Hominid systematics is discussed with respect to two 1.7-million-year-old crania found in the Republic of Georgia, a discovery that "expands both the sample from the region and the picture of human taxonomic diversity." The contributions of mouse genetics in the early 1900s to the study of human diseases are described. And the implications are examined of a study in which the antipsychotic drug haloperidol was used to induce working memory deficits in monkeys through the down-regulation of D1 dopamine receptors, which evidence suggests are reduced in number in schizophrenia patients.

Taxonomy of the Dmanisi Crania

The recent discovery of two hominid crania (D2280 and D2282) from the Georgian early Pleistocene site, Dmanisi, by L. Gabunia and colleagues (Research Article, "Earliest Pleistocene hominid cranial remains from Dmanisi, Republic of Georgia: taxonomy, geological setting, and age," 12 May, p. 1019) is exciting because it expands both the sample from the region and the picture of human taxonomic diversity. At about 1.7 million years old, these specimens are roughly contemporaneous with African *Homo ergaster* and Asian *Homo erectus*, to which Gabunia *et al.* compare the Dmanisi crania. They suggest allocation of the crania to the former species. In light of the significance of this discovery, the following is of potential relevance.

The type specimen of *H. ergaster* is KNM ER 992, a mostly complete lower jaw from northern Kenya (*1*). Although three crania from this region, KNM ER 3733 and 3883 and KNM WT 15000, are also regarded as *H. ergaster*, only the last is associated with a mandible. In terms of the details of dental morphology, ER 992 and WT 15000 are not comparable (*2*). WT 15000 preserves upper teeth, but of ER 3883 and 3733, only the latter retains a tooth, a right upper second molar. This tooth is not morphologically comparable with that of WT 15000, which is consistent with notable differences between the two in cranial morphology. ER 3883 lacks the lower face but otherwise differs in preserved morphology from ER 3733 and WT 15000 (*2*). Thus, in addition to none of these crania being morphologically linked to ER 992, they collectively do not appear to represent the same taxon. But neither do any represent *H. erectus* (another taxon sorely in need of revision). Comparisons of African and Asian fossil hominid crania with the apomorphically configured calotte (skull cap) of the type specimen from Trinil, Indonesia, indicates that only the specimens from Sangiran (not, for example, from Ngandong or Zhoukoudian) are plausibly allocated to this species (*2*). The dental specimens from Sangiran also differ noticeably in morphology from the African ones. Further, because the Sangiran 2 and 4 crania are so unique among primates in having arborizing sigmoid sinuses, it is unlikely that *H. erectus* was ancestral to any known hominid.

What to do with the Dmanisi crania? The mandible previously found at the site (*3*) was analyzed metrically as being like *H. erectus* (wherein the African and Asian specimens were all included in that species) (*4*), but Gabunia and colleagues have now associated it with the two new crania in *H. ergaster*. Detailed morphological studies will surely follow, but photographs of the mandible (*4*) demonstrate lack of morphological comparability with ER 992. As for the crania, the photographs in Gabunia *et al.*'s article not only depict the metrically determined size difference between D2280 and D2282, but also indicate that there are detailed morphological differences to be noted: for instance, in cranial outline and cross section; in the supraorbital, mastoid, and nuchal regions; and in the course of the vault sutures that would reflect intertaxic rather than intrapopulational differences. Perhaps future studies will conclude that D2280 and D2282, and the mandible if it cannot be associated with either cranium, add even more to the picture of human evolutionary diversity than expected.

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Response

Schwartz highlights some important issues concerning the systematics of early Pleistocene hominids. We agree that the relationship between the type specimen of *H. ergaster* (KNM ER 992), KNM ER 3733 and 3883, and KNM WT 15000 remains unclear. In particular, differences in morphology and in dentition between the mandibles of WT 15000 and ER 992 are obvious, as are differences between the skulls ER 3733 and WT 15000. We also agree that only the specimens from Sangiran should be attributed to *H. erectus*, but it is possible that these specimens could be ancestors of hominids from Ngandong or Zhoukoudian.

