may regulate hematopoiesis, including those that encode the transcription factors c-Myc and HES, and CCAAT/enhancer binding protein (C/EBP) (*3*–*5*). Accordingly, agonists of AhR such as TCDD compromise HSC activity in mice (*6*), whereas Boitano *et al*. found that antagonists such as SR1 enhance expansion of human HSCs.

Curiously, SR1 is not active against the mouse AhR but is active against that of dog and monkey. These species-specific activities are consistent with the observed effect, or lack thereof, in stimulating ex vivo expansion of HSCs from these species and suggest the need for developing screens with human target cells.

It will be critical to define the cell population that responds best to SR1. Several types of mouse HSCs, some with short- and long-term repopulation potential, have been described (*7*, *8*). Serial transplantation experiments performed by Boitano *et al*. indicate that SR1-exposed cells can repopulate mice up to several months while preserving their multilineage potential, thus showing intermediate repopulation potential. The development of new reagents and better assays for analyzing pure subsets of human HSCs will be essential to address this clinically relevant issue.

Other molecules such as TAT-HOXB4 (*9*), TAT-NF-Ya (*10*), Notch ligand (Delta$^{\text{ext-IgG}}$) (*11*), pleiotrophin (*12*), and angiopoietin-like molecule 2 and 3 (*13*) enhance human hematopoiesis in immunocompromised mice. However, none of the reported effects are as robust as that of SR1. Moreover, in some cases (e.g., Notch ligand), engraftment was accelerated but the effect was transient, suggesting that more mature progenitors—as opposed to long-term HSCs—preferentially responded to the treatment. Combining treatments that enhance the activity of stem cells with long- and short-term repopulation potential may prove clinically beneficial.

A technology that expands human HSCs by orders of magnitude over what is now achievable with SR1 could rapidly pave the way for using stem cell transplantation to cure genetic diseases (gene therapy) or to protect stem cells from the deleterious effects of chemotherapy. But can human HSCs be expanded further, or have they achieved their limit once exposed to SR1 for several days or weeks? Mouse HSCs can be expanded by several thousandfold if genetically engineered to overexpress *Hox* genes and/or derivatives (*14*, *15*), and human HSCs should behave similarly once the basic molecular machinery underlying self-renewal is dissected. Although AhR has just entered the arena, it will rapidly become a key actor in this search for signaling pathways that determine HSC self-renewal. Equally important, AhR inhibition could lead to expansion of other adult-type stem cells (e.g., skin, gut, central nervous system). Are HSC transplant physicians about to lay their hands on the Holy Grail?

References and Notes

1. A. Gratwohl *et al*., *JAMA* **303**, 1617 (2010).
2. A. E. Boitano *et al*., *Science* **329**, 1345 (2010); published online 5 August 2010 (10.1126/science.1191536).
3. F. L. Casado *et al*., *Blood Cells Mol. Dis.* **44**, 199 (2010).
4. J. S. Thomsen *et al*., *Mol. Pharmacol.* **65**, 165 (2004).
5. D. W. Kim *et al*., *Oncogene* **19**, 5498 (2000).
6. K. P. Singh *et al*., *Carcinogenesis* **30**, 11 (2009).
7. P. Benveniste *et al*., *Cell Stem Cell* **6**, 48 (2010).
8. B. Dykstra *et al*., *Cell Stem Cell* **1**, 218 (2007).
9. C. H. Huang *et al*., *Tissue Eng. Part C Methods* **16**, 487 (2010).
10. A. D. Domashenko *et al*., *Blood*, 10.1182/blood-2010-03-273441 (2010).
11. C. Delaney *et al*., *Nat. Med.* **16**, 232 (2010).
12. H. A. Himburg *et al*., *Nat. Med.* **16**, 475 (2010).
13. C. C. Zhang *et al*., *Nat. Med.* **12**, 240 (2006).
14. S. Cellot *et al*., *Exp. Hematol.* **35**, 802.e1 (2007).
15. H. Ohta *et al*., *Exp. Hematol.* **35**, 817 (2007).

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CLIMATE CHANGE

Farewell to Fossil Fuels?

Barring new CO_2 sources could curb climate change, but won't solve energy problems.

