Editorial overview: Host–microbe interactions: viruses: Viral sensing and activation of immunity

Maria-Carla Saleh

Editorial overview: Host–microbe interactions: viruses: Viral sensing and activation of immunity

Maria-Carla Saleh

Department of Virology, Pasteur Institute, France

A year before receiving an invitation to edit this special issue of Current Opinion in Microbiology, I attended a frontier conference on Non-Self RNA sensing organized by Jean Luc Imler and Raul Andino at Fondation des Treilles. At this conference, it became clear that although we know that the innate immune system recognizes nucleic acids and/or viral components during viral infection and stimulates cellular antiviral responses, very little is known about the players, interactions and exact mechanisms allowing this system to perform.

I decided then, to take this opportunity to develop a special issue on *Viral sensing and activation of immunity* in bacteria, plants, invertebrates and vertebrates. My original intention was to provide an overview of our current knowledge regarding the receptors used to detect virus invasion, the molecular structures these receptors sense, the downstream signaling pathways involved, and the evolution of cellular sensors.

Through the different contributed articles, I hope you will have a sense of the current knowledge in the different kingdoms. For instance, in the first chapter L. Debarbieux discusses the interactions between bacteriophages and bacteria and the importance of this interaction on tripartite relationships: bacteriophage – bacteria – human. He offers insight on how the codes alerting or concealing a phage's presence are deciphere and the consequences on microbial evolution. A clear insight of what is happening in eukarya comes from the review of Padmanabhan *et al.*, in which they discuss how plants use the intracellular Nucleotide Binding domain Leucine Rich Repeat (NLR) class of receptors to recognize viral proteins and initiate an orchestrated signaling cascade aimed at killing infected cells and restricting viral spread. Climbing the tree of life, Lamiable *et al*. confront us with the fact that almost nothing is known about the mechanisms involved in the sensing of viruses in the insect model *Drosophila melanogaster*. The fruit fly has been the model of choice for developing ideas about innate immunity and host–pathogen interactions, yet viral sensing remains poorly characterized.

Not surprisingly, most of the knowledge gathered over the years, come from mammalian systems. In an exquisite way, Fitzgerald *et al.* and Yoo *et al*. take us on a hand-held visit through the world of RIG-I like receptors (RLRs), their domains of unique recognition, strategies of virus evasion and the multiple cellular pathways engaged to assure an efficient antiviral immune response. Kindler et al and Weber et al, expound the intricacies of sensing and sensing evasion by two very different virus models: coronaviruses (such as SARS and MERS-CoV) and segmented negative-strand RNA viruses (sush as influenza virus or Lassa virus). These two reviews carefully delve into the interactions between viral genomes, cellular responses and host-pathogen coevolution, offering hints on future research directions to dissect viral sensing and activation of immunity throughout the species and taxa.

This overview would not be complete without a perspective on evolution of viral sensing. Considering the very little information available, this herculean task fell upon the shoulders of Lewis et al., who discuss the constraints of viral sensing, arms race and a faster evolution of viral sensors compared to other microbe sensors.

Going through the process of putting this issue together, I noted a common trend: we know much more of the downstream cascades and events following viral infection than the initial steps of virus-cell interaction and the sensing of viruses by cells. Understanding downstream processes could provide hints on the upstream process remaining to be deciphered and the availability of new techniques such as next generation sequencing and “omics” (as discussed on Lamiable *et al*.) should facilitate our task.

Studying model organisms other than mammals, as put in evidence by the work of Debarbieux, Padmanabhan *et al*., Lamiable *et al.,* and Lewis *et al*., could provide a richness of information not foreseen before. After all, viral pathogens are present in all species described (from single cell bacteria to animals, as well as plants) and organisms have systematically developed mechanisms to detect and prevent viral infection. A whole complexity awaits and we will surely be thrilled in years to come by the discoveries in the field.

Given the limitations of space and my own natural bias toward all things RNA, I could not sign off this introductory piece guilt free without apologizing for noteworthy research that did not land in these pages, such as the discovery of the cytosolic sensor cGAS, the description of the role of cGAS-cGAMP pathway on immune defense, and more generally, all the work related to microbial sensors, including but not only those involved in RNA sensing, which altogether have greatly contributed to a better understand of the different degrees of essentiality and redundancy of innate immune systems. I can only hope that this set of reviews will, if nothing more, draw us all deeper into the world of sensing to discover what's been eluding us all for years.

Maria-Carla Saleh has a MSc in Biology from the National University of Cordoba, Argentina, and obtained a PhD in Molecular and Cellular Physiopathology from the University of Paris VI. In 2002, she worked for six years as a postdoctoral fellow at the University of California, San Francisco where she focused on RNA interference (RNAi) as the main antiviral immune response in insects. Since 2008, she runs her own laboratory in the Department of Virology at the Pasteur Institute in Paris, France. Using a combination of experimental and bioinformatics approaches, her lab wants to uncover fully the mechanism of antiviral RNAi in insects and its main attributes, such as long-lasting immunity, specificity, and effect on the virus.