The Synthetic Biology Podcast

Episode 4: Rennos Fragkoudis, The Edinburgh Genome Foundry

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00:00 Stevie: Welcome to the Synthetic Biology Podcast brought to you by the UK Centre for Mammalian Synthetic Biology at the University of Edinburgh.

00:09 Stevie: In this episode, I talk to Dr Rennos Fragkoudis, Manager of the Edinburgh Genome Foundry - a research facility specialised in the assembly of DNA constructs. These are artificially constructed fragments of DNA that can be 'transplanted' into a target cell or tissue. These constructs contain a gene sequence of interest that can then be expressed in the host. Rennos explains how he, his team and some very impressive robots are involved in a diverse range of research projects from producing viral vectors for gene therapy to yeast based production of high value chemicals for healthcare products…

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00:52 Rennos: The Edinburgh Genome Foundry is a specialised research facility. We specialise in the assembly of large DNA fragments and to do that we use a highly automated platform. We have the ability to build large genetic constructs and we do that for both academic and industrial customers. Our customers are able to equip cells or even whole organisms with new or improved functions. It's a national facility, it's open access. We are supporting the construction of a large variety of constructs for different projects from viral vectors for gene therapy all the way to yeast based production of high value chemicals for consumer and healthcare products. The platform has recently been used to generate constructs that are used to develop novel assays for SARS Coronavirus 2 for the COVID pandemic. So as you can see we have a huge variety of things we can do and it can touch all sorts of science. That's the important thing that people need to realise is that the foundry can offer something to anyone who uses synthetic DNA and has complex constructs.

02:05 Stevie: So when you say 'highly automated' as well, I'm imagining a lot of robots...?

02:13 Rennos: Yeah, exactly. The heart of the platform is three robotic arms that are moving plates from one instrument to the other. These are routinely found in the automotive industry, so it's the same type but their fingers are a bit different, they are specialised to handle multi-well plates. But these are not the only robots we have in the foundry. We have also robots around them that do a lot of the basic work that scientists do in a molecular lab using pipettes.

02:46 Stevie: Yeah, it's really interesting and I can imagine it speeds up the process a lot as well. Having done a lot of pipetting in my PhD [laughs] I wouldn't want to do it on an industrial scale.

03:00 Rennos: No. That's exactly one of the things that the foundry does very very well. So to give you an example, a very good post-doc would probably produce two plates per week

– so this is two 96 well plates per week of constructs. The way that the foundry is working at the moment, we are able to produce approximately 10 plates per week. We use a combination of the robots with, we have 2 or 3 members of staff. But we can switch to a fully automated schedule and that would allow us to do 20 or more plates per week. So you can quickly see how you are going from 192 constructs in a week that a postdoc can do to something like 1920 constructs per week if you have the platform running fully automated.

03:52 Stevie: Absolutely, and I guess it frees up the postdoc as well or technicians or whoever would normally be doing the lab work, it frees them up to work on other things that, I guess, the robots can't do.

04:06 Rennos: Exactly. A lot of the process that we do in the foundry are very time consuming and very repetitive and the problem that comes with time consuming and repetitive is that the person doing the work will get bored and its where mistakes can happen. Whereas the robots, if you program them appropriately from the beginning, I'm not saying the possibility of a mistake is completely eliminated but it is reduced by orders of magnitude. This is still science so things can go wrong and we have to be there and we have to be able to troubleshoot all these things. I have a team of people, they are all exceptional, in collaboration with other members of the team, if there are problems we are troubling shooting them and trying to find the best ways to do that.

04:51 Stevie: You mentioned it a bit earlier but I just wanted to go into a bit more detail about these constructs, so what exactly you are producing in these plates.

05:03 Rennos: Initially, the customer comes to us with an idea so we have a phase which we call product validation so in this phase we are going to look into is the project feasible, can we do it? And can we do it in the timeframe that the customer wants us to do it. If yes, then the customer will provide us with a design that they have in mind or if they just have the idea then we are helping our customers with the design as well. Once this is completed and we have agreed on the design and designed the constructs – to do that, something we are very proud of in the foundry is the high capacity we have for computational biology. So we have dedicated software that is specialised to design constructs, simulate constructs, make sure that the different parts that are needed to assemble the constructs are working optimally with each other, optimise the different constructs for expression in difference organisms. So once all this is done, we are ordering the DNA parts. A common misconception about the foundry is that we are synthesising DNA. We do not synthesise DNA, we assemble DNA. So we are ordering our parts from commercial suppliers and once these are delivered to us we assemble and QC the constructs on our automated platform. DNA assembly is not the only thing the foundry can do. We can miniaturise reactions. So when you do a PCR reaction in your lab normally it's a 10 or 20 microlitre reaction, we can do that in 0.5-1 microlitre. This is something that especially in times like we are experiencing right now with the pandemic, we have a severe shortage in supplies – this includes pipette tips, plates and things like that. By miniaturising reactions we can use less plates, we are able to reduce the volume of reagents and as reagents are quite expensive you can make a significant saving for the researcher. We are expanding our operation to include much more phenotypes. We already have some in our facility so we can do microfermentations, we have a system called the BioLector. We have a plate reader that can do time courses,

measuring optical density or fluorescence and we can do quantitative PCR and obviously all this pipetting is done using our liquid handling so robots can be used for that.

07:45 Stevie: So just to jump back quickly to clarify on the phenotyping that is just a case of you've made these constructs so now you're testing them in action.

07:59 Rennos: Yeah so you put them for example, at the moment we don't have the capability to do mammalian cells because our platform doesn't have sterility but that is something we are working on, to expand to. But we can do bacteria and yeast. So you insert these constructs in the respective hosts and then you can monitor the growth. So, for example, the system I mentioned, the BioLector, it has the ability to measure growth, it has the ability to measure dissolved oxygen, temperature and if you have your production associated with a fluorescent marker it can measure build-up of fluorescence in this culture and we can do this in both aerobic and anaerobic conditions.

08:46 Stevie: So then, what's your role in the foundry?

08:51 Rennos: It has quite a lot of different sides, if you like. One of the sides is making sure that we are able to deliver to our customers. What's very important is communication. So you have to communicate with people in an effective way. Scientists, we are all creatures of habit, so if we are using one pipette and one kit and it works, we are never going to change it because we know it very well. That's what the foundry is trying to do, it's trying to change the mentality a little bit and see how we can use our time more effectively and also reduce cost in the process, while still delivering high quality science. So I think it is very important to have a scientist in that position who understands two different things: one, how the science works, the other side is how PI come to me and say 'look I have this grant I have to deliver in the next six months can you help me?'. I understand how this person feels because I have been in this position before so I can try to help them as effectively as we can and I think this is very very important.

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10:16 Stevie: A massive thanks to Rennos for highlighting the amazing work going on at The Edinburgh Genome Foundry. Be sure to tune in to future episodes of The Synthetic Biology Podcast.

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