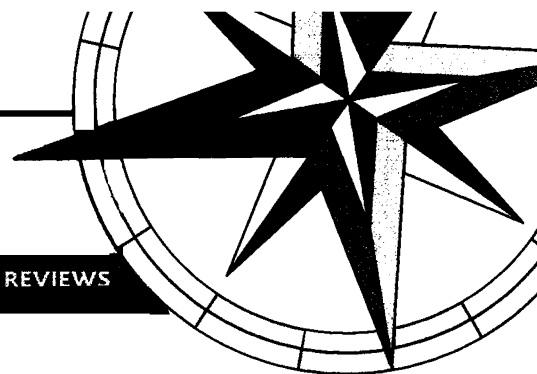




The Rice Genome and the Minor Grains

RONALD P. CANTRELL AND TIMOTHY G. REEVES ("The cereal of the world's poor takes center stage," Perspectives, 5 April, p. 53) correctly point out that the availability of the rice genome sequence has the potential to contribute to food security through the improvement of rice, the staple crop in the diets of half the world's population. They also point to its contribution to future improvement of maize, wheat, and other major commercial grains. A further boon will be felt through its contribution to improvement of the "minor" grains such as tef, sorghum, and the millets.

The world's commercial grain crops have been the focus of enormous public and private investment. The minor grains also feed millions and are a key to food security for the poorest in Asia and Africa. These grains are culturally valued, adapted to harsh environments, nutritious, and diverse in terms of their genetic, agroclimatic, and economic niches. Research on these crops, however, has been severely underinvested, receiving minimal attention by advanced laboratories relative to their importance for the world's poorest regions.

As a result, and because of the close evolutionary relationships among all of the domesticated grain crops [a point well made by Jan Leach *et al.* ("Why finishing the rice genome matters," Letters, 5 April, p. 45) and Jeffrey Bennetzen ("Opening the door to comparative plant biology," Perspectives, 5 April, p. 60)], it is in these crops, too, where the rice sequence will have a significant food security payoff.

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Altered Peptide Ligands and MS Treatment

THERE ARE SERIOUS DISCREPANCIES IN Jennifer Couzin's article "Gently soothing a savage immune system" (News Focus, 19 April, p. 456) regarding a trial using altered peptide ligands in patients with multiple sclerosis (MS). She quotes Roland Martin of the National Institutes of Health (NIH) about a trial that he participated in with a drug termed an altered peptide ligand (APL), produced by Neurocrine Biosciences. She writes that "three of the eight volunteers suffered exacerbated MS [multiple sclerosis] symptoms apparently linked to the peptide-targeting drug supposed to temper immune attacks."

Couzin fails to note that the NIH trial cited by Martin using the Neurocrine drug was published back to back with a placebo-controlled, double-blinded, multicenter trial on 144 patients (1, 2). Not only did the bigger placebo trial

fail to show any signs of worsening caused by the peptide, the trial also demonstrated improvement on magnetic resonance scans in both the volume and number of contrast-enhancing lesions at one of the doses of altered peptide that approached statistical significance. Moreover, there was evidence of a desirable Th2 shift in T cells responding to myelin basic protein (2).

The NIH trial involved only eight patients and was not placebo-controlled or blinded (1). Moreover, of the three patients who worsened, one had inflammatory demyelinating peripheral neuropathy, rendering the diagnosis of MS questionable. Another patient who worsened had a total clearance of T cells reactive to myelin basic protein, after treatment with the altered peptide, making it difficult to blame the peptide for the patient's

worsening. Couzin states that another "patient began the trial with a few brain lesions and ended up with 91." This is inaccurate. The patient had over 20 lesions at baseline and had no contrast-enhancing lesions before starting beta interferon treatment, which was given to the patient after withdrawal of APL therapy and a "course of standard intravenous steroid therapy" (1, p. 1170). This is quite different from concluding that the patient ended up with 91 lesions after APL therapy. It is unfortunate that the figure accompanying the article was labeled "Backfired," because there were no contrast lesions at all at the conclusion of altered peptide therapy and before beta interferon was administered [see fig. 1c of (1)].

Overall, the results of the two trials with APLs in MS show that there was "no substantial improvement or worsening in the whole cohort of 8 MS patients treated at NIH" (1, p. 1169), and there was improvement on magnetic resonance imaging in the placebo-controlled, double-blinded study involving the same drug (2).

APLs are a promising therapy for autoimmune disease, and further trials, with sponsorship from the NIH-funded Immune Tolerance Network, are planned. It would be unfortunate indeed if these conflicting matters were not clarified and if the successful early use of APL was not mentioned (1, 2). To state only one side of the story is regrettable.

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References

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2. L. Kappos *et al.*, *Nature Med.* 6, 1176 (2000).

Response

IT IS CORRECT THAT THREE OUT OF EIGHT multiple sclerosis (MS) patients participating in the National Institutes of Health (NIH) study suffered from exacerbations during the trial of an APL (1); however, extensive immunological testing linked the disease exacerbations to APL treatment in 2/8 (25%) of the patients.



Sorghum, one of the so-called minor grains, is important for food security.