Interview with Kevin Chen of Hyasynth Bio

Completed via email

1. What is your experience with synbio?

   As much as I can of many different things. I'm mostly experience in metabolic engineering with yeast from my work at Hyasynth, although my role is more in business than in science.

2. Where are you from, what is your education, story? (quick bio)

   I grew up in Ottawa, went to school at Queens for biochemistry, and then dropped out of grad school to start Hyasynth.

3. Tell us about Hyasynth Bio.

   Hyasynth is creating the future supply chain for the Cannabis industry by producing cannabinoids using engineered yeast instead of growing plants.

4. What is your role at Hyasynth?

   CEO

5. How did you come to be there?

   Lots of hard work.

6. What were the challenges bringing your project with respect to synthetic biology to the market? How did you overcome them?

   We're still on our way to market. A big part of the challenge is being able to manage the amount of time and risk involved to develop and validate the technology. I suppose I could write a whole book on all the different challenges we've been through, but perhaps my experience is summed up by a statement like this: In our field, there are challenges which cannot be solved by an amount of resources, money or time that a person can give a definition or a prediction to. Most challenges in other fields can be solved or have already been solved in different contexts, which make them easier for people to understand and to invest in. As researchers and scientists, we are attempting to overcome or understand the hard challenges which are potentially unsolvable. Aside from those, I feel like the greatest challenge for most scientists is communication.

7. What were the first few months of starting the company like? Funding, employees, etc...

   We had a tiny amount of money and 4 cofounders. It was chaotic, and stressful, but also very fun.

8. Are there other companies synthesizing cannabinoids? How do they differ?

   There are lots of people looking at this area, all with different teams and strategies to approach the problem. In our case, we have a great and motivated core team, veteran advisors, and strategic partners.

9. What is your experience with Synbio and public perception?

   I've been doing this kind of work since I did iGEM back in 2011. Synbio is still a very new topic for lots of people, and I'm excited to see what happens next.

10. What is your experience with Synbio and the government? What process did Hysasynth have to undertake regarding policy and legislation?

    Hyasynth needed permits to work with cannabinoids and we went through the process of getting those permits. Afterwards, we kept making submissions to public calls from the

government with regards to cannabis legislation, and one of the outcomes of that is the updated definition of Cannabis in 2018. The new definition includes cannabinoids that we make in the same regulation as the cannabis plant, which is important for giving us clarity and a route to market.

11. What were the challenges of scaling your product to bring it to market?
    We're still on our way, but getting really close. A lot of our go-to-market challenges can be addressed with the help of our advisors and strategic partners.
12. Do you involve ethics in your research & development?
    In some ways, yes, but this will be a more important topic as we bring products to market and refine our overall strategy.
13. What made you believe your iGEM project would become a successful career?
    Ha, do I have a successful career already?
14. Do you have any notable stories involving collaboration?
    Probably the biggest one was our relationship with Organigram. They're there to support us all the way to market and were the first ones to seriously invest towards a technology like ours.
15. Any wearable biosensors that stand out in your mind? What are their strengths or weaknesses?
    I only know of things that are kind of on their way to market or new technologies, unless you consider smartwatches and fitness sensors as biosensors. Either way, I don't know if there are any mass market wearable sensors that get into molecular detection. There certainly aren't any for regular consumers.
16. What is your knowledge of the opioid crisis? Of fentanyl?
    It's pretty extreme, and an issue that needs to be addressed. An interesting case is the effect cannabis is having on opioid use in a lot of patients. But, it's surprising how bad things got without further action. I wish the companies that helped fuel the crisis did more to avoid it.
17. How are you inspired as part of a team or how do you inspire a team?
    Clarity in ownership and goal setting is important. We're here to make something real, and use synbio to revolutionize the Cannabis industry.
18. What is your favorite non-science related activity?
    Circus arts – juggling specifically. It's a hobby I've had for a long time, but it's a great one for fun and it's a great community to be a part of.

