result in pathology. In addition, it is likely that individuals who have secondary tumors will have subsets of cells exposed to different stromal factors and under different selective pressures than those at the primary tumor. As practical as whole genome sequencing is becoming, it may still be a considerable length of time before it is practical to profile thousands of individuals and thousands of cells from each tumor. Even with this level of resolution within each patient, it is not clear when we will capture enough variants of each tumor genome to confidently predict therapeutic resistance (or lack thereof) with a high degree of confidence.

In addition to identifying driver mutations, it would also be desirable to decipher the phenotypic contribution of each mutation or combinations of mutations. In the short term, perhaps the greatest potential for understanding the catalog of somatic variants identified in these studies will come not from adding more genomic data on other cancers or on different clonal populations but from

mining complementary information, such as whole genome epigenetic and transcriptomic data. This was already undertaken in the study of clear cell renal cell carcinoma by Dalglish *et al.*², and hints of this promise are also apparent in the recent work of Verhaak *et al.*⁵. In the latter, a correlation of copy number variation, mutational events and expression profiles allowed classification of subtypes of glioblastoma that, critically, differ in their response to radiation and drug treatments. Rather than complicating interpretation of the data sets, such approaches should help us understand pathology by unraveling the functions of driver mutations⁶.

Certainly, the promise of a complete mutational catalog of cancer is attractive. However, the spectrum of observed mutations is likely to be enormous given that many are under very little selection pressure. As clear mechanistic insights have yet to come from these data, the paramount question for therapeutic efforts remains: what are the high-priority

therapeutic targets, and why are they better than our current favorites? After all, it can be argued that industry is already awash in seemingly attractive targets and early drug discovery projects. Unfortunately, until a large number of cancer genomes is sequenced and functional mutations are discovered, cancer genome sequencing will likely provide little benefit to cancer therapy or patient care. As we are now in the midst of an explosive increase in cancer genome sequencing, a case can be made for greater focus on the development of new approaches for functional analysis of the expanding mutational catalog.

COMPETING INTERESTS STATEMENT

The authors declare no competing financial interests.

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Grass genomics on the wild side

Grasses are, in human terms, perhaps the most economically important of all plant families.

BrachyTAG programme (John Innes Centre, Norwich, UK)

And of the twelve grass subfamilies, the Ehrhartoideae, Panicoideae and Pooideae include many of the species with the greatest potential to address humankind's need for

food, feed and fuel. Genome sequences are currently available for crop members of the Ehrhartoideae (rice) and Panicoideae (sorghum and maize). Now, writing in *Nature*, an international consortium reports the genomic sequence of the wild grass *Brachypodium distachyon*—a first for a member of the Pooideae¹.

Many crops have unintentionally been bred to a high level of ploidy after centuries of domestication. This makes genome sequencing and genetic analysis particularly challenging for species such as bread wheat (17,000 Mb). Although it is of no intrinsic commercial importance, *B. distachyon* has emerged as a valuable model for

understanding other grasses, in large part because of its far more streamlined genome (272 Mb). When compared with wheat (right), the much smaller stature of mature *B. distachyon* (center) compares favorably with that of the better-known model plant, *Arabidopsis thaliana* (left). This makes it easier to cultivate large numbers of lines in a relatively small space. And like *A. thaliana*, its rapid life cycle and amenability to genetic manipulation further enhance its experimental tractability relative to most crops.

The new genome sequence enables cross-species comparison of the genomes of the three major subfamilies of grasses, generating results that should prove useful for analyzing members of the Pooideae with larger genomes, such as wheat, oats, barley,

rye and several forage grasses. And coupled with a wealth of mutant strains, detailed genetic maps, and resources for marker-assisted breeding, the *B. distachyon* genome sequence promises to provide valuable insights into how grasses from other subfamilies, such as the bioenergy species switchgrass and *Miscanthus*, might be improved to enhance their potential for sustainable fuel production.

Genes in *B. distachyon* bear a closer resemblance to their counterparts in rice and sorghum than to the relevant genes in their more distant relative *A. thaliana*, suggesting that *B. distachyon* has a valuable part to play in accelerating progress in grass functional genomics.

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1. The International Brachypodium Initiative *Nature* **463**, 763–768 (2010)