experimentally induced mutation of Mfsd12 feature streaky hairs that contain eumelanin, but not pheomelanin, identical to what has been described for grizzled. Indeed, Crawford et al. demonstrate that Mfsd12 mutant mice are unable to produce pheomelanin and that grizzled mice have a deletion of Mfsd12. Hence, the identification of MFSD12 marks a victory for phenotype-driven human genetics.

The MFSD12 findings from Crawford et al. raise several intriguing questions. How does this transporter-like protein expressed in lysosomes affect what happens in melanosomes (the organelle that stores and transports melanin)? Why does reduced expression of MFSD12 cause increased synthesis of black-brown eumelanin in humans, but loss of Mfsd12 in mice does not affect eumelanin synthesis? Finally, is it a coincidence that human MFSD12 variants affect gene expression rather than protein structure? A potential answer to the last question is apparent from grizzled mice, which not only exhibit streaky hair but also have occasional developmental and growth abnormalities (9). It seems possible that regulatory variants in MFSD12 that reduce, but do not ablate, protein function confer positive selection due to the ability of dark skin to block the damaging effects of UV radiation, but avoid negative selection due to impaired development and/or growth.

It is interesting to contrast MFSD12 selection in African populations with that for SLC24A5 in European populations. The regions surrounding both genes exhibit strong divergence between continents, but the derived variant of SLC24A5, which occurs mostly in Europe and South Asia, contributes to lighter skin color, whereas the derived variant of MFSD12, largely maintained in Africa, contributes to darker skin color (see the figure). Although the evidence for positive selection of the dark skin–associated MFSD12 variants in Africans is not as strong as it is for the light-skinned variants of SLC24A5 in Europeans, this may reflect the age of the mutations—light-skinned variation in SLC24A5 is ~30,000 years old (10, 11), whereas dark skin–associated variation in MFSD12 is estimated to have occurred more than 500,000 years ago (2). Like MFSD12, many of the variants at the other three loci identified by Crawford et al. as associated with dark skin are also derived—other hominid and primate genomes carry variants associated with lighter skin at these loci. Taken together, these observations suggest that skin pigmentation of ancestral humans was intermediate, with darker pigmentation providing adaptive protection against UV radiation in east African ancestors.

Studying the genetic architecture of skin pigmentation could provide a platform to explore the extent to which interaction between genes and interaction between genes and environment contribute to phenotypic variation. But such studies require larger samples and new analytic frameworks: Like other studies on skin pigmentation (12–14), Crawford et al. focus on additive effects across loci—approximately one-third of the total phenotypic variation was accounted for by four loci. What accounts for the other two-thirds? Some of the “missing” heritability could represent measurement noise or environmental factors. A study of an African-European cohort from the Cape Verde Islands points to an oligogenic model with four major gene variants and many additional gene variants of small effect (14). It should be emphasized, however, that estimates of heritability are meaningful only to the population being studied. For example, Crawford et al. estimate that 12.8% of the phenotypic variance in skin pigmentation in Africans is attributable to SLC24A5, which reflects both the strength of allelic substitution and allele frequency. By contrast, SLC24A5 contributes almost nothing to skin color variation in Europeans because the derived allele occurs essentially at a frequency of one. Success of the endeavor described in Crawford et al. depends on a diversity of approaches, diversity of genetic variation, and, especially, diversity of phenotypic variation. Perhaps paradoxically, the strongest association signal for skin color comes from SLC24A5, for which variation is of relatively recent origin in Europe. Thus, the power of continental Africa as a substrate for human genetics is enhanced by human migration and gene flow not only out of, but, more recently, back into Africa (15). Ultimately, human genetic and phenotypic variation is not captured in any single continent, and likewise, a complete picture of the genetic architecture of a complex trait—pigmentation or otherwise—cannot be gleaned through studying a single population. As in all things, diversity matters.

**REFERENCES**

although the chemistries already exist, most current processes and technologies that use biobased feedstocks are too expensive to be competitive with traditional petrochemical refining. This needs to change for the polymer industry to become truly sustainable.

