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SPEAKERS

John Sutherland, Unknown speaker, James Tour

J James Tour 00:00

Okay, guys, I'll admit it, I was all wrong on origin of life, these guys have it all figured out, they know where life came from. I am going to take down all the content on my YouTube channel where I've critiqued origin of life on one condition. The condition is this, I am going to name 10 key researchers that have published key papers in the area of origin of life. And I'm going to give all 10 of you a chance to answer five essential questions that need to be answered for origin of life to be solved. What are these five questions? Well, they're the same five questions that I put up on a recent debate that some YouTubers have said have already been solved, show me the prebiotic chemistry that would do this coupling.

U Unknown speaker 00:45

This scheme is what James wanted me to write on the board.

J James Tour 00:50

If their answers good, take their answer. I'd like to see you, as a researcher in the origin of life community, take their answer, and present that as a solution. Who's going to be the judge? The judge will be you. That's right. You can judge yourself whether this really answers those questions. All five have to be answered to have a model for the origin of life. You just answer one, and I'll take down all my content. But if you can't answer any of them, I'll continue to say that we're not just clueless on origin of life. We are utterly clueless, and the world will see. I'm Dr. James Tour. I'm a professor at Rice University. I'm a synthetic organic chemists and I just don't get it. I just don't understand the chemistry. So help me out guys helped me with the chemistry here. The people I'm appealing to are people in the origin of life community, people who have published in it, all of them with the ability to make molecules and assess whether this chemistry can work. And the invitation is to these 10 people. Steve Benner, Jack Szostak, Clemens Reichert, Lee Cronin, Bruce Lipschutz, John Sutherland, Nicholas Hud, Ramanarayanan

Krishnamurthy, Neil Devaraj, and Matthew Powner. Any one of these people can answer just one of the five questions, it will be considered a win. Well, who's going to decide whether the question was properly answered? I'm going to sign three of those Steve Benner, Jack Szostak and Clemens Reichert as the judges. What do I mean by that? So if all three of those judges are in agreement that that has answered the question, then we'll consider it a win for the origin of life community. If none of these five can be answered, then we'll consider it a loss. And I'll continue to say that we're clueless on the origin of life. And I'm giving you 60 days to solve this, because I've always said that I presume one day we'll be able to solve this, we will someday figure out how life was formed. But I'm giving you 60 days, because we have to be able to wrap up this challenge and talk about it at some point, you can send it to me by email, where you just write the thing out, use ChemDraw and write out the structures write out the mechanism, you want to write it by hand, that'll work too, or best just get an iPhone or your smartphone and have somebody filming you at a blackboard. Yeah, I don't need the board I and started a blackboard with the very reagents that I put down and go from those reagents to those products, be my guest. But you're going to have to start with that starting material and make your way to the proposed product. What I'm going to do is I'm going to yield to you all 19 of the canonical amino acids, all the nucleotides and all the monosaccharides in 100% enantiomeric purity. And you know that these things are hard to make in an anti numerically pure form. And you say, well, they might come on meteorites. Well, they don't, don't come in enantiomeric pure form on meteorites, they come as gross mixtures. And it would be very hard to use that.

J John Sutherland 04:03

Don't think neutrons make the right sort of mixtures.

J James Tour 04:06

But let's just say you have all 20 amino acids, the 19 of them that have a stereocenter that you get in pure 100% chiral form 100% and enantiomeric access. Same with any of the nucleotides you want, and also of the monosaccharides the five areas are the same five areas that I talked about in my recent debate, you're going to have to make polypeptides, you're going to have to make polynucleotides and polysaccharides. You're going to have to come up with the origin of specified information where there is a specified code and then the assembly of all those components into an integrated functional living system, namely a cell that bears the textbook characteristics of life not my definition of life, but textbook definition is going to have to be responsiveness to the environment, growth and change ability to reproduce, have a metabolism and breathe, maintain homeostasis, being made cells and passing traits onto offspring. All you got to do is answer any one of those five, and we'll call it a win for you. We're used to as chemists working on moles of molecules, we have lots and lots and lots of the same molecules in there. So we don't worry as much about their stability about how quickly they would hydrolyze. I think more about this, because I worked in an area called molecular electronics for many years, where one molecule would be a switching device, we had to have things be really stable, because one molecule can decompose really quite rapidly. So let me show you the problem here, when you're converting a halflife of a sample of many molecules to the stability of a single molecule, you have to have a conversion of a halflife to a probability, we're assuming exponential decay. So I have some assumptions here, I'm assuming exponential decay, and independent bond breaking events. So if we were hydrolyzing, the polymer chain, I'm just assuming independent bond breaking events, and the probabilities of