Martin I. Hoffert

One concrete goal adopted by some policy-makers is to reduce the risks associated with climate change by preventing the mean global temperature from rising by more than 2°C above preindustrial levels (*1*). Climate models indicate that achieving this goal will require limiting atmospheric carbon dioxide (CO_2) concentrations to less than 450 parts per million (ppm), a level that implies substantial reductions in emissions from burning fossil fuels (*2, 3*). So far, however, efforts to curb emissions through regulation and international agreement haven't worked (*4*); emissions are rising faster than ever, and programs to scale up "carbon neutral" energy sources are moving slowly at best (*5*). On page 1330 of this issue, Davis *et al*. (*6*) offer new insights into just how difficult it will be to say farewell to fossil fuels.

The authors ask this question: What would future CO_2 levels and global mean temperatures be if humans built no additional CO_2-emitting devices (e.g., power plants, motor vehicles) and allowed existing CO_2-emitting devices to live out their normal lifetimes over the next 50 years? Their answer is that this strategy would limit mean warming to 1.3°C (1.1° to 1.4°C) above that of the preindustrial era and limit atmospheric concentrations of CO_2 to less than 430 ppm. They concede, however, that such a radical "age-out" scenario is unlikely, and that a major mobilization is needed to figure out how to power the world carbon-neutrally to stay below the 2°C threshold.

The bitter pill implicit in Davis *et al*. and other, earlier studies of emissions-reducing scenarios is that we are in no position to make this energy transition now, and that it will likely take decades of hard work (*7*). For example, Pacala and Socolow (*8*) analyzed a scenario that envisioned stabilizing atmospheric concentrations of CO_2 at 500 ppm within 50 years. They found that reaching that goal required the deployment of seven existing or nearly existing groups of technologies, such as more fuel-efficient vehicles, to remove seven "wedges" of predicted future emissions (the wedge image coming from the shape created by graphing each increment of avoided future emissions). Those seven wedges, each of which represents 25 gigatons of avoided carbon emissions by 2054, are cited by some as sufficient to "solve" climate change for 50 years (*9*).

Unfortunately, the original wedges approach greatly underestimates needed reductions. In part, that is because Pacala and Socolow built their scenario on a business as usual (BAU) emissions baseline based on assumptions that do not appear to be coming true. For instance, the scenario assumes that a shift in the mix of fossil fuels will reduce the amount of carbon released per unit of energy. This carbon-to-energy ratio did decline during prior shifts from coal to oil, and then from

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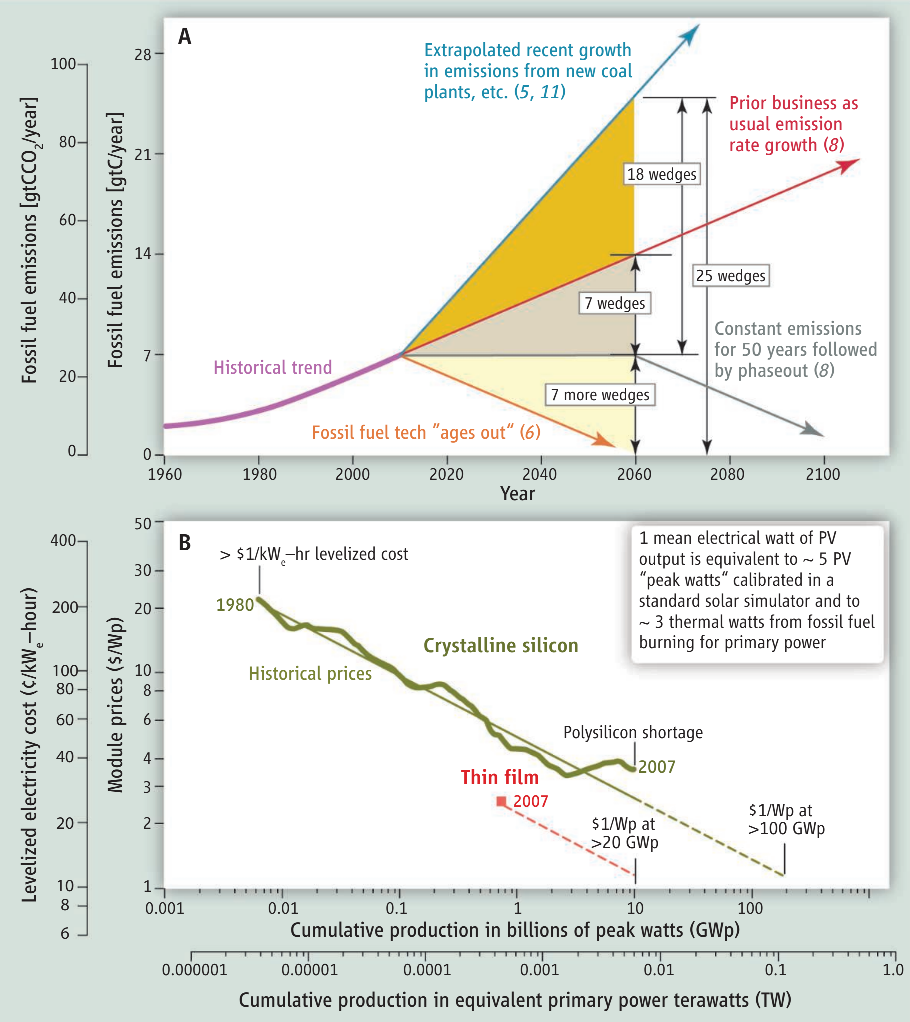

