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I: Welcome to IFLScience The Big Questions. I'm your host Rachael Funnell, and today I'm at the London Natural History Museum for a very exciting episode where we are looking back on 30 years of Jurassic Park. I'm here to speak to dinosaur expert, Dr Susie Maidment about what we've learned in the last three decades and I'll also be speaking to Ben Lamm, CEO and Co-Founder of Colossal about whether or not we could ever actually clone a dinosaur.

So, hello Dr Susie Maidment, it's great to see you again.

SM: Hi there, thanks for coming down to the dinosaur collections.

RF: It's excellent to be here, and we're standing here in 2023, so that means somehow, 30 years have passed since the *Jurassic Park* film came out, no idea where they have gone. But in that time, you know, science has trundled on and we've made some incredible discoveries. So, what do we know so far about the possibility of bringing dinosaurs back?

SM: Well, people have had some ideas about how we might be able to bring dinosaurs back, and of course, the first one in *Jurassic Park* was the idea that we could maybe extract some blood from a mosquito and then take the DNA from that, fill in the gaps in the DNA, and then clone a dinosaur. Well, we can't do that, and we still can't do that 30 years on from the film, and that's because we haven't found any DNA from dinosaurs. In fact, the oldest DNA in the fossil record is probably only around a million years old, maybe a bit more. So, the dinosaurs died out 66 million years ago, so definitely we don't have any DNA for dinosaurs at this point. We do, however, now have some blood, so we have some red blood cells that are preserved from dinosaurs and some other soft tissue features. So maybe in the future we might be able to get some DNA. There are a couple of other different techniques that are going on though. One of those is reverse engineering, so this is this idea that you can maybe take a bird, which of course are the direct descendants of the dinosaurs, fiddle around with its genetics, and produce something like a dinosaur.

RF: Fantastic. So, in the film, obviously when you're talking about the precious dino DNA there, they use a mosquito trapped in amber. So, would that not work for our understanding of fossils at the moment?

SM: Yeah, so when we look at insects in amber - what we tend to find is that the outside of the insect, the kind of chitinous husk, the crunchy bit, it you like of the insect - but the inside stuff isn't preserved, so there isn't any blood found within those. But there has been a beautiful specimen of a mosquito found preserved in lake sediment. So, these are very, very, very kind of finely laminated, finely layered sediments and this specimen had a kind of dark stain around its abdomen and when they tested that, they actually found the breakdown products of haemoglobin in it. So, it was blood in a mosquito's abdomen, however that specimen was only actually 60 million years old, so not old enough to be around at the same time as the dinosaurs.

RF: Fantastic. Massive gap then, between then and where we're at now. In the film, when they manage to extract the DNA from the amber specimen, they get this genome but it's not quite complete, so their idea is well, we'll just get a bit of a frog and we'll plug in the gaps. Is there any reason that might work, or what would be the flaws there?

SM: So, there are some fairly major flaws with this whole kind of concept. Firstly, in order to know where the gaps in the DNA are, you kind of have to have the whole genome to start off with, otherwise you don't know which bits are missing. The second problem is that frogs are the least likely organism you would choose. The organism that you would choose would be birds, because birds are the direct descendants of dinosaurs, and when *Jurassic Park* came out I don't think that was 100 percent accepted. There were some ideas that it might be the case, but it wasn't as widely accepted as it is now. Now, that's just fact, basically, but they still wouldn't have used frog. I mean, humans are more closely related to dinosaurs than frogs are. So it was totally a bizarre choice, but it was needed for the narrative of the film, because they needed the dinosaurs to be able to change sex randomly and then produce offspring. So, they needed this, and this is something that some frogs can do.

RF: And for entertainment value it really paid off, so fair enough Michael, we got it. The animal cloning aspect of *Jurassic Park* is actually the field of science of our second guest, Ben Lamm over at Colossal, who is something of an expert in. He works towards the de-extinction of animals that aren't around today, like the Woolly Mammoth.

