The Synthetic Biology Podcast

Episode 2: Elise Cachat

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00:03 Stevie: Welcome to the Synthetic Biology Podcast brought to you by the UK Centre for Mammalian Synthetic Biology at the University of Edinburgh.

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00:12 Stevie: In this episode we are joined by Dr Elise Cachat, a lecturer in synthetic biology at the University of Edinburgh. We chat about her research and how it can help us to understand the role of immune cells called macrophages in the progression of cancer. We also hear a little bit about an interesting fusion project.

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00:36 Stevie: But first, what got Elise interested in the field of synthetic biology?

00:42 Elise: So, I became interested in synthetic biology through a job advert, really. So, the project was aimed at constructing novel genetic circuits in cells to drive or control specific cellular behaviours. So, for example, getting cells to adhere to one another or getting cells to fuse to one another. It was really the first time I read the term 'Synthetic Biology', my curiosity got peaked, I read around the subject … Also, yes, I think I was partly interested in the technical challenge of engineering cells, that appealed to me. But also, I suppose, by the incredible possibilities that this new field could open up.

In the main project that we are working on in the lab at the moment, we want to be able to detect interactions between macrophages and cancer cells. This is because we know that macrophages are important for cancer cells to establish secondary tumour sites, but macrophages are an incredibly heterogenous group of cells and so being able to distinguish which subtypes are responsible for this interaction with the cancer cells and enable them to establish secondary tumour sites is quite challenging. So, what we want to do is we want to build cells that can detect and report on their contact with macrophages and with particular macrophage subtypes so that we can map these interactions and understand their importance for metastasis establishment.

02:20 Stevie: So how do you engineer a cell?

02:26 Elise: To do this we need to basically build cells that react the way we want. This is quite a slow and painful process. First, we need to design the new biological parts that the cell will need to fulfil a particular behaviour. Then we need, once they are designed, we need to construct them into the cells. We use DNA as building blocks, so we need to make sure that the DNA circuits we insert in cells are behaving the way we want. So, there is a long process of selecting, isolating cells and then testing them to see that they react.

03:07 Stevie: And this would be done in a Petri dish?

03:10 Elise: Yes, so it’s in vitro. To be sure that this works first in vitro there is a lot of testing to be done. Then when this is done, we can move into animal models and in animal models what we can do is engineer cancer cells – in models of metastasis in mice – and then we can, after letting those cancer cells interact with different macrophages, we can collect those cancer cells and then test them to see if they have previously contacted some macrophages. This is quite far away, we are still very much in the in-vitro phase. When it comes to synthetic cells in a body then we need to be extremely careful. There’s always a level of uncertainty associated with engineered cells and also associated with their long-term behaviour in-vivo.

04:03 Stevie: That’s really interesting because you’re essentially putting in this living cell, this engineered cell, it’s alive, it’s replicating and essentially it can just go off on its own evolutionary path, right? And that in itself can actually cause cancer.

04:22 Elise: Exactly. We need to make sure they are safe and that they are stable. Or at least that they can be easily removed from the body or at least easily suicided in the body. So in-vitro already can be useful for diagnosis or screening purposes but in-vivo we could imagine that those cells that are able to detect contact can tell us where the contact happens, when the contact happens in real time. Or even why not start therapeutic program so maybe asking the cell to produce some sort of therapeutic outcome.

05:02 Stevie: That’s really interesting. One thing that I wanted to ask about as well was this interkingdom fusion between yeast and mammalian cells.

05:13 Elise: So this is a project in collaboration with artists and social scientists. It’s called the Crossing Kingdoms project and in this project we are trying to fuse mammalian cells and yeast cells. The scientific reason for creating these hybrid cells is to find a way to channel large chunks of DNA into mammalian cells. This is because large DNA circuits or even entire synthetic chromosomes can be engineered and they are usually assembled in yeast cells first. So you basically have small DNA fragments that are concatenated into larger and larger fragments and at some point need to be channelled into mammalian cells. There’s a big part of synthetic biology aiming at building cells from the bottom up. At the moment, it’s definitely easier to do with bacterial cells that have a much smaller genome but in the future we want to be able to maybe engineer eukaryotic cells and bigger cells and so the amount of DNA needed is much larger.

06:29 Stevie: Obviously, synthetic biology is a subject that is viewed as very much pushing the boundaries and so to link up with social scientists, I can see the obvious link there.

06:44 Elise: Yes, exactly. They are more interested in the questions that those new hybrid cells raise. So for example where do those hybrids belong in the biological world, the biological realm? Do they impact society? And also they were very interested in trying to study the interactions between our different disciplines and trying to see if we achieve interdisciplinary fusion as well. For the artists, they are more interested in the fusion process itself and they want to explore through art what it means to have those new interkingdom hybrids.

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07:35 Stevie: Thank you to Elise for such a fascinating discussion. Be sure to tune 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. Elise's work is also funded by the Wellcome Trust-University of Edinburgh Institutional Strategic Support Fund and the University of Edinburgh's School of Biological Sciences