Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 patients that are severe or critically ill have impaired interferon (IFN) response. IFNs are critical in promoting the transcription of IFN-stimulated genes (ISGs), many of which have antiviral functions. Martin-Sancho et al. screen ISGs and analyze a subset that impede SARS-CoV-2 replication, presenting a network of SARS-CoV-2 antiviral effectors that target different stages of the viral infectious cycle.

Tell us a bit about yourself. What motivated you to become a scientist?

L.M.S.: I grew up in Valladolid, a relatively small city in Spain. As a kid, I was an avid reader, and for years I thought my path was to become a literature teacher. Everything changed in high school when I started advanced biology classes and I learned about the double helix and other incredible scientific discoveries. I was fascinated and I knew I wanted to become a scientist.

S.K.C.: My parents came to the US from India to do their postdocs in biochemistry, so science was always in my family. Ironically, they advised me not to go into science. However, discussion of science at home, in conjunction with some incredible teachers in high school and college really ignited my passion for research. Once I started wet bench internships in college, I had no opportunity to look back—I was hooked.

Talking about being inspired, are there any particular mentors who helped guide you on your path?

L.M.S.: I am incredibly lucky that both my parents and my brother were very intellectually stimulating and always encouraged me in following my own path. For getting interested in microbes and becoming a virologist, I have to thank my fantastic PhD mentor, Thomas F. Meyer, and my co-mentor and fantastic virologist, Wendy Barclay. As a biochemist doing a PhD in virology embedded within a predominantly bacterial-focused lab, her knowledge and guidance were a tremendous help.

S.K.C.: I had the fortunate opportunity to do internships in both Ananda Chakrabarty (UIC) and Inder Verma’s (Salk) labs before I went to graduate school. I remember that the intellectual excitement and prospects for discovery were palatable in those environments. My experiences in those labs continue to shape my thinking and science.

Laura, tell us about your journey to your doctoral studies?

L.M.S.: I did my Bachelor’s in molecular biology at the University of Salamanca, Spain, and a Masters in Biochemistry between the University of Oviedo in Spain and the University of North Carolina at Chapel Hill in the US. After a very inspiring and exciting year of laboratory training at the Max Planck Institute for Molecular Genetics with Sylvia Krobitsch, I started my PhD at the Max Planck Institute for Infection Biology under the supervision of the very talented microbiologist Thomas F. Meyer.

And then what drew you to pursue your postdoc in Sumit’s lab?

L.M.S.: During my PhD in Germany, I studied the tropism of zoonotic influenza A viruses and became very interested in emergent viruses and those with pandemic potential. I met my current postdoc supervisor Sumit Chanda at a conference in Riga. His lab was using functional screening to study host-pathogen interactions for a wide range of human viruses including influenza, dengue, and zika. I thought his lab was a perfect fit for me and I applied for a postdoc position once I graduated. A few months later, I was moving across the world to join his lab in San Diego, US. Little did I know that years later I would be in the middle of a pandemic investigating SARS-CoV-2 host restriction.

Sumit, tell us what drew you to this area of research?

S.K.C.: I did my graduate work in Silicon Valley during the first dot com boom, where I really began to appreciate the role of technology in discovery and innovation. So being a technologist at heart, our lab leverages bleeding-edge...
platforms to understand host-pathogen interactions, unravel new biology, and find novel therapeutic strategies for critical unmet medical needs.

Speaking of Silicon Valley, where is the lab based currently?
S.K.C.: The lab is located in sunny La Jolla, California. We all draw from the natural beauty of southern California to inspire our science.

How has the research focus of the lab evolved over the years?
S.K.C.: A little over a decade ago, we started the lab focusing on systems-level analysis of host-pathogen interactions. It has been exciting transition for the lab to take these global surveys and drill down to novel mechanistic understandings and to leverage this novel biology toward the development of new therapies for unmet medical needs. Having spent about a decade in pharma, bringing together technology, biological discovery, and drug development is an exciting nexus of our research expertise and ability to have an impact on human health.

Let’s talk about the paper. Why did you start working on the project?
L.M.S.: I always found it fascinating how viruses that have a limited coding capacity can subvert our cells’ highly sophisticated antiviral programs. Though our initial studies on SARS-CoV-2 were focused on small-molecule screening and drill down to novel mechanistic understandings and to leverage this novel biology toward the development of new therapies for unmet medical needs. Having spent about a decade in pharma, bringing together technology, biological discovery, and drug development is an exciting nexus of our research expertise and ability to have an impact on human health.

S.K.C.: Like Laura, I have been always been intrigued by the ruthless efficiency of RNA viruses—in the case of the current pandemic, how do a series of ~11 genes bring the world to its knees? The inspiration for this project stemmed from the early implication of innate immune responses in determining disease severity. We felt it would be critical for us to understand the compendium of innate effectors that underlie frontline immune control.

What was your first experiment?
L.M.S.: The first experiment for this project was after receiving the first vial of 100 μl of SARS-CoV-2 at the beginning of the pandemic, having to figure out appropriate cells and ideal conditions to propagate this novel virus to high enough concentrations to enable these experiments.

What previous advances were particularly important for the project?
S.K.C.: This work was inspired by groundbreaking studies from Charlie Rice and John Schoggins on determining global effector functions of ISGs across viral families.

How important was collaboration to the success of this project?
L.M.S.: I am very thankful to all the labs that helped us do this work considering the time constraints and the lockdowns. Specially, I would like to mention the Gattelli lab. Their expertise and scientific input were critical to characterize BST2 as a negative regulator for SARS-CoV-2 replication and its antagonism by viral Orf7a. Besides, they are a lot of fun to work with.

Given the lockdowns and social distancing guidelines, did you get an opportunity to celebrate the acceptance of your paper?
S.K.C.: We have yet to formally celebrate acceptance of any of our papers that have published during the pandemic. However, we hope to visit a favorite Michelin restaurant in San Diego soon to acknowledge all of the hard work, dedication, and sacrifice the scientists in the lab have made during the pandemic.

Sumit, speaking of the pandemic, what’s next for the project and the lab?
S.K.C.: Our lab is now planning to redouble our efforts on pandemic preparedness. This will not only involve developing novel prophylactic and therapeutic strategies to target viruses with pandemic potential, but to gain fundamental molecular understanding of viral-host interfaces that drive zoonotic transmission and disease pathogenesis.

And finally, Laura, what advice would you give aspiring young scientists?
L.M.S.: Rejected grants, long publication processes, and periods of negative data can be sometimes overwhelming. Remember why you became a scientist, be passionate about your work, and don’t lose the joy of planning a well-controlled experiment or getting excited about the results. Also, there is life beyond the lab and hobbies are important. Meeting friends, doing yoga, and surfing are mine.

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