rons with antibodies sends the cells into untimely demise (8). Hence, we are led to wonder whether the damage wrought on neurons by clustered PrP<sup>C</sup> proteins relates to TSE neurodegeneration. If so, could the mechanism by which prion infections lead to brain damage be related to the normal function of PrP<sup>C</sup>?

Mice lacking normal prion protein live a healthy and long life without pathological phenotypes, so loss of function of PrP<sup>C</sup> is most certainly not a cause of brain damage in TSE. Could any gain of function of PrP<sup>C</sup> trigger disease pathogenesis? Morphological findings would appear to depose against this hypothesis as well. Although the clustering of molecules at the cell surface is a common way to initiate signaling, injecting antibodies to PrP<sup>C</sup> into a mouse brain does not elicit spongiosis. Conversely, ordered aggregation is a crucial event in the formation of PrP<sub>Sc</sub> and may represent the true mechanism by which infectivity is generated (9).

Chesebro et al.'s findings yield powerful support for a link between the cell surface topology of PrP<sub>Sc</sub> and prion disease pathogenesis. By disengaging PrP<sup>C</sup> from the cell surface, the authors have effectively uncoupled clinical disease from prion replication, PrP<sub>Sc</sub> formation, and its assembly into higher order aggregates and the hallmark brain plaques. It is almost unavoidable to conclude that prion replication avails itself of membrane-bound signal transducers to elicit brain damage.

Another twist to Chesebro et al.'s story relates to the structural requirements for prion replication. In contrast to GPI-negative mice, transgenic mice that express a soluble dimeric version of PrP<sup>Sc</sup> do not accumulate PrP<sub>Sc</sub> in their brains or spleens upon prion infection, nor do they develop or transmit TSE (10). Instead, the soluble dimeric form effaces competes with endogenous PrP<sup>C</sup> and delays prion pathogenesis in normal mice. In combination with Chesebro et al.'s results, this indicates that detachment of PrP<sup>C</sup> from the membrane does not necessarily abolish its prion replication competence. The soluble dimeric form may act as a dominant-negative form that sequesters PrP<sub>Sc</sub>, rendering it unavailable and thereby inhibiting disease progression.

Brain extracts of prion-infected GPI-negative mice did not elicit plaque formation when injected into other GPI-negative mice. The importance of this failed attempt at transmission is unclear, but such a result may point to some kind of deficiency in the prion replication machinery of these transgenic mice.

For all the insight brought about by Chesebro et al.'s findings, a central question remains. Accruing evidence suggests that signaling at the membrane involving PrP<sup>C</sup> underlies TSE pathogenesis. Infectious prions may damage the brain by distorting signaling events that PrP<sup>C</sup> normally controls. If that is true, the best way to find out what exactly goes wrong in the brains of prion-infected individuals may be to sort out the normal function of PrP<sup>C</sup>. Yet despite 13 years of availability of mice lacking normal prion protein, progress toward resolving the latter question has been painstakingly slow. Although Chesebro et al.'s work exemplifies the awesome power of mouse transgenetics, a next important step may consist of porting the prion signaling system to simpler, genetically tractable organisms such as worms, flies, or fish, whose use is already having a tremendous impact on the study of other neurodegenerative diseases.

References

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CHEMISTRY

Making Fuels from Biomass
Jens R. Rostrup-Nielsen

Recent high oil prices have put the spotlight on biofuels and other alternative energy sources. Energy safety and the environment are high on the political agenda. Biofuels cannot replace oil completely, because sufficient agricultural area is unavailable. However, the conversion of biomass from different sources (including waste) may, in conjunction with other energy sources, help to make our societies less dependent on oil.

The challenge for scientists is not only to find new ways to generate useful fuels, but also to guide politicians toward decisions with minimum costs. The conversion of biomass to fuels is one example, which is illustrated by the conversion of carbohydrates to hydrocarbons reported by Huber et al. on page 1446 of this issue (1).

Carbohydrates—such as sugars, starch, hemicellulose, and cellulose—are found for example in grain, wood, and agricultural waste. Sugars and starch can be converted to ethanol by fermentation, whereas cellulose and hemicellulose require chemical and physical pretreatment followed by enzymatic breakdown of the molecules. Pure ethanol can be added to gasoline; however, this requires an energy-intensive distillation step. This and the energy used in fertilizers, transportation of biomass, etc., should be subtracted from the energy gained from the biofuel to assess the net energy output. One may question the net energy output when the biomass is provided as a primary product at the locations with intensive agriculture. It has been estimated that the ratio of energy output to energy input is no more than 1.1 for corn-based ethanol in the United States; the energy input is provided mainly from fossil fuels (2).

