Herbicide discovery and herbicide resistance: A case of a tail wagging the dog

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"The tail wagging the dog" is an idiom that means something less important is controlling something more important. In this context, the misuse of herbicides is driving the rise in the number of herbicide resistance cases. To illustrate this, we will first review the history and current status of the agrochemical industry and describe why the discovery and commercialization of new herbicides with novel mechanisms of action has decreased dramatically over the last several years. Then, we will survey a few startup companies utilizing novel approaches to provide new tools for weed management. These diverse new tools broaden the scope of discovery, encompassing advanced computational, bioinformatic, and imaging platforms, plant genome-editing and targeted protein degradation technologies, as well as machine learning and artificial intelligence (AI)-based strategies. These new technologies are needed to fulfill the need for more environmentally and toxicologically safe herbicides and to combat fast-growing herbicide resistance.

In the second part of this presentation, we will review how weeds evolve resistance to herbicides and differentiate target-site resistance (TSR) and nontarget-site resistance (NTSR) mechanisms. TSR often involves mutations in genes encoding the protein targets of herbicides, affecting the binding of the herbicide either at or near catalytic domains or in regions affecting access to them. Some herbicides bind multiple proteins, making the evolution of TSR mechanisms more difficult. In these cases, increased amounts of protein target, by increased gene expression or by gene duplication, are an important TSR mechanism. NTSR mechanisms include reduced absorption or translocation and increased sequestration or metabolic degradation. The mechanisms that can contribute to NTSR are complex and often involve genes that are members of large gene families. The vast array of herbicide-resistance mechanisms will be illustrated using examples from Palmer amaranth and kochia, two species with great evolutionary resilience to extreme selection pressures imparted by herbicides. These evolutionary processes drive herbicide and herbicide-resistant crop development and resistance management strategies.