independent events multiply, so the exponents are going to add. So what it works out to be is the half life of the N-mer, whatever that N-mer is, however, number of groups it is the half life of the N-mer is the half life of one of those bonds, divided by the number of those bonds in the N-mer. So, for example, if you have a protein, and a protein has a seven year half life, if you have a single 200 polypeptide in water. if you have one molecule of that polypeptide in water, then its lifetime is to 2555 divided by 200. 13 days, that's all you have. So somehow, if that one polypeptide form, that happened to be the right sequence to do something, it's going to have to find all the substrate that it's going to act upon very quickly, within 13 days. The problem, of course, is exacerbated when you have RNA, if you want to have the RNA hypothesis, let's just take a 600 mer of an identical RNAs say you had a mole of these, let's be generous and say it had a half life at room temperature of 100 days, again, that's probably pretty generous, that's 2400 hours in water at room temperature, then for a single RNA strand, its lifetime would be 2400 hours divided by 600. If it's a 600 mer, which is fairly short for an RNA, but let's just say it's a 600. That would be four hours, four hours, think about that, because time really is enemy number one, when it comes to origin of life, and these organic compounds, time is not the great Savior. Actually time is a real problem. But that's the problem when the free energies are positive. These reactions favor as you know, the starting material, these want to hydrolyze and these are the types of times you have. So if you do have that single RNA strand is like one of my colleagues said, â€œMaybe it only takes one RNAâ€, Josh Swamidass told me when we were discussing this stuff, but you only need one RNA strand, that's all you need. Well, you got four hours, then gonna have to find the substrates that is going to act upon this. Just to give a little bit of background, here's the 20 canonical amino acids, all the ones in red circles have these active side chains, and the ones in dashed circles are reasonably active. So that just paints the picture. Question number one, prepare this dipeptide DK or if you want to prepare KD, I'll accept that too, in greater than or equal to 90% yield from D and K, which I'm giving you D and K to the exclusion of sidechain linked systems using prebiotically-relevant chemistry. So you need to use prebiotically- relevant chemistry. And you guys know what I'm talking about these side chains. This active carboxyl group is quite reactive, very much like the reactivity of that carboxyl group and very much like the reactivity of that carboxyl group, but you're going to have to make it so that that carboxyl group does not react. Remember, that's what's necessary to make polypeptides. This amine group cannot undergo the reaction, only this amine or this amine can undergo the reaction so that we get DK or KD and note the steric chemical purity here I am giving you these in 100% enantiomeric access so that's what you have. Note the stearic chemical retention, the stereochemistry is here have not changed, and the regio chemical control where there's no sidechain reactivity. Now Matthew Powner, you have amino nitriles doing this in a prebiotic setting, Paul Rimmer has suggested that your amino nitriles would work. They can't because there is no amino nitrile you have to start from these amino acids that we know that I've given you. I've given you these amino acids. This is all you've got is these amino acids. This is just the starting materials, you got to start with the starting materials and make this product. Why the starting materials? Because these are the starting materials that people have argued for many years could be made in Miller-Urey type chemistry that you could somehow get these two form agglomerates and get them separated, people have worked out lots of things where they suggest that they can do this cleanly. Okay, so we'll start with these. And also if you start with your amino nitriles, you have no stereo control here. So starting with these two acids get this product. Paul Rimmer tried to answer this question. And poor Paul, he started with a different material. He started with an amino nitrile. That's not what's given here, plus the Amino nitrile would have never controlled stereochemistry. So everything was planar. You guys know better than that, you've got to show stereochemistry because that's going to be important for making polypeptides. Reza Gadari, a good friend of mine, he and I were in school together. How about your carbonyl sulfide chemistry, which is prebiotic, will this work? Or will it have Sidechain Competition here? How

about Bruce? Bruce Lipschutz? Will your hydrophobic pockets work for this, bring this forward and see if the three judges agree that you could cleanly get this dipeptide in greater than 90% yield? And you say, well, that's a really high yield, that's really not a high yield. Remember, you are going to have to do condensation polymerization. And condensation polymerization is generally need to be in 99.99% yield to give you any decent molecular weight compound. 90% Yield is being very generous on this. This may be the easiest question among all the five. Question number two: polymerize two greater than or equal to a 200-mer, which is actually quite short for RNA, but polymerize, this nucleotide with less than or equal to 2% of the 2'5'-linked, and less than or equal to 2% of the two prime branch system using this prebiotically-relevant chemistry. Is there a method to take this nucleotide, you can take it as the triphosphate or you can take it as an aminazole derivative if you want to? Either way, I'm okay. So you could be the phosphor imidazole, that would be fine to show me how you would polymerize these to the exclusion of the 2'5' prime linkage and to the exclusion of the branching? And so that's the question so you have to be able to make a 200-mer or longer and you can use it with this base or any one of the bases that you want to use. I don't think Steve Benners chemistry address this because Steve Benner had plenty of the 2'5' linkage and plenty of the branching and that's why Jack Szostak said that he went with the hype and not the science. That is the question, take a nucleotide and polymerize it because this is what we're going to have to have. I mean, a YouTuber suggested something I mean, is what he suggested Mount Morlandite clay does that solve it?

