

08.01.2018

Location: zoom

Present: Anthony, Michael, Thomas, Maria, Alex, Winnie

- The HPLC in CCL is about to work
- Michael and Eddy tried to reproduce Yann's work on yeast. Didn't quite work out. They do need to run a gel
- Maria is doing a workshop on making antibodies with hybridomas
- Oskar Laur makes constructs. Put enough in for us, too, possibly in two weeks.

27.11.2017

Location: zoom

Present: Anthony, Michael, Winnie

- Anthony and Winnie were in Milan. The most concrete outcome was a group in Senegal that wants to start up. Macoumba is setting it up. They seem capable.
- Lucia can help us with putting together a group of government officials from Milan that can help us put together a strategy on how to involve the government.
- For patient cooperative we can frame it as a blockchain project and get access to a large pot of funding through the European Commission.

02.10.2017

Location: Zoom

Present: Anthony, Alex, Winnie

Anthony: continue to consider gene therapy possibilities. Signed letter of intent with ligandell (?) folks (gene therapy delivery vehicle). Bill Liao invested in a company with a delivery vehicle of genes, will get in touch.

Oakland yeast: about to design own strain.

Also working on long acting strain from Biocon. Duplicate work, but also do it in *S. cerevisiae* to duplicate human insulin pathways for expression & mod of insulin, to just mimic in vivo.

They will address legal problems by making a strain themselves. Josiah has them covered, has done it before.

Jim Wilkins: got it from graduate institute under restrictive MTA. Didn't allow to share officially (he's working on it in our space). He's taking the strain to go with it as it is -> incubator space. Does he still want to be affiliated with Open Insulin? Anthony will figure it out. Else they need to stop working on it.

As multiple opportunities for research open up, so does the partition of work among global groups.

We need a Code of honour or something similar. What do want to do? What are our shared values? Each group has autonomy. Idea of a commons of projects, where you share within the commons and you gain admission by agreeing to share openly within that group or other groups that hold the same principles or are economically compatible with what we do. Like a P2P patent pool.

Another idea: manufacturing efforts. Try to set it up as patient owned and managed cooperatives. Invest time, dividends from owning the factories and buying the product.

Misalignment of incentives. Drug companies: take money from patients, who needs medicine. But patients want a cure, more R&D for better treatment. But in the end the company invests in marketing and approvals, ... We want to put the decision power in the hands of the patients -> more competitive market (patients are happy w 100% profit instead of 10000%).

Anthony and Winnie will be travelling to Milano in November to spread the idea. Italy: discourse around city and regional autonomy. Compatible with how we see the scaling. Naples has already started to do this type of thing with water, control over their utilities.

Alex: gone back to updating plasmids. They have to rush to finish everything before the iGem deadline.

21.08.2017

Noel will need large network of people doing lab work. Lots of constructs. Wants to attend the opencare workshop.

Work on paper for nature biotech on microproduction.

07.08.2017

CCL is exploring the yeast route.

New team member: Nathan. Igor works on strain 1244 Yann on strain 1245 and Nathan on 1246. Three strains from Jim Wilkins. Non-IP strains of yeast. Pichia Pastorus.

Equipment problems. HPLC is down. They have 1,5. So not really rolling at the speed they were.

Papers? On the Drive.

https://drive.google.com/drive/u/0/folders/0B_51GdQ-X3JzbFE2WXZVSV9xY1E

Pichia for Jim Wilkins as expert. A lot of success with that strain.

New strains for discovery. Anything to produce insulin non protected by IP.
No more gfp in the yeast. Was in E. coli for demonstration purposes.
Yeast: A and B chain, no more C chain.

Sydney doing human insulin
Second is thermostable. But on patent. Other one is chimera of 10 different animals.
Famous guy written big report on insulin market. David Henry Beran.

10.07.2017

Confirm yeast proinsulin in two out of three strains. Not good for scale-up, but by the end of the year they should have a fancy construct.

Next up is open source part, maybe gene therapy? Nothing will adequately replace the body's ability to regulate blood sugar levels.

Low cost & generic, eliminate profits -> perverse incentive to ignore a cure disappears. Chronic treatment will be less lucrative.

Gene therapy: animal studies are pretty far along. Eg. 8 year study on dogs went well: gene therapy was perfect, dogs were perfectly healthy.