Reducing emissions. (**A**) Estimates based on one emissions scenario (red line) (*8*) found that technologies capable of removing 7 "wedges" of future predicted emissions could stabilize future CO_2 emissions from fossil fuels. Other scenarios (blue and gold lines) (*6*, *11*) suggest that removing up to 25 wedges will be needed. (**B**) Cost of producing electricity from silicon and thin-film photovoltaics (PV) are declining, but extensive development is needed to scale up cost-effective solar power to produce needed terawatts of primary power.

oil to natural gas. Now, however, the ratio is increasing as natural gas and oil approach peak production, coal production rises, and new coal-fired power plants are built in China, India, and the United States (*10*).

The enormous challenge of making the transition to carbon-neutral power sources becomes even clearer when emissions-reduction scenarios are based on arguably more realistic baselines, such as the Intergovernmental Panel on Climate Change's "frozen technology" scenario (*11*, *12*). Capturing all alternate energy technologies, including those assumed within this BAU scenario, means that a total of ~18 of Pacala and Socolow's wedges would be needed to curb emissions (*13*) (see the figure). And to keep future warming below 2°C, even under the Davis *et al*. age-out scenario, an additional 7 wedges of emissions reductions would be needed—for a total of 25 wedges (see the figure).

Maintaining world economic growth and keeping atmospheric CO_2 concentrations below 450 ppm, even with continuing improvements in energy intensity (the amount of CO_2 emitted per unit of energy, and a proxy for increasing energy efficiency and less consumptive lifestyles), will require ~30 terawatts (TW) of power from carbon-neutral sources at mid-century (*2*). Some forecasts envisioned market forces spurring the creation of 10 carbon-neutral terawatts (*2*), but that now appears optimistic. The difficulties posed by generating even 1 TW of carbon-neutral power led the late Nobel Laureate Richard Smalley and colleagues to call it the "terawatt challenge" (*14*–*16*); we have yet to mobilize enough talent and resources to meet it. It has proven difficult, for example, to tap the huge, if diffuse, solar flux on Earth using photovoltaic (PV) cells to generate electricity in a cost-effective manner, particularly for routine "baseload" generation. Costs of PV technologies are dropping (*17*) (see the figure), but greater economies of scale, perhaps accompanied by a switch to thin films—a less efficient technology, but less expensive in terms of cost per kilowatt—will help. Achieving massive market penetration of solar and wind electricity will require utility-scale systems that can store intermittent supplies of power until they are needed. Denmark, for instance, uses intermittent power to pump water into Norway's hydropower impoundments; the water is later released through turbines. That approach, however, isn't widely feasible in the United States, and other approaches that use compressed air, flywheels, and "flow batteries" to store power are expensive and need substantial research and testing.