U Unknown speaker 12:35

So first of all, this is completely idiotic. Our nuclear nucleotide polymerization has been demonstrated on my Mount Morlandite clay for decades.

J James Tour 12:44

Yes, yes. With 30 to 70% 2'5', I asked you for 3'5', which is what you need to have life. You three are the judges, you guys understand the difficulty with this? You guys understand that these are active hydroxyl groups, you can have branching from here. How do you stop that branching from occurring? And you guys understand that this hydroxyl group can be hooked on to this position to the 2'5' which is a problem here. So we want to be able to solve these problems make this material. That's the question. The question is not whether that you could get it to be active in something the question is, with this, can you polymerize this, limiting the two prime five prime linkage and limiting the branching to less than 2%? In each of those? Now, we'll look at the molecule glucose. So here's glucose, so YouTubers suggest it's no problem getting glucose, because the foremost reaction makes it.

U Unknown speaker 13:35

Foremost most mixed sugars, for most reaction mix sugars, what are you talking about?

J James Tour 13:38

And it does, butit's unusable. You know that, as John Sutherland has said,

J John Sutherland 13:43

but we need to have more constrained chemistry to actually make the right sort of mixtures.

J James Tour 13:48

You have to have more constrained chemistry, you have to have selective chemistry, nobody ever has made glucose in its enantiopure form from the foremost reaction. And nobody has ever even separated what they've been able to make, because it's unusable. And you know, this, the foremost reaction doesn't provide it, but I've given it to you already. Remember, I've given you all the monomeric sugars in 100% chiral form and just so that you understand how gracious it is to be giving you this, here's what nature has to go through to prepare glucose doesn't use the foremost reaction because that would be unusable that material. Just to make glucose, it takes 11 different enzymes, four of those enzymes are unique to glucose formation, and it takes four activators on top of that. So there's 15 different activation steps, enzyme-induced and activator-induced four of those enzymes being unique. And so you have all of these different enzymes, you say, well, this enzyme might form randomly. Well, if this enzyme were to form randomly, it would be 10 to the 6368 possibilities,

U Unknown speaker 14:54

Big numbers, big numbers, guys.

J James Tour 14:56

That would take you more time than 10 of universes. So you know that this is not going to form randomly, and then fold up randomly. I mean, some people think that enzymes can just form randomly without using any of the active enzymes. And then those would fold and make other enzymes. And it's really wishful thinking, but you guys are above that you guys aren't going to propose that kind of nonsense. Got all of these different steps, this is what nature has to go through to make glucose, but I've given it to you, I've given you glucose. And if you add up all the amino acids, all of these polypeptides, it's 10, to the 65,000 possible combinations here, you know, this isn't going to happen. So but I've given it to you anyway. Now, here is the enzyme phosphorylase. This is the enzyme that dimerizes glucose, look at this enzyme, it's 98 kilodaltons, that's a molecular weight of 98,000. It says 842 amino acid units ten to the 1094 possible combinations. And then it has to get folded, right and all of this. So this is what nature has to go through just to dimerize glucose, and all I'm asking you to do is dimerize, glucose. Prepare this disaccharide in greater than or equal to 90% yield from glucose to the exclusion of the other regioisomers. to the exclusion of the furanos on this side, you can have a furanos could open and close here, but to the exclusion of the furanos here, and it has to have this anomer is this is the anomer we're going for. So you've got to control that anomer, and you can't have any of the other regiochemistries. Just show me. I mean, you just dimerize in glucose, for goodness sake, help me out here. Why do I think that this chemistry is so difficult? The world thinks that this chemistry is simple? Why is it what am I missing here? I mean, certainly you guys know that we've made lots of synthetic molecules. We've made lots of complex molecules, we've done this sort of thing. I've done this in my career, why is it that I

have such trouble with this, but YouTubers can provide the answer. I want to know if you guys can provide the answers to these you guys think that we're really not far from cracking this problem? Some of you have even said that, that we're all set up now for Darwinian evolution to take over? Well, let's see, can you even just make the dimer because you guys know that you're going to have to do this 1000s upon 1000s of times in a prebiotically relevant manner. And if you want to say that we started with the sugars, and you can't just say enzymes, I mean, this YouTuber just said, well, enzymes,

U Unknown speaker 17:26

there you go, enzymes, enzymes, did it.