Concerning the Dmanisi findings, we would like to stress their geological context and dating. The depositional nature of the site, the orientation of the bones, and the presence of the axial skeletons indicate rapid burial of the fossils and a lack of postdepositional movement. The two skulls (D2280 and D2282) were found in the same stratum within a 4-square-meter area, suggesting that these specimens belong to a single population [see our Research Article and (*1*)]. We interpret that these remains represent individuals who died during a single event and were buried together. The morphological differences between the Dmanisi specimens mentioned by Schwartz cannot be explained, we believe, on taxonomic grounds, but rather can be attributed to sexual dimorphism, age differences, or individual variation.

Although we agree with Schwartz that the Dmanisi mandible differs from type specimen ER 992, the taxonomic significance of these features is not well understood. The similarities between these specimens should be stressed, which include narrow width and robustness, the anterior position of the ascending ramus, and reduction of the retromolar space, as well as lack of a trigonum mentale and some other traits (*2, 3*).

The interdisciplinary study of the Dmanisi site indicates an age of 1.7 million years ago, which means that these fossils represent the oldest hominids yet found in Eurasia. We suggest that these specimens represent the first lineage from which the Sangiran specimens are derived. A detailed comparative study of Dmanisi skulls with specimens from Java is in progress and should help clarify this issue.

In conclusion, we agree with Schwartz that the Dmanisi hominids show human evolutionary diversity, which typically is overlooked in current, generalized hominid systematics.

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Early Mouse Models of Human Diseases

The News Focus article "The rise of the mouse, biomedicine's model mammal" by David Malakoff (14 Apr., p. 248) highlights the mouse as a mammalian model for human diseases, with the emphasis being on the provision of mouse strains and mutants by suppliers. In this otherwise fine survey of the role of the mouse as a prototype of human genetics and physiology, there is, however, little mention of the numerous mouse mutations as counterparts of human diseases that were already discovered in the early part of the 20th century. For instance, mouse pituitary dwarfism was discovered by Snell in 1929 (*1*). A^y, the top-dominant allele of the agouti coat color series, was discovered by the French geneticist Cuénot in 1905 (*2*). Many animals with the A^y gene become remarkably obese and thus offered an early model for human obesity (*3*). At least six genes were known early in the century to produce neurological and labyrinthine disturbances, the prototype being the Japanese waltzing mouse (*4*).

An outstanding resource that would have been valuable to mention is the volume by Hans Grüneberg titled *The Genetics of the Mouse* (*5*), a scholarly treatise about the mouse, including detailed descriptions of mouse mutants, gene action, genetic strains, and cancer genetics. It was first published in 1943 and enlarged greatly for the second edition in 1952, which includes more than 1700 references. Modern physiologists and geneticists should be aware of this gold mine of information about mouse mutants, many of which can still be obtained and studied using modern biochemical and molecular techniques. These mutants exhibit many abnormalities, including those in the central nervous system, the eye, blood and blood-forming organs, skin, and skeleton.

My criticisms should not detract from the thrust of the article, which is that the mouse should be recognized as the prime mammalian model of human genetics and physiology.

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Antipsychotics and Working Memory in Schizophrenia

Patients with schizophrenia suffer from substantial cognitive deficits, notably in the realm of memory functioning (*1*), which warrants considerable research efforts aimed at developing pharmacological treatment strategies. S. A. Castner, G. V. Williams, and P. S. Goldman-Rakic describe in their Report (17 Mar., p. 2020) the reversal of antipsychotic-induced working memory deficits in monkeys by stimulation of short-term dopamine D1 receptors. They suggest that the results of their study may have therapeutic implications for schizophrenia. However, the putative implications of their results for treatment of cognitive dysfunction in schizophrenia may be somewhat overstated.

Castner and colleagues propose that chronic haloperidol treatment should induce