COVID Information Commons (CIC) Research Lightning Talk

Transcript of a Presentation by Kazushige Yokoyama (SUNY Geneseo) January 30, 2024

Title: Investigating Reversible Aggregation of SARS-CoV-2 Spike Protein-Coated Gold Colloid

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Transcript

Slide 1

Right, thank you very much for your patience. I hope you can see my screen here. Ok, so my talk is focusing on chemistry. I hope it's not going to be too boring for all of you! I'm going to focus on the study which we did for the spike protein of the SARS-CoV-2 virus. That's the icon of the coronavirus, a coronavirus spike-like formation.

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I'd like to acknowledge first my group. Those who were involved heavily are indicated with the bold font. I'd like to thank NSF especially for the major grant.

Slide 3

Talking about spike protein, I want to show you an animation showing the part of the spike protein which has an S1 S2 domain. On the left hand side I'm showing the process which is going so S2 comes in as a receptor that takes off the S1 part. Now the S2 part is going to anchor onto the human membrane. Then, they are going to fold back and merge the virus cell and also the human cell together. Then it spits out the RNA into to the human body which is then infected. This is the intro of the infection so the spike protein plays a huge role to start infection. Also, as you may have heard, the MRNA vaccine basically asks human cells to copy the spike protein and train us to have the antibody to fight against it. So the spike protein can be a little bit of the 'behind the scenes' but it's a very interesting thing to talk about.

Slide 4

The methodology that I like to use here is - since I'd like to focus on only spike proteins, I don't want to think about the rest of the virus part. So simply, to just try to anchor or place the spike protein on the particle. In this case, I'm going to use a gold nanoparticle, a gold particle. It has the two parts accepting the S2 and also taking off this S1 part. Then the S2 part is the fusion protein part that you saw in the animation. It's going to go onto the cell and try to merge.

Slide 5

Now, the first question of course is does this spike protein attach onto the gold surface? Nobody knew. So I took the microscopy which uses the electron to probe the object. As you can see, it's very fuzzy thing but so excited to see this. If you focus on the left hand side and look at the edge of the this gold nanoparticle, a dark sphere, then you see a very fuzzy part which is spiking out definitely. So it's really obvious compared to the case when you have an acidic condition. Then, two things happen: number one that if you take a look at the surface of the gold nanoparticle, there's no fuzzy thing. So it's actually acting like a sheet. Then at the same time they are trying to make friends with other nanoparticle and they try to attach to each other so they're making interactions. That's actually a cue for the next point that I like to make. The reason why I'm am so interested in doing spike proteins is the thing that we have in the paper reporting that the spike protein is making amyloidogenesis. It's making fiber. So it's similar to what you observe in Alzheimer's disease. In that case amyloid beta is the major thing that the people think is a cause of the fiber. That is the reason - the major motivation.

Slide 6

Now, I'm sure that you are asking why I want to use a gold nanoparticle. Here is the first reason why: because they have color so that I can actually monitor what's going on. For example, if I can use the example for aBeta 1-40 - that's the iconic protein for Alzheimer's disease - then for pH7 or pH10, so either neutral or basic conditions, then they don't want to make aggregates. They just want to keep the structure of the protein as folded. So they are not welcoming to interact with each other and it has the color of the red. However if you make it Ph4, which is an acidic condition, then we can control the structure of this protein. They they unfold, and then they're going to welcome or invite other proteins and they start connecting gold to each other. So you can see that the chunk of the aggregates here. Then, the color also changes into blue. So by looking at the color of the solution, we are able to tell what's going on on the protein on the surface of gold, so that's the huge advantage.

Slide 7

Also, another thing is I want to show you this example. This is very artistic, I think, but this is actually coming from the gold colloid aggregates. Gold colloid aggregates have the amyloid beta on the top. My point here is that by creating gold colloid aggregates, we are able to make the stage to detect something which would contain protein- protein induction. In other words, if there's no interaction between proteins, in this case spike proteins, then you won't see the

aggregate. So the finding that gold colloid aggregate, this chunk of particles that's showing that we have something to study about the protein-protein interaction.