BL: So Colossal Bioscience is, to our knowledge at least, the worlds' first de-extinction company and species preservation company. What that means to us is looking and understanding what are the genes associated with the core phenotypes or physical attributes that existed in an extinct animal. So, for example with the Woolly Mammoth, it's like the dome cranium, that's the curved tusk that's making cold tolerance, to a lot of things under the hood. Things like how nerve endings respond to negative 40, how the body produces haemoglobin […] and obviously the shaggy wool coat. So, how can we at Colossal understand the core genes that made elephants cold tolerant that those genes are now extinct and then how do we then de-extinct those genes and put them into the architecture, if you will, of an existing living animal, in the case at the moment, the Asian Elephant which is 99.6% the same genetically, and then de-extinct those genes so that you then have the mammoth 2.0.

RF: Fantastic. And so, you mentioned the mammoth there, but as I understand it, your company works with a few animals. Can you tell me what else you are working with?

BL: We're working on obviously the Woolly Mammoth, we're working on the Thylacine, also known as the Tasmanian Tiger and then the iconic Dodo from Mauritius.

RF: Amazing. When you're looking to do these projects with these different animals, what kind of materials do you need to begin with to bring them back?

BL: First you need to look at, what is the closest phylogenetic relative? What is the animal that is still existing on the planet that's the closest on the family tree? For example, for the Woolly Mammoth, that's the Asian Elephant. As I mentioned its 99.6% the same genetically. Most people don't realise this but an Asian Elephant is closer genetically on the family tree to the Woolly Mammoth than it even is an African Elephant. Sometimes that fact blows peoples' minds, like, the Mammoth isn't here anymore, but these two are still here. So, you've got to find and build a reference genome. You've got to get tissue samples; you've got to be able to build a reference genome. We did that last year with the Asian Elephant. We just announced this week, the African Elephant reference genome that we built for comparative genomics, and then you've got to get tissue samples in ancient DNA from those extinct species and ancient DNAs are different than existing living DNA because it's massively fragmented, it's not all exogenous, meaning that there's other microbes or other things that kind of contaminated it over time. Then you've got to basically piece together that, so like with the Mammoth, we actually use 54 different Mammoth genomes to build our reference genome to then do the comparison. Then lastly, you obviously need surrogate that will be able to house the genetically modified embryo once you get there.

RF: Getting those ancient samples, does that get harder and harder the further back in evolutionary time that you're working with?

BL: Yeah. It's also conditions. So, there are animals that are extinct more recently than Mammoths that went extinct in very hot and wet places. That's not a great place for DNA. Cold, dry places is great. So, things like caves or the arctic, in the case of the permafrost. There were some circumstances like the Thylacine, where they went extinct in 1936 where people preserved some pups in ethanol and alsoin alcohol for scientific study and we were able to sequence those to get a nearly complete genome. So, it really depends. Sometimes you get lucky, but generally speaking the further back you go and the hotter, wetter places you are, is bad.

RF: Great. Just before we move on to the dinosaur stuff, you mentioned there about a species that have gone extinct in more modern times. I think that's a really interesting point because your company, a lot of people think of the really old stuff like the Mammoth and the Dodo but you've got plans for supporting conservation projects, right?

BL: All of the technologies that we develop on the path to de-extinction, some of them have applications to human healthcare which we are monetising. We did that last year, we spun out our first computational biology platform, but all the technologies that could add to assisted reproductive technologies or conservation groups for zoos or animal groups worldwide, we are subsidising and giving to the world for free. So those are tools like better semantics on nuclear transfer techniques. Those are things like better computational biology for research, all the data we built on Asian and African elephants we publish to science so that people can use those. A lot of these technologies can not only be used to bring back Mammoths but can help critically endangered species. So, if we are successful long term and we even get to technologies like artificial wombs - which are a way out, it's much more likely you will see extinct animals from us before we see artificial wombs - but once we get to artificial wombs think, about that for species like the Northern White Rhino, where there are only two females left. If we could clone them or create genetically modified versions of them, inserting DNA from other lines that are now extinct, that don't exist anymore and you insert that biodiversity and then you can grow them in a lab and work with great re-wilding partners and put them back in the wild, that's pretty awesome. We think it could be transformative for conservation. So, this de-extinction tool kit that we're building over time with our species we want to make available for free to every conservation group out there.