Basically, there are two therapies that look promising. One is the dog study: glucokinase gene in skeletal muscle. Will transport glucose into the cell on a concentration dependant manner. No transmitter molecule trigger, but automatically when concentration drops.

Another was adding insulin gene to liver cell in mice. Under promotor tied into glucokinase pathway. When high blood glucose is detected -> insulin expression turned on at a high rate. Expression stops fairly quickly when concentration of glucose is reduced. Liver cells kind of act like the pancreatic cells should act. Enhancer of aldolase in the gene. Seems to work fine, though sometimes expression didn't go down fast enough.

Another thing, a bit less relevant to OS biotech. The main mechanism behind eye retina leaking is an inflammation enzyme. Key step in pathway that further inflames more and increasing permeability of blood vessels. This high concentration in glucose results in high enzyme activity. Highly correlated with diabetes. Some companies are already into this and developing drugs.

Reducing suffering of complications would be a good alternative, as gene therapy will be expensive. A low cost, simple molecule would be helpful.

An organic synthesis robot. No cell cultures etc., just organic chemistry. Make your chemical. A lot of things you can also do with small molecules (the same as with protein, but even stuff you can't do with a protein).

26.06.2017

Science going great in CCL. Moving to yeast actively, some results (*Pichia pectoris*). Did a gel and saw that they got proinsulin. They're working with 3 strains from a collaborator of Jim Wilkins (Fair Access Medicine). Will optimize now. They have 1 inducible strain, 1 constitutive, 1 both. For the easiest possible system they want to go towards an organism that secretes whole insulin straight away.

How to confirm the structure of insulin? Antibodies will suffice for an announcement within the next few months. Human receptors bound to a surface and measure binding activity.

Alex: iGem team is dedicated. They're also testing 9 different plasmids. Three kinds of insulin for periplasmic in *E. coli*, bacillus cytoplasmic and cytoplasmic in *E. coli*. One called Winsulin. Combo of 9 most similar mammalian insulin. Looked at homologous regions -> conserved. Complete chimera, no idea how it will work. Alex will be in Africa for the next weeks.

12.06.2017

CCL got the plasmid to Josiah to ship, it gets to us whenever customs feel like it.

They are starting with yeast work this week. They have someone who has gotten a yeast strain via connection. Three strains: one constitutively expressing & excreting, one inducible, third is both promoters. Now looking which one has best yield. The terms & agreement are that we can't transfer to other groups, though they will develop own strain of yeast. Fair Access Medicines. Jim Wilkins. Joined up with Open Insulin. Also helping in fixing the HPLC.

Groups in Biocurious are looking at microfluidics for diabetes and other types.

Winnie is meeting Claudio, a filmmaker who proposed to make a movie about Open Insulin, on Thursday. Another film maker in Miami was excited, but then disappeared. For her it was hard to get funding sorted out. We could pool resources for a movie. There's several people in the network who have similar ambitions. It takes multiple people anyway. We could introduce everyone to each other.

A lot of people come on to help, non-scientists, but they don't necessarily have organisational skills. We should have some sort of path for people to get involved in technical or organisational stuff.

Technical stuff: direct people's attention, curate educational material. Every minute should be relevant, not encounter friction. Not wade through irrelevant information.

Anthony doesn't know if there's primers on project management. A beginning resource to get started on things. They had a project manager who works @ Google. She moved on to another project after a few months. She did simple suggestions: coordinate schedule, running cultures more efficiently than even research labs. But it was hard to reconcile this with the usual chaos.

It went: you are PM, what should we do? "make spreadsheet, figure out how long everything takes." Elementary thing, being able to approach things from a certain mindset. Planning vs navigating chaos. Anthony's skill: good at navigating chaos. A combo with planning is best. But CCL always defaults to fostering chaos and navigating it.

Now biggest problem is ordering supplies. CCL doesn't have an account with suppliers, nowhere to receive packages. People nick it from their work, but this doesn't always work. Sometimes down for a month. Lots of logistics and navigating bureaucracy. Either suppliers don't really get what it is (even though they might be willing). Or they aren't willing to supply a non-profit.

Logistics take a long time. Sister space Biocurious does a better job though. More business minded people, because in Silicon Valley. More money, more organisational skills.

29.05.2017

Anthony: plasmids are ready to ship. Speaking with Josiah, maybe also the organisms.

Yeast-based protocols. Jim Wilkins (fair access medicine). They have an interesting strain in mind that's in an academic lab he knows. They will get it donated.

