**Biochem COVID: Research Paper I Activity. ACE2 – Spike Protein Paper Discussion**

For this activity, you will read and analyze a pre-published paper on SARS-CoV-2 S Spike protein. Before (and after) you read the paper, watch the informative interview by the author Dr. Procko linked from your resource page. This activity can work in groups to discuss the paper but the assignment MUST be done independently.

1. Watch the interview from Dr. Procko and the zoom recording of Dr. Provost’s discussion of some of the methods including flow cytometry.
2. Read the [paper](https://www.biorxiv.org/content/10.1101/2020.03.16.994236v1?fbclid=IwAR3b-8BEVi-LKb6zr2u22T6fkykg4zYXYgvsdegl9I9lBHYfsVcSLc5fjYs) and look up questions on techniques and terms you may be unfamiliar with. We will have a help session devoted to these types of questions. I have also provided a video discussing the key assays / methods of the paper. You should watch this to help to get to the heart of the paper…
3. Answer and submit your answers to each question via the LMS.

**Questions to answer.** Work with your video presentation group to discuss and answer these questions. Submit one answer per group. Ensure all names of the participants are recorded. IF someone did NOT engage in the process, you may email or zoom me. You may need to go back to the videos your peers made to understand some of these concepts.

1. What was the big picture purpose of the paper?
2. The method used two fusion proteins: Myc and GFP. What are these fusion tags/proteins and how were they used in this paper?
3. Recalling Dr. Procko’s description of deep mutagenesis and reviewing the methods section of the paper, can you simply describe how he generated so many mutations of the ACE2 receptor?
4. In broad terms, describe how Dr. Procko used cells expressing ACE2 receptors and S protein-GFP to identify protein – protein interaction between the two proteins?
5. In the results/discussion section the author states “.. shows that residues buried in the interface tend to be conserved, whereas residues at the interface periphery or in the substrate-binding cleft are mutationally tolerant”. What does it mean to be “conserved” or “mutationally tolerant” in this context?
6. Consider that same paragraph of the results/discussion section). In your words, describe how the S protein and ACE2 receptor interact.
7. In the next section,– interpret the role post translational modification plays on S protein binding.
8. Lastly – using the information provided in this paper, is the S protein – ACE2 receptor a good “fit”? Do these proteins bind optimally? Could other S proteins from SARS or MERS bind differently? How could you determine this?
9. How could the results of this paper be used in an applied or practical sense? Think really big picture here…