RF: It's really cool to think that some of the ideas that underpinned Jurassic Park could actually help us keep endangered species alive, but what if we brought some back, including really old ones like the dinosaurs? As Susie explained, animal welfare doesn't get any easier when you're dealing with long extinct species.

SM: There's all sorts of problems. First of all, the dinosaurs lived for 170 million years on earth. That's a really, really, really long time. So, *T-Rex* is closer to us in time than it was to *Stegosaurus*. Many dinosaurs were already fossils by the time other ones lived, so you're bringing all these different animals together and putting them living alongside each other, already that's weird, and then you're bringing in living animals and putting them alongside. So, how do they al interact? They're not in a natural environment. But also, what about the things that they eat? So, grass hadn't evolved when the dinosaurs were around so the herbivores weren't eating grass, and grass is quite difficult to eat, it has lots of bits of almost glass-like material in it which causes your teeth to wear down really, really fast. So, things like horses have evolved these very high crown teeth which wear down over time. Dinosaurs didn't have that, they replaced their teeth continuously through their lives, but if they were eating grass, could they have digested grass? Could their teeth replacement rate keep up with being worn away? Would some of these plants today be poisonous for these dinosaurs that lived in a world where flowering plants hadn't even evolved yet. So, I think there is a bit of concern over what they would eat and how they would get on with each other. But of course, what rights would they have today? So, would they be treated like living animals? Would we afford them the same rights that living animals have, or because we've invented them or reconstructed them, would they have a different status? So, I think there is a bunch of ethical concerns around it as well.

RF: I suppose there would be an element where we could open up a new era of dentistry, that would be exciting. But maybe more problems than it solves. A difficult sell for modern zoos then, but as Ben told me, we probably don't need to worry about seeing a living breathing *T-Rex* any time soon.

BL: We are asked the dinosaur question all the time. People love Mammoths, people love Dodos, and obviously Thylacines too, but people really do want dinosaurs. We get probably two or three emails a day about dinosaurs. People love dinosaurs. I don't want to break hearts, but it is not possible to de-extinct a dinosaur. Every so often, you will see some press or paper that's like, 'oh we got some dino DNA'. Like Ken Lacovara who is arguably the number one Palaeontologist in the world that discovered *Dreadnoughtus*. He's amazing, he's one of our scientific advisors, he's probably been the closest because he's actually developed a process to de-mineralise dinosaur bones and get basic fragments of amino acids but, you know, we've just had amino acids for our mammoth project but we're not working on it because it's not possible. So, it's not possible to scientifically bring back a dinosaur. I do think that the tools over the next

20 years could get to the point where you could start engineering species that had kind of those dinosaur-like traits, but unlike our work with the Mammoth, we can't really look at the genome and identify those core genes and de-extinct them so I don't think it's possible to bring back a dinosaur or de-extinct one, but I do think over time you could probably engineer dinosaur-like things, but I think then you've really got to ask yourself why. Why are you doing it? What's the purpose? How does this help the world? How does this help our ecosystems? How does this help humanity? I think you've got to be really thoughtful about it at the time.

RF: Yeah, makes for a great movie but not necessarily useful science.

BL: Yeah. It sounds really cool. As a sci-fi nerd myself yeah it sounds cool, but what is the true purpose?

