That review also stated there would only be a 12 year window until a generic would become available.

My question is this, what do you think the best way forward for governments would be to negotiate prices that more closely represent the QALY value (as that is how they determine what a drug is worth) while also ensuring that companies are incentivized to continue pursuing orphan drugs with small target markets. Should market exclusivity be extended? As a CF patient I am wary of the fact that a "good drug" is being kept out of the hands of patients solely because the government wasn't willing to find a way to negotiate a price they were willing to pay for it. This is also complicated by the fact that the pricing negotiated is I believe based on the average of what the G7 countries are willing to pay but isn't that a chicken and the egg scenario?

Thanks for reading, not trying to go after Vertex just using them as an example of a scenario that's happened.

Your blog is awesome and I find it really helpful when trying to point science skeptics in the right direction for looking for information about how the pharmaceutical industry actually works. You're doing good work!

Cheers,

Mike

thatcfkid

This is a tricky area for me to talk about, but in general, there would seem to be possible solutions (such as extending exclusivity) that are probably not politically feasible, and things that are politically feasible that probably wouldn't solve the problem (!) Which is a very hard one indeed. I think one of the hardest things in policy-making is setting up an incentive structure that's strong enough to influence behavior but not so tempting as to invite people to game it.

It's an excellent example of why I wanted to bang my head on the wall when Trump said "Who knew health care could be so complicated?"

Do you see any male pattern baldness cures on the horizon that have potential to be a real breakthrough?

browniancoffee

Can't say that I do! Doesn't seem to be a problem in my family line, but that would be a big seller. There is research going on, though: http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1006594

After the pharma industry was practically decimated in states like NJ do you think bench level pharma research will be largely outsourced? And as a followup, do you think pharma research is a good profession for a young scientist in the US?

Cantholditdown

I think that there will always be bench level research here in the US, but it's going to be run at a higher level, on average, because the routine stuff will be (and is being) done offshore or by automation.

As for being a good profession, I think so - if you keep the above in mind. It's a bad time to be a just-average medicinal chemist in a high-wage country, but if you like and you have something to offer, I'd say go for it.

This will probably get buried, but maybe you'll see it so here goes nothing!

I'm currently an undergraduate majoring in Chemical Engineering. My current plans for post graduation is industry first (in pharmaceuticals - probably process engineering of tablets or something along those

lines), then Grad school for Pharmaceutical Sciences. One day, I want to either be the person designing the drugs/vaccines or determining the mechanisms for drug delivery.

I've heard very conflicting advice between industry first then grad school vs grad school right away. My main reason for industry would be to just pay back the debt I've accumulated thus far, but I'm open to any future plan.

I'd be very happy to hear any advice you may have! Thanks for doing the AMA, and I'm very happy tow start following your blog to get more immersed in the industry!

Ab-Eb-Bb-C-Eb-G-C

Nah, I'm trying to answer everything! I've seen people do this both ways. Industry first can be good, but I wouldn't stay too long before going back to grad school, so you don't look too out of place compared to your degree and experience.

If you want to be the person designing the drugs, though, Chem E and/or Pharm Sci are not the fields doing that. Drug delivery mechanisms, though, could definitely be a thing to get into.

Is Alzheimer's still just a money sink? Are there any new developments there you're excited about?

RRautamaa

I wish that I had something exciting to report. But I don't see anything out there at the moment (that I'm aware of) that makes me hopeful.

Hi Derek, any upcoming breakthroughs on possible cures for Crohn's disease?

iwinagain

Haven't worked in the area myself, but my guess is that the microbiome work that's going on (gut bacteria and all) is the best shot at making real progress there.

What impact do you believe neuromodulation will have on the traditional drug market? What are your thoughts on neuromodulation in general?

ORD_to_SFO

"Neuromodulation" is a pretty vague term - what specifically do you have in mind?

Does Pharm feel any blame over the opioid epidemic?

fantasyfest

Looks like Purdue Pharma should, from what I can see. But very few companies actually work in this area.

Hi Derek! Really excited to see you doing an AMA, I am a long time reader of ITP, and it is a staple at my workplace for casual conversation. As a student still trying to get my footing a lot of the time, it has helped me understand current industry tech and progress a lot better than I would have on my own.

That being said, I was wondering what your opinion is on how you think DNA encoded library technology could change the way we approach drug discovery, and if you think it will ever gain a real foothold in big pharma production? Thanks again for an awesome blog!

irreverent_villager

I know that a lot of the large companies are using it pretty routinely. It's another tool in the collection - not a magic cure for what ails you in screening, but certainly worthwhile. At a smaller company, it's harder to keep DEL stuff going, though, because the number of projects and screening campaigns that are suitable for it may not be high enough to keep everything running smoothly. But I like the idea, and have seen some interesting results out of it.

Hello Derek,

My question is: What's the strangest place your blog or career has taken you? I saw your interesting articles on chemical warfare, and wondered if either your work or your blog have led you into some other odd areas of research.