Broad investment will be crucial to enabling such basic research findings to cross the "valley of death" and develop into applied commercial technologies. Carbon taxes (*1*) and ramped-up government research budgets (*2*) could help spur investments, but developing carbon-neutral technologies also requires, at the very least, reversing perverse incentives, such as existing global subsidies to fossil fuels that are estimated to be 12 times higher than those to renewable energy (*18*). We have to stop marching the wrong way before we can turn around.

Davis *et al*. show that breaking the world's fossil-fuel addiction will be hard. To create carbon-neutral power sources, we may well need programs with the scale and urgency of the Manhattan atom bomb project. One goal should be to develop technologies that can first meet the terawatt challenge, and eventually provide 30 carbon-neutral terawatts of power by mid-century; perhaps 10 TW each of primary power from "clean coal" and from nuclear and renewable technologies. Without these alternatives to fossil fuels, the age-out scenario painted by Davis *et al*. evokes Havana after the 1959 Cuban Revolution: no new cars, only constantly repaired but still running old Chevys in the streets, as a beautiful old city crumbles around them.

References

1. J. Hansen, *Storms of My Grandchildren* (Bloomsbury, New York, 2009).
2. M. I. Hoffert *et al*., *Nature* **395**, 881 (1998).
3. K. Caldeira, *Science* **299**, 2052 (2003).
4. J. Rogelj *et al*., *Nature* **464**, 1126 (2010).
5. M. R. Raupach *et al*., *Proc. Natl. Acad. Sci. U.S.A.* **104**, 10288 (2007).
6. S. J. Davis *et al*., *Science* **329**, 1330 (2010).
7. V. Smil, *Energy Transitions* (Praeger, Santa Barbara, CA, 2010).
8. S. Pacala, R. Socolow, *Science* **305**, 968 (2004).
9. A. Gore, *An Inconvenient Truth: The Planetary Emer-*

gency of Global Warming and What We Can Do About It* (Rodale, New York, 2006).
10. E. Kintisch, *Science* **311**, 1702 (2006).
11. B. S. Fisher *et al.*, in *Climate Change 2007: Mitigation. Contribution of Working Group III to the Fourth Assessment Report of the IPCC*, B. Metz *et al.*, Eds. (Cambridge Univ. Press, Cambridge, UK, 2007), p. 220.
12. R. Pielke, Jr, T. Wigley, C. Green, *Nature* **452**, 531 (2008).
13. R. Socolow, in *Avoiding Dangerous Climate Change*, H. J. Schellnhuber *et al.*, Eds. (Cambridge Univ. Press, Cambridge, UK, 2006), pp. 347–354.
14. R. E. Smalley, *MRS Bull.* **30**, 412 (2005).
15. N. S. Lewis, *Eng. Sci.* **2**, 12 (2007).
16. K. Zweibel, *The Terawatt Challenge for Thin-Film PV* (NREL/TP-520-38350, National Renewable Energy Laboratory, Golden, CO, August 2005).
17. S. Chu, Meeting the Energy and Climate Challenge: A Tale of Two Countries, presented at Tsinghua University, People's Republic of China, 15 July 2009; www.slideshare.net/Calion/meeting-the-energy-and-climate-challenge-a-tale-of-two-countries-usa-china.
18. A. Morales, "Fossil fuel subsidies are twelve times renewables support," Bloomberg Businessweek, 29 July 2010; www.businessweek.com/news/2010-07-29/fossil-fuel-subsidies-are-twelve-times-renewables-support.html.

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MATERIALS SCIENCE

Shape Memory Bulk Metallic Glass Composites

Glass-forming and shape memory metals may provide a route to fabricating materials with enhanced mechanical properties.