Quantifen

Our Project Description:

We are designing a non-invasive wearable biosensor for fentanyl detection in sweat. Imagine a Fitbit-inspired design for fentanyl monitoring. We aim at harm reduction and safe drug use with the use of our monitoring device. We recognize this is not a solution to the opioid crisis but potentially a tool in

accidental overdose reduction as many recreational drugs, such as MDMA or cocaine, are laced with this deadly opioid. The genetic system is currently in yeast, but aims to be cell-free for distribution and environmental concerns.

A small electric current delivers sweat-inducing drugs which creates an electro-osmotic flow in the skin, uptaking small molecules into a hydrogel. If fentanyl is present, it binds to our biosensor inducing expression of glucose oxidase or amilCP (chromoprotein). AmilCP when expressed changes the hydrogel to blue, visually, yet discreetly (the gel is under the device) showing fentanyl presence as a visual aid for emergency responders if the wearer is incapacitated. The enzyme glucose oxidase binds to glucose already present in the hydrogel and produces hydrogen peroxide. Hydrogen peroxide reacts with Prussian Blue ink through a reduction oxidation reaction, creating current. Current is carried to our PCB where the signal is transferred to the user's cellular device.

In the App presets are able to notify a close friend via text message or a group such as PLURI (party-safe groups present at events such as electronic music festivals) who would have Naloxone or Narcan on site. Naloxone or Narcan are an injection or nasal spray which can delay the effects of an opioid overdose for 3-4 minutes when administered, long enough to allow emergency services to arrive.

Data collected is protected by privacy and consent measures to ensure the privacy of the user is maintained, especially as they are consuming illicit drugs.

Our customer base is primarily recreational drugs users with viable income and organisation skills. Through interviewing medical professionals and addiction centers we also found a customer base in rehabilitation centers where a patient/ doctor agreement would allow for monitoring of the patient while in recovery as relapses often occur, but could occur more safely, as well as collect data.

An aspect we are especially excited about it the modularity of the device. The biosensor can be adapted for a tremendous variety of small molecules such as cortisol. Therefore the monitoring device could have a multi-gel which not only detected fentanyl but cortisol or estrogen at the same time.The gels are designed to be disposable, durable and interchangeable.

See supplementary figures below.

19. Do you have any insight or opinion on our current design?

    It's still very early, of course, so there's probably some insight from manufacturing and also real-life use cases that would improve the design. Some questions that seem like might be missing are like how durable is it? Who would use it and why would this person use it? How would people find out about it? Who would pay for it? Another important question from the real world is whether or not a biosensor is necessary for this approach or if a chemical or electronic sensor of some kind might be possible as well. FredSense is a company that got started from iGEM Calgary that did environmental biosensors. Their story is a great inspiration for biosensor development.

20. How would we go about taking our project to market? Estimated cost of production.

    Make a prototype, show that it works, and then check any regulatory clearances you need to sell it. I'm not sure what standards are required for drug testing kits (if any). But you might be looking at a similar business model. A big question for a lot of companies in synbio is: Who will pay for the technology? Will be a government or insurance like in many healthcare products? Direct to consumer? Or perhaps you're selling a specific

person in the chain of events related to a fentanyl overdose? (ie: friends/family members of drug users? Or perhaps even drug dealers themselves?) I've seen quite a few startups with great ideas like this that struggle with this question. Lots of the hold up and where startups fail are in understanding this overall timeline.

21. Anything else you have to say regarding iGEM (any advice!)

    Have fun! Be bold and ambitious! Meet lots of people! This is a rare chance to have almost completely freedom and creativity with your scientific work. Everyone loves to see that crazy shit you come up with, and not so much you filling up a rubric. Also, here is a quick list of things that someone should do (I regret not doing these things after I finished my iGEM tour):

    i. Thank your instructors and funders with a recap presentation, cards and with swag. (This is also your chance to ask them for more funding next year! Give good reasons why they should give you more money! – especially if you didn't get gold this time.)
    ii. Do iGEM again! Probably many of you are pretty burnt out, but in my time at Queen's we always had at least one repeat attendee.