Slide 8

This is a little bit busy and I'm hesitant to sort of go fast, but what you're seeing here on the left hand panel is - it's like a doing the experiment. So this is what exactly we did. We actually add acid or base externally and make the pH condition either 4 or 10 back to back. Why do we do this? Because we want to see if the protein colloid gold aggregates can make a disassembly. Either make aggregates or disassemble so that we can - if we can control the structure of the protein on the top of the gold. In this case, we see that things are actually going quasi-reversible. We can actually plot that the peak - it's it's not exactly reversible but we can see it's going back and forth. This video is not really synchronized with this panels but they're actually showing the idea - I think it gives you idea what kind of color you will see. This is great. This is what we probably expect to see if the spike protein is attached. Also, we'll see if they perform the same way that amyloid beta 1-40 does.

Slide 9

Here is the result for the spike protein. I am plotting the the peak shift. As you can see above, it goes back and forth. In this case, if you're wondering I'm showing lots of the waves here so it actually has a label of D from 10 to 100 nanometers. What I did here is I changed the core size of the gold nanoparticle and see if there's a certain threshold that they start making this reversible process of aggregation. Then you can see that clearly between 20 and 30 there is a difference so that it has the point that the spike protein seems to attach and then make the reversible process if the size of the core is larger than 30 nanometers. From the report, as far as I know, the size of the spike protein overall is reported to be 100 nanometers. Therefore the spike protein I think report says to be about 10 nanometers. I think the the spike protein that we are seeing is a case that corresponds to when d equals 80 nanometers. There's a 10 nanometer spike sticking out. Now my point here is I'm so excited to see that the spike protein can make aggregates. That is actually the reason why I wanted to study so that it has the good stage that they were able to study how they are going to make an interaction and leading to the fiber.

Slide 10

So that's pretty much the things which are done. In the rest of the three or four slides I'm going to talk about the study in progress. I have two questions to ask: number one, I know now that the spike protein colloid gold can make aggregates. That's good. However, how does the spike protein absorb on the gold surface? What's the first stage to go into the nanoparticle? Then question number two is: what is the structure or like a confirmation of the spike proteins when they forming aggregates? For that, I recently published a paper which talks about the amyloid beta 1-40 reaching to the gold surface. It actually revealed that benzene ring contain part of Y or F approaches to the surface. After that, beta sheet formation is used to network the protein. That could be maybe the hint or maybe could be the answer for the spike protein case. For that study I use this - it's kind of confusing, but it's not SARS, it's SERS, it's Surface Enhanced Raman

Scattering imaging. This is basically images created using raman signals. This is another reason why a nonoparticle of gold was used, because it has a huge signal on the top of the gold surface.

Slide 11

Very quickly, I just want to talk about the preliminary result. When I have the spike protein called the gold colloid and am trying to see the raman imaging, I Imaging I was successful to get the raman imagine. Like a thermal camera - if you see the people then you have a different temperature, different color - I'm actually showing this as a spectroscopically different color corresponding to different component of spectrum so that you can actually image the particle. This is the gold nanoparticle aggregates with spike protein has different component. I have been successful to find out some of the part which is around this region called the fingerprint region. It's well studied we know what kind of motion of the molecule is going on but I'm more interested in the part which is not well reported. This is the part that I'm trying to study harder.

Slide 12

Also, it's possible to make three-dimensional slides of the spectrum and find out the particular section of the networking or not networking part.

Slide 13

Also, lastly, you are able to make the mobile section of the spike protein by adding the ACE2. This is the trigger of the infection, and then you are able to make the colloid aggregates to be mobile because of the ACE2.

Slide 14

That allow us to study which section of the spike protein would be mobile. This is just trying to show you that the video and also the image. I can actually tell which part of the color corresponding to the mobile sections.

Slide 15

Sorry I'm going too long, but this is my conclusion. I have three conclusions: the spike protein likely absorbs onto the gold surface and also the spike protein coated gold nano-particle can form aggregates and can be used for studying further details. Also, by adding the ACE2, we are able to create different set of the study to find out the mobility of the spike protein. Thank you so much.