J James Tour 17:29

I mean, come on, who of you is going to give an exam and just say, how would you carry this out? And somebody writes enzymes? Why don't you just write with chemicals? If you think that's an answer, what enzyme? What enzyme is going to do this? It's phosphorylase hanging around here? What enzyme are you talking about? That's why I'm asking you 10 Guys that are real chemists. Show me how you do this. If this is pretty simple, show me how you do it. Question number four, account for the origin of specified information rather than Shannon information. Shannon information is trying to gather information out of random sequences, but specified information embedded in the sequence in polypeptides, polynucleotides, or polysaccharides. Any one of the three, whichever you think arose first, and consider how that would translate its information in irrelevant time. If it's just one polymer molecule, think about that. But the question is, what is the origin of the information? How do you gather together the information you're going to need to build a cell? I don't know YouTubers has said it's already encoded in the DNA

U Unknown speaker 18:36

DNA is inherently information because of the way genes code for proteins when expressed.

J James Tour 18:42

No, that's Shannon information if there's no particular sequence to this, the origin of information critical for life is the origin of information, DNA, RNA, the order in which these things are attached. This information is primary matters, secondary matters secondary, so if I have a thought in my mind, alright, and I write it on a piece of paper, it was stored in into pathways in my brain, now it's written down on a piece of paper. Now I take that paper and I type it into my computer, it goes into a flash memory goes actually into SRAM right away. And then when I hit save, it goes into, into flash memory. Now I take this and I upload it to the cloud. So it goes to an RF wave to the to the box on the wall, wherever that is, and it'll go into that box just to an RF wave. So that information has been here, it's been on a piece of paper, it's been on SRAM. It's been on flash memory, now it's in an RF wave. Then when it hits that box, it goes down a wire, that information is going down to where it goes to a server farm into another flash memory. The matter upon which it resides is secondary. The information is

primary, the information is the key. Nobody knows where this informational code came from. If somebody tells you that the DNA itself is the code, that's a bunch of garbage that's like saying, this this this memory stick, you know, I just bought it memory, I have a memory stick in my pocket. So this memory stick. This is the information. I haven't written anything on it. But that's inherently the information. No, this is the medium upon which it's stored. Where did the blueprint come from? Where did this specified information come from? That's question number four. Question number five, assuming you had access to all the poly peptides that you wanted your choice, whatever you want, all the enzymes you want, that's fine, too. All the poly nucleotides, DNA, all the RNA, and I'll even give it to you in any sequence you want. So you can have any sequence you want I'll give you the information, it's yours. And you have all the polysaccharides, which are the hardest class to make, as you know, all the polysaccharides you want. And I'll give you all the lipids of your choice. Could you in your research group, not on an mindless, early Earth? Even in your research group in your laboratory? Could you assemble those in your lab into an integrated functional living system? Namely a cell? Could you assemble those into a cell? Because I'm lost on this guys, I'm just lost. I don't understand that even if you had all these molecules, even if you could make all these polymers, which I don't think you can, because you can't solve numbers one, two, and three. And even if you had the informational code, the answer to question number four, how would you address in your laboratory not trying to figure out how it did it on a mindless early Earth? How would you figure it out in your laboratory to make the simplest of cells. And remember, a cell is going to have these characteristics, responsiveness to the environment, growth and change, ability to reproduce, have a metabolism and breathe, maintain homeostasis. And that's what constitutes a cell. And you have to be able to pass on traits to offspring. This is the characteristics of life, not my definition, textbook definition. I don't understand why there's this suggestion that we're very close to solving this problem on Origin of Life. My contention has always been that we will get there. But that target is very far away, because it moves away from us faster than we get toward it, because we find out all the complexity of what has to go on here. But you have to solve all five of these questions. In order to make life. I'm just asking you to solve one. For those of you in the research groups, go ahead, just point out to your advisor that this challenge is out there and all they've got to do is answer one of those questions and Jim tour will shut up these guys who work in origin of life are absolutely clueless. Everybody's clueless on this. They were utterly clueless. I'll stop bothering you guys and stop bothering your research group. If you guys just answer one of those questions. I won't talk about origin of life publicly anymore. Origin of life research is a scam. So that's the challenge Guys, help me out here. Teach me you guys understand the chemistry. You understand the magnitude of this challenge? YouTubers don't. But you guys do. I will email you the link to this video. And I'll have those five questions and PowerPoint slides to you and have at it guys. The clock starts now. If you're enjoying this series, give us a thumbs up and click the subscribe button. And that way you'll hear when we're coming out with new videos. There are no salaried employees in this organization, all the accounting, all the legal work, it's all done by friends of mine. The only thing that I have to pay for is the production work. And if you could help us out with that, I'd appreciate it. There's a link below where you can just click on that and help us in several different ways. Thank you