22. Anything else you have to say to a group of undergraduates (any advice!)

    Don't let the academic world drain your soul. Being a student is fun, and easy (compared to my job), it's also a good time to try strange ideas and test yourself. Starting Hyasynth was a personal experiment which seems to be working out so far. Aside from all my other reasons for starting this company, one of the big ones was also that I dared myself to do it.

23. Anything else you have to say to anyone wanting to start a business (any advice!)

    Try it. If it doesn't work, stop, and go back to school, or work, or whatever. Maybe find a group of friends and start two companies at the same time, and then watch each other's progress. That's kind of what my first experience was like in a startup accelerator. Once you seriously start something, you will learn everything you need to know very quickly and you'll also very quickly find out if it's something you really want to do. If it doesn't work out, you'll already have learned a lot and whatever you do next will be easy.

24. A quote (if you have one)

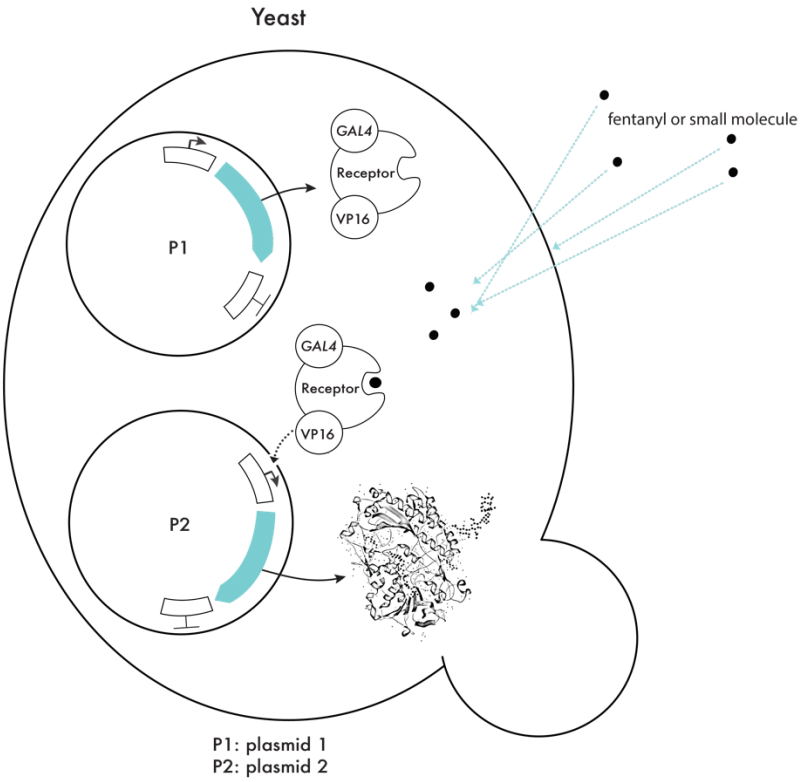
    From me? Or from someone else? Perhaps there's something wrong with how we have been interpreting the saying "Look before you leap". From my personal experience, and from history, I think we'll find that the "looking" part might be far less important, and also not practiced as often as one would think, than the "leaping" part and we, as already well-educated and great scientists, should "leap" more often. I think far too few of us do. Maybe that's vague and insightful enough to be a quote.

Thank you for your participation and feedback at the mini Jamboree and for taking the time for this interview.