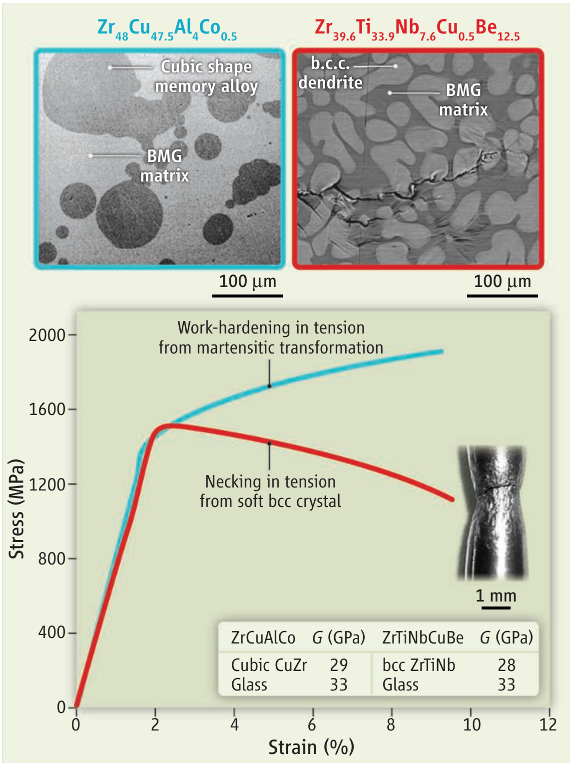
Douglas C. Hofmann

Bulk metallic glasses (BMGs) are being studied extensively as potential structural materials as they have a unique array of mechanical properties compared to traditional crystalline metals (*1*–*4*). Their amorphous microstructure and variable composition give BMGs ultrahigh-yield strengths, large elastic strain limits, high hardness, corrosion resistance, and the ability to be processed like a plastic. So far, however, BMGs have not found many structural applications because of their catastrophic failure under tension (tensile loading) and their typically low fracture toughness (resistance to cracking), both resulting from the same amorphous microstructure that differentiates them from crystalline metals. This shortcoming has been addressed in recent years with the development of BMG matrix composites (BMGMCs)—two-phase alloys consisting of soft, crystalline dendrites grown in situ in a glass-forming matrix (*5*–*9*). When designed and processed properly, BMGMCs retain the positive structural features exhibited by monolithic (single-phase) BMGs, but can also exhibit enhanced tensile ductility, fracture toughness, and fatigue endurance, which makes them desirable as engineering materials (*5*, *10*, *11*).

In conventional crystalline metals, strength and ductility are typically inversely proportional, a result of the interactions between dislocations and microstructural features, like grain boundaries. In contrast, BMGMCs exhibit plasticity through a complex interaction between the dislocations in the crystalline phase and the highly localized shear bands in the glass matrix. This results in mechanical properties (like fracture toughness) that exceed the "rule of mixtures" expected for each phase individually (*5*).

Dendrite-reinforced BMGMCs do exhibit some drawbacks, however. The two-phase alloy must contain a dendrite in thermodynamic equilibrium with a glass-forming liquid. This necessitates a system that has very sluggish crystallization kinetics, in order to prevent the dendrites from causing heterogeneous nucleation of unwanted brittle phases. This typically requires the use of Be-containing composites, which have very few stable compounds and are excellent glass-formers, but which require special consideration during processing owing to the toxicity of Be. Improvements in mechanical properties (e.g., tension ductility) have been confined almost exclusively to Zr-Ti-Be–based BMGMCs, which has limited the scope of applications.

Recent advancements in metallic glass composites come at the intersection between two different areas of materials science research—shape memory alloys and metallic glasses—whereby a shape memory alloy has been integrated as the crystalline phase, effectively using the concept of transformation-induced plasticity (*12*, *13*) (see the figure). The most widely studied shape memory alloy, NiTi (or Nitinol), undergoes a stress-induced martensitic transformation from a cubic to a monoclinic phase, which imparts an appreciable work-hardening capability (the alloy becoming stronger as it deforms). Less well known is that CuZr also exhibits the same shape-memory effect as NiTi. In a remarkable coinci-



Tensile ductility in metallic glass composites. (**A**) A scanning electron micrograph (SEM) from a CuZrAlCo composite showing the isolated shape memory alloy phase embedded in a glass matrix. (**B**) An SEM micrograph from a ZrTiNbCuBe composite showing isolated body-centered cubic (bcc) dendrites embedded in a glass matrix with a crack arrested by the microstructure. (**C**) Two tension tests representative of the work-hardening behavior observed in shape memory–reinforced composites and the necking behavior observed in bcc dendrite–reinforced composites. The shear modulus of the crystal and glass matrix of both composites is shown in the inset, demonstrating that the inclusion is a soft phase, one of the criteria necessary for tensile ductility.

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