**BIOBASED COMMODITY POLYMERS**

Two major approaches highlight the importance in chemistry to moving toward polymers made from renewable resources. The first is focused on generating, from biobased resources, the small set of monomers used to produce the commodity polymers that dominate the polymer industry (see the figure).

Consider the fermentation of sugar to make ethanol, a process carried out in the United States at a scale of billions of kilograms every year (see the photo), for use in transportation fuels. A commercially viable process is available for dehydrating this bioethanol to make bioethylene, which can be polymerized to produce a whole family of polyethylenes, the most abundant class of synthetic polymers (6). Isoprene—the precursor to polyisoprene, a principal ingredient in car tires—can also be produced through catalytic conversion of fermentation products derived from sugar in processes that have commercial potential (7). Some manufacturers are using ethylene glycol from bioethylene as a component in polyethylene terephthalate (PET), the polymer found in hundreds of billions of beverage bottles globally produced per year. Efforts are also under way to produce other key high-volume monomers used in commodity polymers—propylene, styrene, and terephthalic acid—from plant-based materials (8).

The principal roadblocks to further progress in this area are associated with biomass-to-product conversion efficiencies. Fundamental research is needed to find highly active and selective catalysts, formations with new high-yielding and atom-economic metabolic pathways, and new organic chemistry transformations with high efficiencies. These strategies must be able to act on abundant biomass to provide sustain-able monomers in the purity needed for the polymer industry.

For example, a recent technoeconomic analysis of the biobased production of styrene from sugar through the L-phenylalanine pathway with engineered bacteria pointed to low productivities, titers, and yields as major limitations to a commercially viable process (9).

Combining more efficient biochemical pathways and making bacteria less susceptible to the toxicity of the product styrene are formidable challenges in this specific case.

**NEW BIOBASED POLYMERS**

A second major theme is the conversion of renewable feedstocks, either directly or after some chemical manipulation, into unprecedented polymers that exhibit new and useful properties (10). The chemical functionalities available in biomass-derived molecules are much more diverse than those found in typical petrochemicals; oxygenated functional groups, reactive moieties, stereochemical features, and complex molecular topologies abound.

This diversity poses two main challenges. First, converting these molecules into polymers with controlled molar mass, microstructure, and architecture requires polymerization schemes with catalysts, initiators, and mediators that are matched to the reactive moieties in new monomeric compounds. This can be difficult because of, for example, low efficiency catalysis, uncontrolled polymerization processes, or thermodynamic limitations associated with emerging monomers that have largely been solved for commodity monomers (11).

The second challenge is in generating materials with useful thermal, mechanical, optical, and other physical properties. Sensitivity to hydrolysis, degradation induced by processing at high temperatures, poor mechanical properties, and unsuitable glass transition temperatures are just some of many characteristics that can render new materials ill-suited for practical commercial applications. Scientists are working on addressing these deficiencies with new additives and comonomers and by controlling of macromolecular architectures (e.g., block polymers discussed below).

Polyactide offers a good example. Fermentation of sugar to lactic acid, followed by conversion into this compostable polyester, is one of the leading commercial processes in industrial biopolymer production. This polymer can be used in place of polystyrene or PET in applications ranging from disposable plastic cups to durable textiles. Polyactide is produced on a global scale of about a billion kilograms annually. Fundamental research carried out in both industry and academia over the past three decades has been critically important to the commercial success of this bioplastic. By all accounts, the development of polyactide has blazed a trail that should give us confidence that if there is a will, there is a way in the biobased polymer arena.

The discovery of new biobased polymers with tunable and competitive properties will also require innovative polymerization strategies that allow the preparation of precisely controlled macromolecular architectures such as block, graft, and star polymers. This level of control can translate into materials with exquisite toughness or resilience, while retaining favorable optical and/or processing characteristics. Biobased block polymers, in particular, hold tremendous promise because they can marry the properties of multiple components into a single material, thus imparting benefits associated with each constituent (12). For example, my colleagues and I have recently reported new, high-performing aliphatic polyester block polymers derived from biomass (12).