Alex has also been looking into it, although he doesn't have much more time to spend on new avenues of research/organisms, their effort gets spread too thinly.

Alex's updates: they're really happy with the many events of the last weeks. They're moving forward with an iGem team. They are about to start with their own plasmids.

Winnie's update

- Michiel, a postdoc in computational biology and machine learning is in touch with Noel for computation.

- Microfluidics group getting together, hackathon in start of July. First building one, then during the hackathon working with the organisms hopefully.
- Some hiccups with the BL2 lab, as we're limited by this. It makes it harder for us to start with practical things. Looking into the options.
- I've noticed that I'm not the most technically skilled in our team. These meetings are kind of technical, which makes them very interesting, so it would be a shame for me to be the bottleneck. How do we cooperate more effectively, github style, so that people are better up-to-date with each other? Is there a precedent for this? Can we put someone on this? Consensus: we can find someone or each put someone on it. As it stands we do not have the capacity to invest much, but there are some people who might be into it.

17.04.2017

Anthony

Last round of lab work for the next weeks

Mixture of protein attached to Insulin, gfp. Problems with column, they tried to fix it. They have one band that is the right size, which is encouraging. Now troubleshooting. Thinking how to move to production, so revising construct for better process and higher yield. They have a band for 40kDA (gfp-proI), but also the 30kDA. Protease inhibitor to help during lysis: many proteases around in the cell.

Two phders joined, so there's more talent in the project now.

Still need to check on Ile and The ODIN for shipping.

We should have good yields of gfp prol few days after receiving samples

The people who work at companies aren't particularly interested. It's a bit of coincidence. They will have a HPLC in the future soon.

More formulation patented than production method. Vector is PET22b. Gfp might be as well.

Make a blog post, ask others. To publish.

Rita: ask specific questions regarding the consumables and protocol.

03.04.2017

Location: Zoom

Present: Anthony (CCL), Michael (CCL), Alex (BioFoundry), Winnie (ReaGent)

Michael has taken an interest in producing insulin with transgenic plants.

Anthony has spoken to someone doing work with plants and insulin. She said it's interesting, but difficult. Because of long lifetime cycles of plants.

CCL is ready to ship through the ODIN of Josiah Zayner. Alex: he has shipped to Australia and Germany before. We just need to give them the address and it'll be on the way.

20.03.2017

Anthony (SF):

We need to digest the protein, we have pro insulin alone and isolated. Now we're trying out SDS page to separate it. Experimenting more with electrophoresis.

Alex (SYD): BioFoundry is getting lab work underway now. They've made a cool flow chart (on Draw.io, see BE Drive) detailing their process.

Alex thinks it's a good idea to modularize tasks to share work. Everyone can contribute where they can then.

They're collecting stuff from Alibaba to help their experiments and development of kits to support their own activities.

Alex would like infographics to visualize their data, it would help with communication. He likes both the idea of having separate social media channels and crosspost a lot. Still, he would also like an overarching open insulin blog and other channels that unifies everything.

Anthony has trouble with regular media updates, summarizing what they're doing. A modular media package would help a lot.

They can send us samples to get into the research faster.

Michael wants us to make clear how to collaborate. Local and global stuff need to be compatible.

Everyone:

Google drive is good for sharing. Facebook as frontend.

Alex: A lot of diabetes support groups on Facebook. We could generate content and interest.

Also put a focus on the people who cannot afford insulin.

Anthony mentioned Labarchives as a way for tracking data, but it wasn't clear to me what he meant.

Winnie mentioned the Edgeryders platform. He will send an invitation to Alex.

A discussion on what we are doing. Is it a social enterprise? A humanitarian effort?

Michael: End goal is communication. Eg. With the view of reaching a foundation like the Macarthur foundation.

Antony: small scale production. Allow local production for poor communities.

Winnie: citizen science proof of concept, humanitarian effort

Regulatory stuff. Alex did a write up on what is a biosimilar. It's quite complicated.

There are some OS alternatives in the diabetes sphere. Glucose monitoring. Alex knows. See also a popular media article, and some projects on Edgeryders.

Anthony shared some of their experiences locally. They have a talk by Jennifer Doudna, who is a local, to raise awareness for the project. She revolutionized biotech with her discovery of CRISPR-cas. Share events that we do locally with the group. Event outreach is a good way to do things.

We will Skype fortnightly. Involve people who are up to date. Belgium time is Monday at 7 am. Next call is April 3.