I've been an infrequent visitor to your blog over time, mostly to read up on amusing "Things I won't work with", "Things I'm glad I don't do", and "How not to do it" articles. My knowledge of chemistry doesn't stretch much beyond cement hydration, and the odd scrap of oil & gas refining trivia my chemical engineer colleagues have let drop. Thank you for publishing some entertaining stuff even the laymen like me can appreciate!

51Gunner

Glad to hear from nonchemists who like the site, I have to say. I think the oddest things I've wandered into are inorganic X-ray crystallography and some odd metal-organic complexes. I never thought either of those would come up, but you never know. Which means that there's no telling what the next oddity might be. . .

In the movie "Bourne Legacy" one of the characters goes through this process called: "viraled-out"

In the real world is there such a thing?

Can this be possible with Adderall? Can you somehow fix yourself permentally and not rely on using Adderall the rest of your life?

DeerSpotter

We definitely don't know enough to do this sort of thing yet, and I certainly wouldn't line up to be a test subject for the 1.0 version. All of the body's systems are tradeoffs - sleep, stamina, brain activity, reproduction, longevity, immune function, etc. There's only a certain amount of metabolic energy available to run all these things, and if you ramp one of them up, you run the risk of ramping something else down that you might have wanted to keep. To pick one example, it's going to be tricky to extend lifespan without also messing with the defenses the body has against cancerous cells.

So no, we know of no way to permanently change things in the way you're talking about, and especially not brain function.

Hi Derek, love your blog.

Was wondering about your take on *in silico* target identification and drug discovery. Do you think it is an area that has any potential for finding lead compounds? Or is it a waste of time and money?

eeyore102

It has, in general, been a waste of time and money over the years. But it doesn't have to remain that way, and you'd have to think that it's not going to. We keep learning more about the things we're trying to model, and we keep getting more and more powerful hardware and more capable software, so at some point it's going to be the way to go. But not yet. For years now, it's been "not yet".

What field in pharmaceuticals do you believe to be the most exciting to work in?

noahharrison64

I've always loved the very early-stage research, way out there, on things that no one has tried before (and that most people probably think is going to fail). There's plenty of that around in the business, fortunately (or unfortunately!)

What do you know about SARMs and the effect it has on the human body? I understand that there isn't much research for the drug used on humans, but is there anything you might know?

alexisloraine

There are actually a number of clinical programs going on with selective androgen receptor compounds. Interesting and tricky field, as are all the nuclear receptors. The same compound, in this area, can have completely different effects in different tissues, because the underlying mechanisms are complex and varied. The only way to straighten out what's really going to happen is in human trials, so we'll see what comes up!

Hey! What do you think is the biggest thing preventing us from developing new antibiotics?

SkepticShoc

Hard to pick one. Among the issues are that the need is greatest for gram-negative organisms, but those are really, really protected well from foreign molecules because of their complex and active cell membrane structure. Another problem is that it's very hard to come up with new mechanisms - most of the natural products we find hit the same pathways that others have already hit before, and attempts to expand the repertoire (and I've been on some of those projects) have not worked out.

Hi Derek, thanks for the AMA!

How do you feel about data science in pharma?

Where do you think it can help the most? Discovery/reg/marketing/patient data etc? Are there any other helpful resources you could point me to? Thanks again

outchecksnameuser

I think that digging through the huge piles of clinical data is the first thing, and the one that's most likely to have an impact. Second would be dealing with high-content assays back in the discovery phase of things. This isn't quite my field, though, so I hope that someone else has some resources to offer!

Aaaaaaaaah you're seriously one of my favorite bloggers on the entire internet, and on par with Elise the Great's End of Shift Report. I don't always know what's going on, but you explain things so evocatively and beautifully that I get at least the gist of it. Thank you for your "Things I Won't Work With" and "How Not To Do It".

RedMadeline

Thanks! I always enjoy reading stuff that gives me sort of a tour into another person's work and thinking, and that's what I try to do as well.

Hello Derek and thank you for your time.

Do you think that any cancer cures will ever see the light of day or will treatment rule the day as it is more profitable. What are the ethical implications of pharmaceutical companies hiding research to increase profits? Do you feel this is standard practice?

Thank you.

Unusual_wookie_hobo

Absolutely! The drugs that have come along so far, in many cases, were hoped-for cures that didn't work as well as people thought. A cure would be vastly profitable, so there's no incentive not to find one. After all, almost all cancer treatments eventually wear down because of resistance developing, whereas a cure would be for life.

Could you explain what you mean by "hiding research to increase profits"? We have to patent things in order to own them and make money off them, and patents have to disclose the invention, and provide the means to reproduce it, or they're invalid.

Do you feel that CBD oil and cannabis deserve to be marked as schedule 1 drugs?As far as my research goes I haven't found what traits qualified them to be marked as such, any information would be much appreciated!

bkscrambob74

As long as they're being used for their psychoactive effects, it's going to be hard to change their regulatory status - at lest that's my take on it. The standard reply is "Well, alcohol", and while that's correct, it's not an answer that leads anywhere in the real world. . .

