The Synthetic Biology Podcast

Episode 3: Jane Calvert and Rob Smith

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00:01 Stevie: Welcome to the Synthetic Biology Podcast brought to you by the UK Centre for Mammalian Synthetic Biology at the University of Edinburgh.

00:10 Stevie: In this episode we talk to Drs Jane Calvert and Rob Smith who work in the department of Science, Technology and Innovation Studies, also known as STS. Jane and Rob talk about the Crossing Kingdoms project, which is part of their work in the Centre for Mammalian Synthetic Biology, but we also cover Jane's work on synthetic yeast, funded by the BBSRC, and Rob's work on gene drives, funded by the British Academy. We chat about the social, political and ethical dimensions of synthetic biology research and discuss the fundamental value of interdisciplinary collaboration.

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00:48 Jane: I work in the area of science and technology studies and this is a field where we study science and technology, but we are not scientists, or technologists or engineers. We are actually from the social sciences, but some people come from philosophy or history, so it's quite an interdisciplinary perspective on science and technology. I bring interests in the sociology of science, the philosophy of science and science policy.

01:13 Rob: Yeah, so I also work in science and technology studies. Originally, I trained as a biologist and this is something that is also quite common in our field so the kind of move over from the sciences. But I've always had this interest in humanities so after my undergrad I realised that I didn't want to work in a lab for the rest of my life, but I quite liked policy, so transitioned away from that. But I have always been interested in biological sciences over any of the other things.

01:42 Jane: Yes, so, I think we don't just go to the most hyped or controversial field, we actually have quite detailed interests in how the science is done in that field. Like Rob said that often comes from starting out with a real interest in the science. So what I really love about being in science and technology studies is that in the morning I can be reading a philosophy article and in the afternoon I can be reading an article about genomes and then in the evening I can be … watching tele! [Laughs] No, reading something else about something else, you know, so it allows you to continue traversing across disciplines. Some people say it's a bit like being a theatre critic or a restaurant critic, you appreciate what you are studying but you simultaneously want to apply a critical lens to it.

02:35 Stevie: So would you say that synthetic biology lends itself quite well to this type of study? You know, looking at social implications and cultural implications of the work that synthetic biologists are doing?

02:45: Yes, so synthetic biology is definitely interdisciplinary, and I think this is one of the reasons why I became interested in it. Also, because they are very open to people from different disciplines. So, engineers are talking to computer scientists who are talking to biologists, so everyone is talking to someone who doesn't know their field so that makes it very open. But I don't think we are just interested in the social and cultural dimensions of these fields, although this is kind of a tricky point because we don't separate the social from the scientific. And that sounds a bit weird but actually we think that scientific knowledge is inherently social – its produced by people, its driven by agendas and not to bring in COVID but we can see this at the moment with all these competing scientific claims and how politicians are arguing for some and not the other. So, this is a really nice example at this moment of how scientific knowledge is not one thing, its contested, its influenced by agendas and priorities.

03:48 Stevie: Yeah that's a really good point. One of the things that I am just trying to wrap my head around is how this collaboration looks. Would you come on board early in the project, you know if someone is writing a grant to do something you would have a role at that stage or is it the case that you come in a bit later down the road when they have things up and running, maybe in the lab?

04:09 Jane: I really think the earlier the better. So, we've known the synthetic biologists at Edinburgh for a long time because they are just open and friendly, and they have been for years. So, most of the things we have been involved with have been at the grant writing stage which means that we can put forward our own research agenda at the beginning because we are researchers, we do our own research. But then again, also I like riffing off what they do as well so with the synthetic yeast project that I studied I didn't know much about yeast or yeast biology, so I did follow and develop my interests around what they were doing to reengineer this organism.

04:47: Can you explain a bit about that project actually because that's really quite fascinating?

