

Stability means the persistence of the message, the degradation of the message. It could be that in certain cells, the message is protected so that it hangs around longer. And, in other cells, perhaps, it's unprotected and it's degraded very rapidly. If it's degraded very rapidly, it doesn't get a chance to make a protein or maybe it doesn't get to make too many copies of the protein. If it's persistent for a long time, it can make a lot of copies of protein.

All of those things can and do occur. Then, of course, there is the regulation at the level of translation. Translation, if I give you an mRNA, is it automatically going to be translated? Maybe the cell has a way to sequester the RNA to ramp it up in some way so that it doesn't get to the ribosome under some conditions, and under other conditions it does get to the ribosome, or some ways to block, in other manners than just sequestering it, but to physically block whether or not this message gets translated. Well, it turns out that there's a tremendous amount of that. It's, again, not the most common, but we're learning, particularly over the last couple of years, that regulation of the translation of an mRNA is important. There are, although I won't talk about them at length, an exciting new set of genes called micro RNA's, teeny little RNAs that encode 21-22 base pair segments that are able to pair with a messenger RNA and interfere in some ways partially with its translatability. And so, by the number and the kinds of little micro RNAs that are there, organisms can tweak up or down how actively a particular message is being translated. So, the ability to regulate translation in a number of different ways is important. And then, of course, there's post-translational control.

Once a protein is made, there's post-translational regulation that could happen. It could be that the protein is modified in some way. The proteins stay completely inactive unless you put a phosphate group on it, and some enzyme comes along and puts a phosphate group on it. Or, it's inactive until you take off the phosphate group. All sorts of post-translational modifications can occur to proteins after the amino acid chain is made that can affect whether or not the protein is active. Every one of these is potentially a step by which an organism can regulate whether or not you have a certain biochemical activity present in a certain amount at a certain time. And, every one of these gets used. This is the thing about coming to a system that has been in the process of evolution for three and a half billion years is that even little differences can be fought over as competitive advantages, and can be fixed by an organism.

So, if a tiny little thing began to help the organism slightly, it could reach fixation. And, you're coming along to this system, which has had about three and a half billion years of patches to the software code, and it's just got all sorts of layers and regulation piled on top of it. All of these things happen. But, what we think is the most important out of this whole collection is this guy.

The fundamental place at which you're going to regulate whether or not you have the product of a gene is whether you bother to transcribe its RNA. But I do want to say because, yes? Which exons are used and which aren't? Yeah, well, there are tissue-specific factors that are gene-specific that can influence that. And, surprisingly little is known about the details. There are a couple of cases where people know,

but as you'd imagine, you actually need a regulatory system in that tissue to be able to decide to skip over that exon. And, the mechanics of that surprisingly are understood in very few cases. And, you might think that evolution wouldn't like to use that as the most common thing because you really do have to make a specialized thing to do that. So, that's what happens on these.

That's one in particular where I think a tremendous amount of more work has to happen. mRNA stability, we understand some of it but not all the factors in this business. I was telling you about translation with these little micro-RNAs. Its stuff that's really only a few years old that people have come to understand. So, there's a lot to be understood about these things. I'm going to tell you about initiation of mRNAs, because it's the area where we know the most, and I think it'll give you a good idea of the general paradigm. But, any of you who want to go into this will find that there's a tremendous amount more to still be discovered about these things.