Recent notable advances in making biobased polymers include alternating copolymerizations between biobased epoxides and carbon dioxide to make polycarbonates, and between biobased epoxides and biobased anhydrides to give polyesters (14). In many cases, such polymerizations have led to new materials with attractive property profiles for possible use as plastics and/or elastomers, provided that catalytic efficienc-
OUTLOOK

Biobased polymers can frame the future of plastics, provided that scientists continue to develop efficient, often catalytic, conversion of biomass to useful polymer ingredients; generate new and established monomers from biomass in high yields and purities; and discover new polymers with outstanding properties that are comparable or superior to their petrochemical analogs. An exciting contemporary example of this future is the substitution of terephthalic acid with the bioderived 2,5-furandicarboxylic acid to produce a high-performing fully biobased PET replacement (15). Support for this type of research should come not only from government. University-industry partnerships can be very effective at producing basic research that is couched in the economic realities of the polymer marketplace.

For polymers from renewable resources to penetrate the marketplace, they must outcompete traditional materials in both price and performance. But as the fundamental research in the conversion of biomass to polymer precursors continues to evolve, the resultant technologies will become more and more practical. Similarly, as the basic research on converting these compounds into polymers with exceptional property, processing, and performance profiles continues to be established, the resultant materials will be increasingly competitive. If the economic and environmental costs of extracting fossil resources and converting them into plastics continue to rise, there will likely be an inversion point where biobased polymers become the less expensive alternative, akin to what is starting to happen in the renewable energy sector. Societal pressures and policies that are conducive to environmental stewardship will only help the cause. We are not there yet, but there is good reason to stay the course and continue to push the frontiers of biobased polymers for the sake of sustainability.

REFERENCES AND NOTES


ACKNOWLEDGMENTS

The Center for Sustainable Polymers at the University of Minnesota, a National Science Foundation–supported Center for Chemical Innovation (CHE-1413862), is recognized for support. Thanks to F. Bates, P. Drausnauer, T. Hoye, L. Selkirk, and D. Schneiderman for feedback and suggestions. The author has equity and royalty interests in, serves as secretary for, and is on the board of directors of Valerian Materials, a company involved in the commercialization of β-methyl-α-valerolactone. The University of Minnesota also has equity and royalty interests in Valerian Materials. These interests have been reviewed and managed by the University of Minnesota in accordance with its conflict of interest policies.

POLYMER CHEMISTRY

The future of plastics recycling

Chemical advances are increasing the proportion of polymer waste that can be recycled

By Jeannette M. Garcia and Megan L. Robertson

The environmental consequences of plastic solid waste are visible in the ever-increasing levels of global plastic pollution both on land and in the oceans. But although there are important economic and environmental incentives for plastics recycling, end-of-life treatment options for plastic solid waste are in practice quite limited. Presorting of plastics before recycling is costly and time-intensive, recycling requires large amounts of energy and often leads to low-quality polymers, and current technologies cannot be applied to many polymeric materials. Recent research points the way toward chemical recycling methods with lower energy requirements, compatibilization of mixed plastic wastes to avoid the need for sorting, and expanding recycling technologies to traditionally nonrecyclable polymers.

Roughly half of the annual global production of solid plastics, or 150 million tons, is thrown away worldwide each year. The United States generates ~20% of the global amount of plastic solid waste generated (1). Not only is plastic waste residing in landfills harmful to the environment, but it also represents missed economic opportunities. For example, the commodity market value of the total landfilled packaging material waste in the United States has been estimated to be $11.4 billion dollars; $8.3 billion of this is attributed to plastic waste (2). Furthermore, recycling plastic for reuse saves energy compared with producing virgin materials; 1 ton of recycled plastic can save up to ~130 million kJ of energy. The potential annual energy savings that could be achieved from recycling all global plastic solid waste is...
The promise of plastics from plants
Marc A. Hillmyer

Science 358 (6365), 868-870.
DOI: 10.1126/science.aao6711