

The dedicated insect researcher

How do pest insects become resistant to crop protection agents? This is just one of the many questions to which Dr. Ralf Nauen of Bayer CropScience is searching for an answer. The insect toxicologist studies resistant pests and, together with his team, develops solutions to make farming more sustainable.

When caterpillars, beetles or aphids attack fields and no crop protection agent is able to stop them, it's time for Dr. Ralf Nauen to step in. Although new, powerful insecticides are being developed all the time, insect pests can adapt to their environment and rapidly evolve mechanisms that render insecticides less effective. Resistance mechanisms in crop pests are the subject of the insect toxicologist's research at Bayer CropScience. Together with his team, Nauen studies how modern insecticides become harmless to some voracious insects – like the pollen beetle, a hugely magnified image of which appears on a poster hanging over his desk. "There is a risk of massive crop losses when crop protection agents become ineffective against pest insects," the biologist explains. "The development of resistance in insects is one of the greatest challenges facing modern farming today." This universally acknowledged problem was a touchy issue for a

long time, and few industry researchers were prepared to talk openly about it. But Nauen was opposed to this stance. "It is our responsibility to provide information on this subject," the dedicated insect researcher says. Accordingly, it is hugely important to Nauen for all research results to be published. The Bayer expert has published over 150 scientific articles which have been cited over 4,000 times worldwide, and presented hundreds of papers on the subject. What's more, his forthright attitude has been an encouragement to the entire research community. "Many external researchers get in touch with us today because of our proactive approach, enabling us to establish an outstanding network – and gain valuable new insights," Nauen says. Using this knowledge, Bayer's scientists can develop new solutions to keep insect pests in check. "Our resistance research unit is one of the top addresses in the world in the field of pest control," he says proudly.

From child bug-hunter to dedicated insect researcher

But behind every success is a good team, as Nauen repeatedly emphasizes. "Without my practiced team in the laboratory, we would not be where we are today," he maintains, adding, "Research is all about teamwork." He is constantly in contact not only with his eight co-workers and junior researchers, but also with renowned scientists around the globe. For Nauen, working in the laboratory with his team is another matter close to his heart, because research is not just a job, it is part of his hobby: nature. Even as a child, Nauen was fascinated by insects and spent time outdoors collecting specimens. Today he combines this recreational activity with another passion of his: hiking. "I'm always on the go. After a long day at work, I need the change: cooking together with my wife, watching a movie, traveling over the weekend or meeting friends," Nauen says. The biologist is communicative by nature and cultivates close ties with his co-workers, as evidenced everywhere by the positive team spirit. "We not only have a great deal of freedom to do our own



Tracking down pests: as Dr. Ralf Nauen well knows, an infestation of pollen beetles can lead to extreme harvest losses. One of the insect toxicologist's fields of interest is the resistance mechanisms of this pest.



Successful team: for Dr. Ralf Nauen, shown here with his colleague Antje Rottmann, research is all about working in the laboratory with an established team while also being able to engage in dialog with scientists all over the world.



Always on the go: as a resistance manager, Dr. Ralf Nauen not only studies scientific literature (photo above), but also conducts research in the lab together with his doctoral students Denise Steinbach and Marion Zaworra (photo right, left to right). In 2013, he was given the Fellowship Award by the Entomological Society of America (photo below, right). Nauen enjoys getting back to nature by going hiking (photo below, left).



research, we also benefit from the experience and tremendous intellectual capital in the department," says doctoral student Marion Zaworra.

The development of such outstanding know-how at Bayer CropScience is also to Nauen's credit. He began his training as a biology lab technician at Bayer in 1981 and then worked in the field of insect biochemistry. "An early collaboration with a doctoral student inspired me to pursue a scientific career, which my supervisors and Bayer both supported," Nauen recalls. For his doctoral thesis he studied insects and how they absorb, metabolize and eliminate certain active ingredients. "Most of them break down insecticides in the digestive system and neutralize them there. The longer this process takes, the better for the efficacy of the product," he explains.