In what capacity are Pharmacists utilized during the research process, if at all?

tekn1k_

Hardly even, in my own experience. But I've been working up at the very early stages of research, and as you get closer to the clinic, pharmacists would have a better chance of being encountered.

Hi, Derek, big fan of the blog!

Have you ever thought about food blogging (more often than your 1/year holiday food posts)? I would really enjoy stories about your cooking adventures written as well as your medchem content!

A_S00

That seems to be a lot more crowded field than blogging about chemistry and drug research, but probably more lucrative, too. I'll keep it in mind as a possible sideline!

Hey Derek! What could we in the United States do to effectively lower costs of medication? Legislation of some kind? IS there any realistic way of helping to take the gouging out of phrama drugs?

Also, do you think the cost of drugs in the U.S. is higher than other countries, and if so, does it give us "better" medical intervention outcome success drug-wise?

piggydog

The cost here is definitely higher - and that's why the cost in other countries is lower. I think those two are definitely and closely related. As for pricing in general, let me recommend Jack Scannell's take to

you: https://www.forbes.com/sites/matthewherper/2015/10/13/four-reasons-drugs-are-expensive-of-which-two-are-false/#15ddea024c3b

What is your process for efficiently scanning the current literature for material worth blogging about?

rhizome_at_home

Partly I go through a customized RSS feed of journal abstracts, but I periodically get behind on that one. And I also cheat a bit, because a lot of people email with interesting papers, so there's a crowdsourcing effect going on that I very much appreciate.

Hi Derick, just wanted to say hi, I remember reading your blog in grad school some 10+ years ago (is that right?) Glad to see you are here.

gibbie99

Thanks! I started blogging in 2002, so there could be people who started reading me in high school who have now finished their PhDs. Sheesh.

Hi Derek! Thank you so much for your time and dedication. I've loved your blog for a long time.

In an answer to a previous question, you discuss the process of finding new medications. Another answer goes into other details about the process.

With drug discovery being so costly and so high risk, does the industry leverage any sort of machine learning assistance in reducing costs/risks? I am particularly interested in potential uses of multi-armed (MAB) and continuously-armed bandit (CAB) algorithms, the latter of which might allow researchers to find the right dose range in fewer trials than traditional experiment design, for instance. (I've developed probability matching CAB algorithms and had success in using them in other industry problems, hence my interest).

BeardlessNeckbeard

That's out of my expertise, but I think that there's a lot of room for improvement in trial design. That said, though, there's a lot of room to screw things up terribly there, too, and a lot of careful regulatory work that has to be done before you start changing things. The FDA has an effort going on to look at new trial procedures, though.

How does pure cbd (cbd distillate) factor into the future of pharmaceuticals?

I know many chronic illnesses can be treated this way such as epilepsy, migraines, and opiate withdrawal.

When is this medicine going to be available and accepted by the general medical community?

whitekanye

You're not going to like this answer much, but I haven't seen any hard data on this that have impressed me. I know that there are a lot of cannabis fans who talk up its uses against these diseases and more, but pharmacologically, the stuff's not as interesting to people who've worked a lot in the field. A lot of plant extracts do a lot of things.

How often do you get confused with Derek Lowe, the ex-MLB pitcher? Have you ever watched him play or had someone ask you to autograph a baseball, or something?

sprite_n_halo

I did have someone email me a few years ago wanting me to autograph a 2004 World Series ball. I told him that he really didn't want me to do that. Besides, I'm a Cardinal fan!

When are you bringing back "Things I won't work with?"

pandemik

I have a few entires saved for the book, but I keep my eyes open for worthy candidates! It gets harder, though, since some of the best ones have already been used. I am always open for nominations, though, that's for sure.

Hi Derek! You are the author of the oldest science blog, so I ask you how is the internet changing for communications? What do you think about Medium? It seems to me that Medium will sostitute the blog.

Tuco_91

Medium has a lot of good stuff on it, and it's a good platform for longer pieces. For shorter, more frequently updated things, though, I think the blog format occupies a good spot between Twitter and Medium.

I'm an ethical daytrader, can you give me any insight into the biopharma world that may make me money in the future?

LazyOldPervert

Hah! Good luck to you, is all I can say. The publicly available information in this business is often of poor quality, and even when it's good stuff is often insufficient to make good decisions. Investing in individual biopharma stocks is best done only with money you can afford to lose.

Hello there sir, I'm a bit late to the party but hopefully you see this! Thanks for doing the AMA firstly. Second, my question is, because it is 4/20, where do you stand on marijuana and the legalization of recreational use, as well as it's aspects and benefits for those who need it for a sickness or condition like cancer, PTSD, Chronic Pain, etc.

dpmallon122092

Looks like the world is heading your way, considering the number of states in the US who are loosening regulations in that area. I'm a poor candidate for asking about recreational use, though, because I use no recreational drugs whatsoever (not even alcohol). Medicinally, I think it does have uses for pain, nausea, etc.

What do you think about B17 (Laetrile)?

occultcry

Unfortunately, I think it's basically useless. I've never seen any evidence to convince me otherwise. Sorry!