All the best,
Lancia & iGEM Concordia

IGEM CONCORDIA 2019

Supplementary Figures



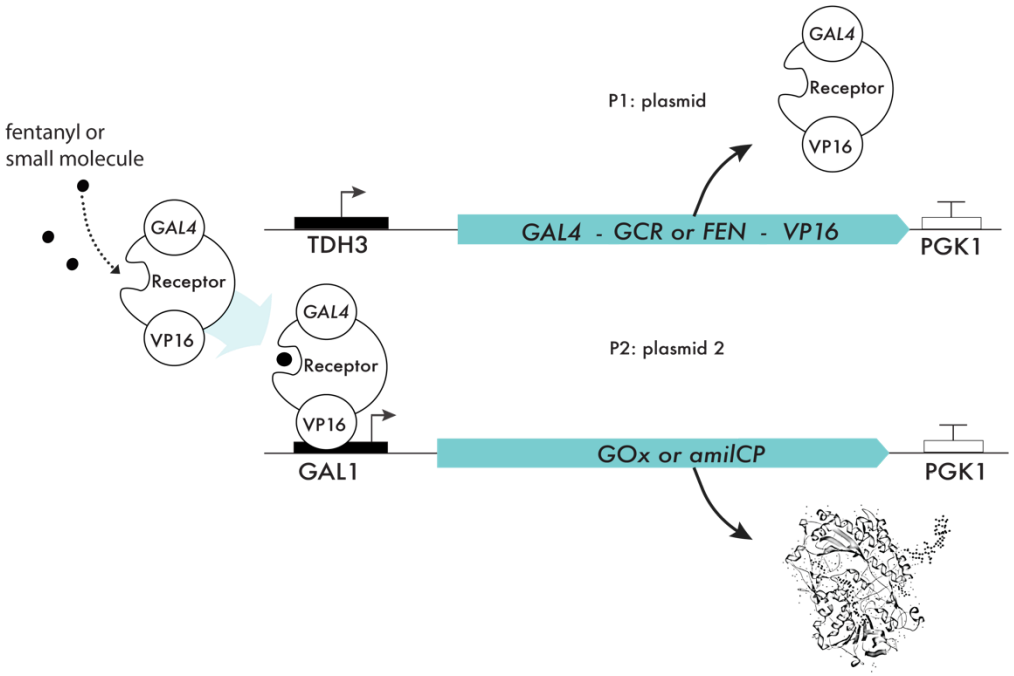


Fig. 1&2 Plasmid 1 constitutively produces our receptor. The receptor, when bound to fentanyl, binds to plasmid 2 inducing expression of glucose oxidase or chromoprotein.