04:53: Yeah, so the project is an attempt to build an entirely synthetic version of the yeast genome of the yeast, *Saccharomyces cerevisiae*, which is very familiar brewer's or baker's yeast. It's kind of audacious in a sense, it's like 'we're going to build a new genome, we're going to build a better genome' so a lot of it involves reducing and shortening existing genomes because they have lots of redundant – well, to be honest, yeast doesn't have so much redundant DNA – or is it even redundant? - as mammalian cells do - so getting rid of unneeded, excess DNA but also introducing mechanisms to be able to evolve the DNA at will. So, there is a system engineered into the yeast genome called SCRaMbLE which allows the scientist to add a chemical and then force the evolution of the yeast genome to produce new variants. It's real idea of rebuilding, redesigning yeast according to our desires as human beings.

05:55 Stevie: It's definitely one of those things though, even as someone outside the field you can immediately see okay, that's very interesting and very cool to be able to modify a genome in that way or to force evolution to go in a particular direction that might have benefits for humans or for a particular task that maybe we want this organism to perform …

But I think there must be a lot to consider in terms of how do you control that? And when it comes to modifying a genome, how much can you edit a genome before it is no longer the thing you started with?

06:28 Jane: Exactly! These are the types of things I'm really interested in. When is it a new species? How do you assess whether or not it is a new species? There are so many different criteria for species, many of them involve mating but then yeast can be both sexual and asexual. Then there are little bits of the genome which are used as a barcode for species identity and they have actually cut them out of the *Saccharomyces cerevisiae* just because they don't actually do anything. Then you are like well, is it a new species then? So, I find those questions really interesting. A lot of the synthetic yeast project is actually about understanding yeast better so if you take away loads of what you consider to be unnecessary genes does the yeast then die and then that teaches you more about the yeast.

07:09 Rob: But also the thing that, I guess, is interesting is that you use the word 'control'. That is often the kind of language that sits behind a lot of engineering, a lot of biotechnologies, this idea that we can control yeast, and I think one of the things that – I wasn't involved in the synthetic yeast project – but I think one of the things that is notable when you listen to the talks of the scientists doing that is that they have had to give up a lot of control to be able to do the work. So a lot of the work they are doing, there are design choices and they change the way the genome goes together and the way that it works but basically they just then go like 'bleugh' and let it go. So they are kind of giving up loads of control and still have this idea that they are rationally designing or engineering. And I think that's one of the things that Jane is interested in …

07:59 Jane: Yeah, so what does that mean for the idea of engineering if you are letting evolution do it and you are kind of giving over control to evolutionary forces, are you still designing? And what we love to do at STS is really challenge categories, I suppose, so when people say this is natural, this isn't, we won't be saying 'yes it is' or 'no it isn't' but we will be saying well what does that mean? What comes into that word? But also, Rob's been doing some work on gene drives and I think with gene drives you don't want them to go off and do their own thing necessarily. So, there are definitely circumstances where control is really important, I think.

08:41 Rob: So, basically there is this proposition that you can get naturally occurring, they are called selfish genetic elements. So these are things which would normally expect to be 'evolved out' over time because they confer a fitness burden but they don't. They kind of persist through time. So that's quite strange. So that's been termed gene drive. There are these naturally occurring things which should disappear over time but that persist. There's obviously been a lot of hype around CRISPR and things like that, these new gene editing technologies. One of the things that is actually has made possible is the ability to build these selfish genetic elements artificially, begin to choose which traits you want to pass down through generations and which ones you kind of might not want to. Scientists have begun to think about, can we force things like sterility down through populations? The thing that they want to use it for really is for pests – organisms that we as humans have decided are pests or are problems. So things like, in the US there's a lot of work on mice because they carry ticks and so they cause Lyme Disease and things like that. The other big one is malaria so it's

mosquitos. There's a lot of work at the moment to build these genetically modified organisms that will spread traits so sterility traits for instance from one generation of mosquito to another generation. I think that there are these kinds of classes of technologies that people have begun to build which, you can see why … solving malaria is clearly a good idea, but you can also see why this seems like it might inherently be a terrifying thing to do. When you do that you often get lots of controversy and contestation, and also lots of calls for public dialogue and public discussion.