RF: Definitely. So dino DNA you mentioned there, that's a great Mr DNA segment of the movie. Obviously when Michael Crichton wrote this book it wasn't intended as an instruction manual for cloning animals but I just thought it might be fine to touch on some of the, kind of, as someone who knows animal cloning pretty damn well, some of the most glaring errors they make in the film when they're attempting to do this.

BL: Absolutely. It's a weird fun fact. George Church, my co-founder, and this is really George's vision. I feel like I'm just a steward of George's vision, he's my partner at Harvard, he's incredible. If you don't know who George is, look up George. Every scientist in the world should follow George because he's just arguably one of the smartest people on the planet and some of George's early work actually was one of the sequences that showed up in Michael Crichton's book and so, I feel like in a weird way, Michael Crichton, if he were still here today, and George would be close friends because especially with the launch of Colossal because there is that alignment which is pretty cool.

RF: That is an amazing fact, I love that. So, if you ignore all of the glaring flaws and the very real risk of death when you do these things, what would you most like to see alive if you could clone a dinosaur?

BL: So, we aren't working on dinosaurs. I don't know if anyone should ever work on dinosaurs or dinosaur-like species, but Mammoths are probably one of the biggest iconic species of extinction and so I would lean towards the *T-Rex*. Once again, I'm not encouraging anyone to work on the *T-Rex* because I think that would be big and scary and terrifying for the world. We already have enough existential problems right now, so updating *T-Rexes* should not be on our current list of problems. We need to focus on politics and climate change, let's focus on other problems before we introduce new ones.

RF: Over at the Natural History Museum it seems like the scientific, logistical, and safety concerns around bringing dinosaurs back from the dead have actually put Maidment off entirely.

SM: Well firstly, did you watch the film? It didn't end well. So, I'm going to say that maybe it's not the best idea. I think if I had to choose one, it's really tricky, because I would say *Stegosaurus* because it's what I work on, it's a dinosaur that I know really well but then I'd be out of a job, so you know, I don't know that I'd choose any to be honest with you.

RF: That's an unexpected answer but I like it. Then another question I had about the film, and it's not necessary science but I just have to ask, because I think it's been burned on the brains of many people since they read the books, could a Velociraptor really open a door?

SM: Well actually, the meat-eating dinosaurs, they had their hands facing each other, so their palms together. So, they were clappers rather than typers. So, their palms couldn't face the floor. For most meat-eating dinosaurs, they couldn't have rotated their wrist round to open a door, their wrists don't work like us. Things like Velociraptor and animals quite closely related to that actually had the ability to almost fold their arms backwards like a wing, because this where wings evolved from dinosaurs very similar to them. So, they had this bone in their wrist that would have allowed their wrist to fold back, but I'm still not totally convinced that to open a door handle. So, I think we're safe.

RF: There we go. All you need to do to beat a Velociraptor is build the door, job done. We've teased the movie a bit but I know for me, it's a film that I've watched probably more than anything else in my entire life. What did *Jurassic Park* mean to you?

SM: I was 12 when *Jurassic Park* came out. I went to see it with my first boyfriend. We held hands in the queue, it was a very special moment. I think *Jurassic Park* for me, because I was a young teenager, it made liking dinosaurs and thinking dinosaurs were interesting and cool a little bit more socially acceptable, which as a girl in the early nineties wasn't always necessarily the case, I think. So, I think it made the discipline a bit more socially acceptable and I think also, it made dinosaurs really star in peoples' minds. It brought them to the forefront of peoples' consciousness and I think that did a lot for Palaeontology as a whole because I think that increased funding to the discipline, I think it really shone a light on dinosaur research and I think that helps all of us in the end.

RF: Absolutely. Thank you so much for your time Susie, that was great. So, as far as the science goes it seems like cloning dinosaurs is probably not that likely but then, what is it they say? Life finds a way.

Thanks for listening to IFLScience, The Big Questions. Head over to iflscience.com and don't forget to sign up to our newsletter so you don't miss out on the biggest stories each week. Until next time.

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