Duel with pests makes necessary different strategies and active ingredients

However, some insects have a natural talent for metabolizing the active ingredients very rapidly. They survive the insecticidal attack and continue to reproduce. After several years, virtually the entire pest species becomes resistant. "That can only be pre-

vented by using mixed strategies, in other words varying products and confronting the pests with different active ingredients," Nauen says. Random mutations are another cause of resistances, such as the dreaded target site mutation, where a molecular change occurs in the target structure – i.e. the site where the insecticide docks – in just one insect in a billion. The substance can no longer take effect, the pest survives and multiplies. "Mutations of this kind are difficult to predict and can take decades to become established," explains Nauen, who today works in Research & Development in Product and Project Support/Life Cycle Management, part of the Pest Control department. There Nauen supervises resistance management, precisely what he aimed for 30 years ago. "I am just as fascinated by my work today as I was back then. The only difference is that the research questions have changed and the responsibility has increased," he says. And the challenge also has its rewards: for example, Nauen is a fellow of the Royal Entomological Society in London and the Entomological Society of America, and in 2014, the Bayer expert received the International Award for Research in Agrochemicals from the American Chemical Society, one of the world's largest and most influential research associations. Nauen was also president of the Insecticide Resistance Action Committee for five years, lon-

Survival artists: bees



Bees are insects. Developing an active ingredient that eliminates voracious beetles but spares beneficial bees is one of the challenges facing the Bayer team of researchers headed by Dr. Ralf Nauen. For this purpose, they must identify which natural detoxification mechanisms are used by honeybees, bumblebees and solitary wild bees to metabolize specific chemical substances that are toxic to other insects. The insect researchers have now discovered a number of enzymes involved in this process. They plan to take the genetic blueprint of these enzymes, incorporate it into insect cell lines, and then utilize the modified cells for selectivity investigations. The researchers can then determine how the bee gene responds to other chemical substances, and facilitate research outside the bee season.

ger than anyone else before him. One of the most important achievements for Nauen and his team involves the tiny pollen beetle whose likeness hangs in his office, and which can cause widespread devastation. "This beetle developed alarming resistances to all known insecticides. It destroyed entire oilseed rape crops in 2006 and 2007," Nauen remembers.

The problem was that all the insecticides used belonged to the same substance class, the pyrethroids, and had a similar mode of action. Naturally resistant beetles multiplied for decades unimpeded and the insecticides became ineffective. Nauen's team analyzed the resistant beetles and tracked down the molecular mechanism protecting them. Based on these findings, they worked with government authorities to develop new control strategies. "It is important to recognize and minimize the risk of resistance development at an early stage," Nauen explains, "because insects that produce several generations a year can develop resistance in a very short time due to the corresponding selection pressure."

Analyzing molecular mechanisms and tracking down new targets in insects

But Nauen and his team face other challenges as well: for example, the process governments use to approve new insecticides is becoming increasingly strict. One important requirement, for instance, is that insecticides must spare bees, which can likewise suffer from the effects of an insecticide if it is used incorrectly. "We therefore study what distinguishes bees from other insects on a molecular level," Nauen explains. "For example, which detoxification mechanisms enable them to tolerate certain active ingredients and which genes are responsible for these mechanisms." In collaboration with other colleagues, he wants to find out which target structures the active ingredients must attack



Teaming up to combat pests: Dr. Ralf Nauen (4th left) is researching new strategies with his colleagues Harald Köhler, Bettina Lueke, Dr. Cristina Manjon, Ángel David Popa Báez, Denise Steinbach, Marion Zaworra and Antje Rottmann (left to right).

to avoid harming beneficial insects. "Then we can subject crop protection substances to much better tests to determine if they are safe for bees, and design modern insecticides to have a more targeted effect," says Nauen, defining his goal. "Research is a never-ending process. To me, that means research is all about teamwork," he concludes.



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