10:40 Stevie: That's really interesting and I think what you say about the fact that you can clearly see the benefits but also, you know, genetically modifying things and then releasing them into the world, it does seems like a scary thought because say you do decide to go ahead with it, and do something like that, is there any retrieving it? If it turns out that it's not a great idea or it's not going to work, what's the plan then?

10:55 Rob: So it's like, is it reversible or not? Yeh, we often think about technologies as they are just a thing that we have, and people talk about them as though they are inevitable. But actually, if you begin to unpack how they are made you can see lots of choices and decisions that would shape the kind of technology that we have and then shape the political and environmental consequences of that technology. So gene drive, the way that I described it makes it sound like it's always going to be irreversible but you could design it in ways which would mean it's local and that it wasn't irreversible and that's a decision. That's a decision that affects the way you would design the technology. So part of what we try and do is show that there are these decision points that will affect how the technology is built, what it will do and then question, who should be making those decisions.

11:46 Jane: I think the point about inevitability is really important because scientific and technological developments are often presented as if they are inevitable, but I think one of the things STS does is says we always have choices. So, for example, with large scale synthetic genomics, people are deciding what organisms of the future might look like but who is going to be involved in that discussion? Is that just a question for the technical experts? And I think one of the things that's really interesting about synthetic biology is that because it is about design, it's about choices because whenever you design something you can always make choices about what is a good design, who is the design for, using this design or that design… So there's an intentionality to it.

12:32 Stevie: One thing that I think leads on quite nicely from that is your involvement in the Crossing Kingdoms project because obviously that's something that creates a lot of discussion and there were a lot of choices made there. So can you talk a little bit about that?

12:47 Jane: Yeah, well it actually started quite serendipitously at a conference where Susan Rosser and Alistair Elfick who are the director and co-director [deputy director] of the mammalian centre and myself and another social scientist and also a couple of biological artists, we were all at this conference and one of the presentations talked about using, I think it was yeast, mammalian and viral cells – three kingdoms of life! So I think she wanted to make a yeast, ebola, human hybrid and the artists were just like 'woah this is something we would like to investigate", they are called Ionat Zurr and Oron Catts from the University of Western Australia. They are very well-known biological artists who have kind of explored

biological questions through their art for many years but since myself and Alistair knew them already from another project called Synthetic Aesthetics we talked about the possibility of doing something with them again. I particularly like working at these intersections of disciplines because people raise questions that you would just never raise yourself so having artists, synthetic biologists and social scientists all in the room together, you have these conversations that interesting because you are all coming from different perspectives. I find that really valuable in itself.

14:02 Rob: So I think, Oron, one of the artists, has quite a good way of talking about this which is like synthetic biology and biology and biological sciences have always kind of brought these new things into the world and we don't, as a society, really have a good way of talking about them. We don't really know what to call them, we don't really have a vocabulary to be able to make sense of these things and I think that's what Crossing Kingdoms is really about. There's been a big backdrop to a lot of the work we do which is to think about what's the impact of it? What's the point of it? And a lot of it is justified in terms in making science ethical or making it responsible or making it publicly acceptable and to then try and quantify that. And I think one of the things that is really good about this project is that it kind of resists that because clearly lots of things have happened – we've done exhibitions and people have come and engaged with the ideas that are associated with synthetic biology, but we haven't really changed the science in any way. We haven't made it responsible or ethical or anything like that, but I think it does contribute to this broader public debate about the kind of things that someone is going to ultimately end up creating somewhere in the world.

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16:01 Stevie: A huge thanks to Jane and Rob for such a brilliant discussion and for giving us some food for thought when it comes to scientific innovation.

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Be sure to join into future episodes of The Synthetic Biology Podcast. Our work is funded by the BBSRC, EPSRC and MRC and the UK Research Council's Synthetic Biology for Growth Programme.