iGEM 2019 Concordia

PostDocFellowship Concordia. Working on an opioid biosensor in yeast
Interviewed by Lancia Lefebvre

Lancia
In general, what is your opinion about the opioid crisis?

Post-Doctorate Fellowship
I think it's pretty tragic what's happening. Think it's a rough combination of prescription opioids and ease of access coming from the absolute prohibition in general. Lack of things like safe injection sites and other care facilities.

Tell us about the project in the Martin lab where opioids are being synthesized in yeast.

I haven't been part of that specific project the group here hasn't synthesized any opioids, at least yet, but they've produced high levels of precursors for those opioids. We've had something like five to 10 more steps to get to opioids. But right now the production strain that we have has stopped at the last non-controlled substance which is reticuline.

What are you working on?

I'm working on developing an opioid biosensor to help in the production of opioids in yeast and also to try and screen for other compounds that could similarly bind to opioid receptors and might have more of the. analgesic effects without the euphoric effects to help with the mass potential of addiction.

Has this been a challenge to do this research in Canada?

For my project, it hasn't been too much of an issue.
You do have to have a controlled substances permit to be able to test any opioids with a biosensor, with regards to the production strains there it is more of an issue. Obviously there's a reason why the project's kind of stopping at this stage and I guess the next few steps down the line is to thebaine which is a non controlled substance in some other countries, like Denmark but is controlled in Canada and now with the levels of production that's going on in the yeast stream you would actually need to get a production license to be able to do that research even though we're not really considering producing opioids in this lab per se.

You mentioned that you want to you are currently developing a biosensor. Do you think there are different ways that this biosensor could be used in society in general, in your opinion?

The two main reasons for developing this biosensor as I've already mentioned are developing the yeast strains to produce opioids and also to screen for other compounds that could have analgesic effects similar to opioids. I think because the biosensor I'm using is a yeast-based biosensor it's not exactly going to be the fastest or most effective way to check for opioids in samples and that sort of thing I think that will still be mass spec-based or using other biosensor platforms.

You mentioned other biosensor platforms do you have any other examples of what that might be?

One example is finding proteins that are capable of binding compounds and measuring the change in electrical potential. Trying to make a faster readout by hooking up biological systems to a chip.

Have we told you a bit about the project we're working on right.now?

I vaguely know what you guys are working on but you haven't told me.

We're kind of working on a biosensor based in yeast that would detect fentanyl in a chitosan patch. This would detect fentanyl which is 100 times stronger than morphine and prevent or warn people that they are in danger of overdosing. It is connected to an electrical system that would send a message to either people around you or to the authorities or someone with a Naloxone kit available to help.
What's your opinion on the project?

It's interesting. I guess some questions I would have around how fentanyl will be distributed throughout the body. If it's possible that you'll get a spike if it just happens to go down…Say somebody is injecting the opioid and it's going to pass down that artery, capillary structure that's going to be detected by the biosensor in advance. Will you get a false positive there before the opioid has been entirely distributed through the body? Another question I have is with respect to how fast you can respond to that biosensor signal and how fast that biosensors signal would be itself. I'm not sure how you're making the biosensor, what's the readout that you'd have?

We are not sure about the concentrations yet.
We have two plasmids, one constitutively on producing a transcription factor which then binds to fentanyl and then expresses GOx which then undergoes a redox reaction sending a signal to the chip.
We are modelling it, but we're not at the speed we need for detection and generally, there are very low concentrations in sweat.

Do you know what the timeline is from injecting too much fentanyl to...

Because drugs are laced with it we're looking more at use where people would be doing cocaine or ecstasy and then they don't know that there is fentanyl in their drugs so they accidentally overdose. We're hoping to detect it before it even reaches overdose levels.
It detects fentanyl in your system so you would know, hopefully before you take in too much.

Yeah makes sense. And then. If that's the case would you consider linking that to an auto-administering Naloxone system?

Somebody else brought it up in a new interview. That it could be possible.
It could work but we are not too sure. What did he say? It's like an EpiPen, the addictions counsellor were saying depending how much you've taken that they almost administer two doses of Naloxone.
That's quite a lot of drugs to put in a small system. But most places have a Naloxone on location like at the bar or at the club. I think it was like one to one hundred micrograms per litre is what we're expecting in sweat for fentanyl.

My other question has to do with the longevity of the biosensor be maintained. How would you changing them on the weekly basis because it is a living system?

It's supposed to be cell-free eventually… On a side note, does yeast uptake fentanyl? Do you know anything about that?

I think to some extent opioids can permeate. Hi there. I'm not sure to what extent. It seems quite possible.

The idea is that it is like a Fitbit and you would switch out the patches, replacing them. We are hoping for a minimum of six hours of wearability.

How would you contain the cell-free?

In the hydrogel, dehydrated and then it rehydrates. Currently, it's in frozen storage and then it's rehydrated by sweat.

Ok

Are there any changes to the face of our product. But I think you've already answered that question. Is there anything else you'd like to add concerning our approach our design, the ethics or in general?

I guess you'd have to look at the population of people that would be most susceptible to opioid overdoses. And what their behavioural pattern would be. I'm not 100 percent sure what the uptake of a product like this would be like. If they're actual addicts I'm not convinced they would have a Fitbit- type electric product already. That would become a pretty big barrier to entry. You know, economically to try and get most people in this at risk population to have some sort of detector like this. That would be one of my concerns about it.

What are you making your biosensor for? Detection or a new analgesic?

Detection. In terms of making a very fast assay for the people developing opiate production strain. Because right now I think that method is about 15 minutes per sample. To analyze the amount of opioids that are in this class of compounds that are called benzophenylaniline alkaloids. To analyze the production of these alkaloids it takes about 15 minutes. And if you have hundreds of samples that's very quickly going to be days worth of time. The liquid chromatography, mass spec downstairs. To accelerate that it's one of the main reasons to work on it.
And then also I think more exciting is the possibility of screening small molecule libraries very quickly. So not sure if you guys are aware of the existence of these libraries. So there are a bunch of different ones out there. Pharmaceutical companies often have these libraries of tens if not hundreds of thousands of small molecules that have either been tested for things before or haven't been tested. And then other groups are finding small molecules and isolating them from a whole bunch of different wildlife.
At UBC there's one group that goes out and collects up from sponges and coral reefs and that's their thing. To just try and store them and then if you have a good assay for, say inactivation of an enzyme, you can put all of these molecules through this assay to see if any of them have that quality that you're looking for. In this case, it would be binding to an opioid receptor. And depending on how that interaction takes place you could have something that kills the pain but does it in a less addictive way.

We have a new project every year. Do you have any suggestions for when the new team starts to choose a new project? Twelve undergraduates from all over the place that don't necessarily know what synthetic biology is.

Trying to keep things simple and manageable is quite a good idea.
Like, in this case, I'm sure you guys are running into issues like you won’t be able to make a biosensor for fentanyl here, because then you'd have to have fentanyl to test with. Which is fine because it'll be a proof of concept project but it could be cool to think about working on a project that you can pursue to that final point that could be interesting. And to some extent, an interesting area that I think synthetic biology has yet to fully expand into is biological remediation.

Trying to find pathways to break down some compound that is difficult to break down that can be an interesting area to look into in the future.