Overcoming multiple herbicide resistance

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(Phys.org) —British scientists from several research facilities across the country have found that an enzyme called *glutathione transferase* which is known to neutralize toxins meant to stem the growth of tumors in humans, also appears to be responsible for helping two kinds of invasive grasses develop multiple herbicide resistance (MHR). The team has published the results of their study in the *Proceedings of the National Academy of Sciences*.

Black-grass and rye-grass are considered by farmers, to be weeds. They are not only invasive—causing reduced yields in fields where they mix with crops—but can also harbor ergot, a type of fungus that can spread to crops, killing them. For these reasons, farmers have used herbicides to keep the grasses at bay. Unfortunately, the grasses have begun to develop immunity to the toxins traditionally used to kill them. In this new effort,

the research group has found what appears to be the source of the plants' new-found strength, and perhaps, a way towards creating a new way to kill them.

Specifically, the team found that a gene called AmGSTF1, appears to be responsible for causing overproduction of an enzyme called *glutathione transferase*. In plants, the result is the production of more than normal amounts of antioxidants, which help ward off the toxins meant to kill them. The team made this discovery by adding the AmGSTF1 gene to thale cress, which does not have MHR. Doing so, they found, caused the thale cress to become just as resistant to herbicides as black or rye grass. Interestingly, the same enzyme has been found to be at least partly responsible for doing something similar with tumors that grow inside of humans.

Because the enzyme has been known to help tumors in humans fight off toxic drugs, researchers have developed another drug called 4-chloro-7-nitro-benzoxadiazole—it blocks the production of *glutathione transferase* and as a result makes tumors easier to kill. Because of that, the researchers studying the invasive grasses tried spraying it on the thale cress that had been made resistant to herbicides and found that doing so caused it to lose its new-found abilities and to be once again susceptible to the chemicals meant to kill them. Unfortunately for farmers, the same drug cannot be used on invasive weeds because it's toxic to people as well. But, the researchers suggest another similar drug might be developed that could do the job without harming those that eat the crops the farmers are trying to protect.

More information: Key role for a glutathione transferase in multiple-herbicide resistance in grass weeds, *PNAS*, Published online before print March 25, 2013, doi: 10.1073/pnas.1221179110

Abstract

Multiple-herbicide resistance (MHR) in black-grass (Alopecurus myosuroides) and annual rye-grass (Lolium rigidum) is a global problem leading to a loss of chemical weed control in cereal crops. Although poorly understood, in common with multiple-drug resistance (MDR) in tumors, MHR is associated with an enhanced ability to detoxify xenobiotics. In humans, MDR is linked to the overexpression of a pi class glutathione transferase (GSTP1), which has both detoxification and signaling functions in promoting drug resistance. In both annual rye-grass and black-grass, MHR was also associated with the increased expression of an evolutionarily distinct plant phi (F) GSTF1 that had a restricted ability to detoxify herbicides. When the black-grass A. myosuroides (Am) AmGSTF1 was expressed in Arabidopsis thaliana, the transgenic plants acquired resistance to multiple herbicides and showed similar changes in their secondary, xenobiotic, and antioxidant metabolism to those determined in MHR weeds. Transcriptome array experiments showed that these changes in biochemistry were not due to changes in gene expression. Rather, AmGSTF1 exerted a direct regulatory control on metabolism that led to an accumulation of protective flavonoids. Further evidence for a key role for this protein in MHR was obtained by showing that the GSTP1- and MDR-inhibiting pharmacophore 4-chloro-7-nitro-benzoxadiazole was also active toward AmGSTF1 and helped restore herbicide control in MHR black-grass. These studies demonstrate a central role for specific GSTFs in MHR in weeds that has parallels with similar roles for unrelated GSTs in MDR in humans and shows their potential as targets for chemical intervention in resistant weed management.