Podcast Interview: Francesco Pennacchio

PNAS: I’m Jessica Johnson. Welcome to Science Sessions.

Colony collapse disorder emerged in 2006 as a mysterious killer of 30% to 50% of honey bee hives on average across the northern hemisphere. Today, no direct cause of the disorder has been identified, but many researchers agree that it is likely triggered by combinations of factors that may include exposure to pesticides, parasitic mites and other pathogens, poor nutrition, and compromised immunity. I spoke with Francesco Pennacchio, a professor of entomology at the University of Naples Federico II, about his investigation into one potential aspect of colony collapse disorder – the apparent immunosuppressive effect of neonicotinoid insecticides on honey bees. Pennacchio and his colleagues published their results in a PNAS paper titled, “Neonicotinoid clothianidin adversely affects insect immunity and promotes replication of a viral pathogen in honey bees,” for which they earned the 2013 Cozzarelli Prize for excellence and originality in the Applied Biological, Agricultural, and Environmental Sciences.

PNAS: Franco, how did you become interested in investigating the potential link between neonicotinoid insecticides and immunosuppression in honey bees?

Pennacchio: There were several reports in the literature showing that bees exposed to neonicotinoids were more highly susceptible to pathogens and parasites. So there was some kind of immunosuppression mechanisms going on, but nobody knew at that time what was the mechanism controlling this kind of immunosuppression response. What we did is to start first with some basic studies on Drosophila, a model system. Indeed what we discovered first in Drosophila was that we had some leucine-rich repeat protein which when an immune response is triggered by infection, they are downregulated in order to allow an immune response to be produced by the fly. And these negative modulators are essential for controlling the immune response in order to avoid an overreaction which could be detrimental to the organisms.

PNAS: Did exposure to neonicotinoid insecticides change the way in which these leucine-rich repeat proteins modulated the immune response?

Pennacchio: With Drosophila we discovered that neonicotinoids were indeed upregulating this negative regulator. With this in mind we switched to bees and what we observed was that the presence of neonicotinoids like clothianidin was upregulating the expression of these leucine-repeat rich proteins and this upregulation resulted in a reduced activation of NF-κB, a transcription factor which is important in modulating a number of stress responses and immune responses in animals.

PNAS: What are the consequences of a depressed immune response in honey bee colonies?

Pennacchio: Deformed wing virus is one of the major viral species associated with colony decline. This deformed wing virus has the capacity to be strictly associated with bees in a form of infection which is asymptomatic. The virus is vectored by the Varroa mite, and in those areas
where the *Varroa* mite is present, this virus is present in nearly all colonies of bees. So the virus is there but is not causing any problem with the bees. As soon as you may have other stress factors in place, like *Varroa* mites or like poor nutrition or like neonicotinoids, which are in some way interfering with the antiviral immunity, you may have that this kind of negative influence can enhance the replication of viral pathogens. When the virus starts to replicate and then is causing trouble because the viral titer increases, you may have that the bees can be seriously influenced and can die.

**PNAS:** So in your research you found that two different neonicotinoid insecticides decreased activation of NF-κB which resulted in suppression of the immune response and increased titers of the deformed wing virus in bees. You didn’t get a similar result when you tested organophosphate insecticides. Can you explain why?

Pennacchio: The organophosphates are not acting like neonicotinoids because they have different modes of action. And probably, what we speculate, is that these neonicotinoids, which are agonists of acetylcholine receptors, can indeed act on immune cells which have receptors for that kind of neurotransmitters, which indicates that insects like in other animals including humans and vertebrates, there could be neural circuits controlling immune response by the nervous system. So there is no doubt that it will be interesting in the near future to investigate in depth how it works, this cross-modulation between the nervous system and the immune system in insects.

**PNAS:** How significant is the role that neonicotinoids play in colony collapse disorder?

Pennacchio: We have shown that it can interfere with the immune response and by doing that they can modulate indirect mortality caused by the proliferation of pathogens associated with bees. This means that if you have healthy colonies with a low level of viruses, the same amount of sublethal doses of neonicotinoids is harmless to the bees but if you start with bees which are already highly stressed by considerable level of viral presence, presence of *Varroa* mites, other kinds of stressors in the environment, then even short exposure to sublethal doses of neonicotinoids can add significant stress to the whole system. Neonicotinoids can contribute to colony decline and collapse but there are different factors that can interact in a synergistic way. The neonicotinoids are a problem but it’s not the only problem that we have to face to solve the colony collapse problem.

**PNAS:** Thanks for listening. The Cozzarelli Prize is awarded annually by PNAS to acknowledge recently published papers that reflect scientific excellence and originality. You can find Science Sessions podcast interviews with all of the 2013 Cozzarelli Prize winners at PNAS.org.