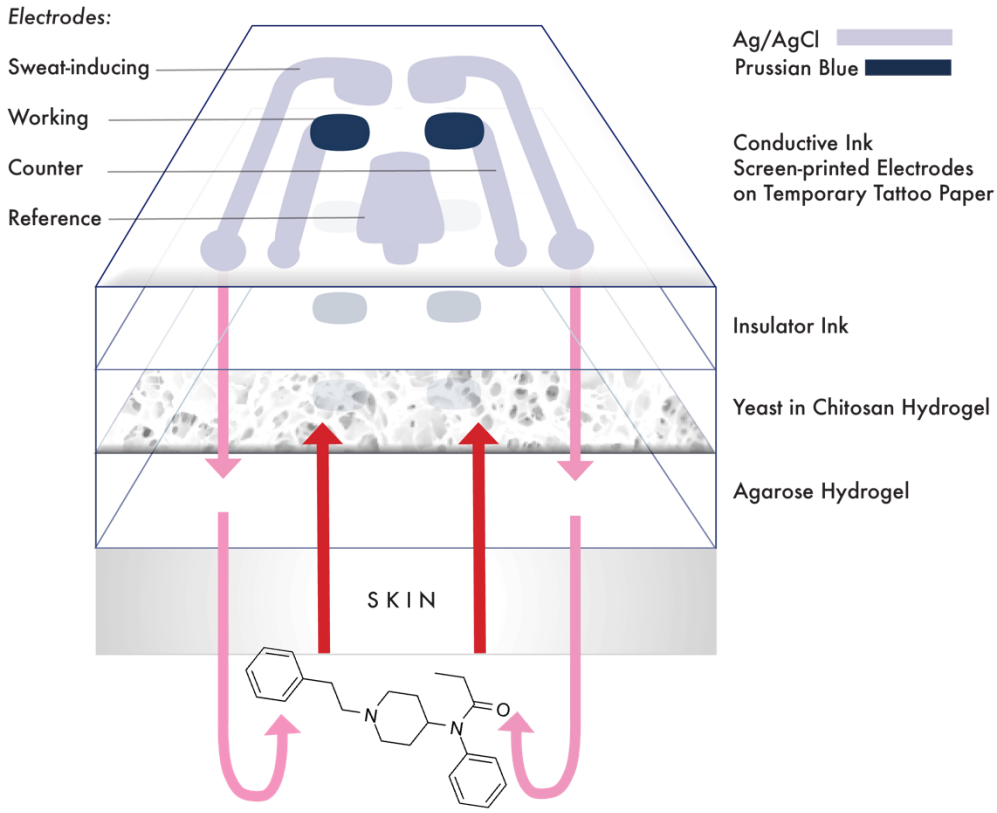


Fig. 3. Electro-osmotic flow induced by sweat-inducing electrodes creates uptake of small molecules into the hydrogel. Thickness of layers approximately 0.2mm.

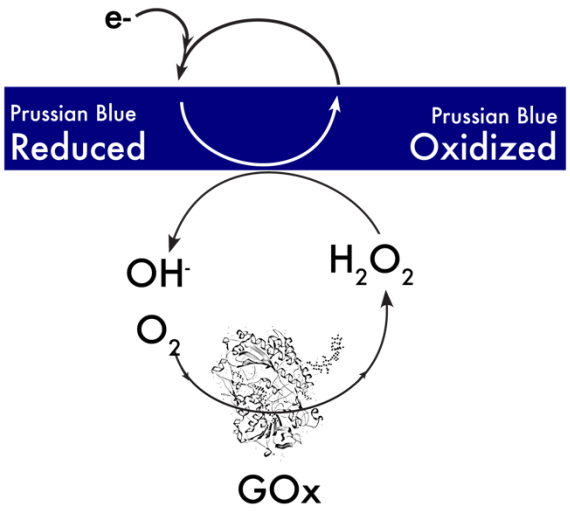


Fig. 4. Reaction of expressed glucose oxidase (GOx) bound to glucose results in the oxidation of Prussian Blue. Current is created by electron flow.

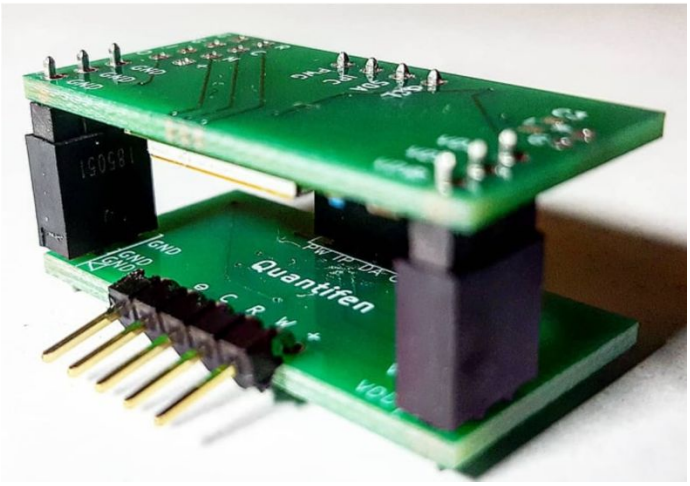


Fig. 5. The PCB (printed circuit board), 36mm x 18mm.
Electrons from the reduction-oxidation reaction caused by glucose oxidase are carried by conductive inks to the PCB which sends the signal to the user's smartphone or induces a signal in the device itself such as a strobe light or tightening of the band (in the case where the user is high or drunk and not organised enough to be aware of their smart phone).

LOL