The distillation problem can be reduced if ethanol is converted to hydrogen. Ethanol may thus serve as an energy carrier for a future hydrogen society. The technology for this conversion is available (3), but as demonstrated in an earlier paper by Huber et al. (4), hydrogen may also be formed directly from the carbohydrates by reaction with water (steam reforming) in the liquid phase, hence saving the energy and costs associated with distillation.

Fuels via synthesis gas. One can use synthesis gas to make hydrogen for fuel cell driven cars or convert it into synthetic diesel or gasoline (synfuel) to be used in conventional internal combustion engines (ICE). The conversion of fossil fuels to synfuels does not solve the CO<sub>2</sub> problem. This is achieved by using biomass or by coupling centralized production of hydrogen from fossil fuels with CO<sub>2</sub> sequestration.

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Now, Huber et al. (1) raise the question why one should not make hydrocarbon fuel directly, instead of aiming for hydrogen as a fuel, which would require an expensive new infrastructure. Modern diesel engines are almost as efficient as fuel cell–driven cars that use hydrogen fuel are likely to be. Why not then make “sustainable” synthetic liquid fuels (synfuels) instead of hydrogen (5)?

The same question may be asked for a hydrogen society built on fossil fuels and sequestration of carbon dioxide. Fossil fuels may be converted by gasification or steam-reforming to synthesis gas (a mixture of carbon monoxide and hydrogen) (see the first figure). Carbon monoxide may be further converted to hydrogen and carbon dioxide; the latter may be reinjected in oil fields or in cavities (sequestration). Alternatively, the synthesis gas can be reacted to synthetic liquid fuels in the form of synthetic diesel or gasoline (synfuels) (see the first figure).

Automotive fuels (that is, diesel and gasoline) have an atomic hydrogen-to-carbon ratio, H:C, of 2 (“CH₂”). Ethanol can be converted to hydrocarbon fuel by catalytic processing over zeolites, but the conversion of carbohydrates faces a fundamental problem: Although carbohydrates (\(C_nH_{2n}O_n\)) contain a lot of hydrogen, this hydrogen is bound to oxygen, meaning that the “effective” H:C ratio is 0.

The earlier liquid-phase reforming method of Huber et al. (4) solves this problem by extracting oxygen as carbon dioxide, and then making hydrogen. Now, Huber et al. (1) show that the use of well-known organic syntheses makes it possible to convert carbohydrates into hydrocarbons that are of interest for use as fuels. The process scheme eliminates the expensive distillation process, because separation of the hydrocarbon product from the aqueous phase is simple. Although the reaction paths should be optimized and the cost of the process must still be analyzed and compared with alternative routes (see the second figure), the work of Huber et al. (1) shows how explorative work can create new options for the supply of energy.

**References**


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**ECOLOGY**

**Rediscovery of the Ivory-billed Woodpecker**

David S. Wilcove

A book on North American wildlife, published in 2000, scoffed at the notion that the ivory-billed woodpecker (Campephilus principalis) might still be alive somewhere in the southern United States: “Although it remains the Holy Grail of American bird watchers, with persistent rumors of its presence in remote forests, most ornithologists now concede that it vanished from the United States sometime in the past 40 years...Its presence today in the sterile, industrial forestlands of the South, however wonderful a thought, would be as out of place as a buckskin-clad settler with a musket in the streets of modern-day Atlanta” (1). As the author of that book, I now know that sometimes it’s great to be wrong. As reported by Fitzpatrick et al. on page 1460 of this issue (2), the ivory-billed woodpecker has been rediscovered in eastern Arkansas, its presence confirmed by multiple sightings and a grainy but diagnostic videotape. The rediscovery stunned bird watchers and generated headlines around the world. But those not under the spell of this charismatic species might well wonder what all the fuss is about. What is the ecological significance of the ivorybill’s reappearance?

The outlook for the species is uncertain. Fitzpatrick et al. did not find any breeding pairs in 14 months of nearly continuous field work, and they concede that all of their observations may refer to a single individual. Ivorybills naturally occur at very low densities. J. Tanner, who undertook the only field studies of the species in the late 1930s (3) estimated the density of ivorybills to be no more than 1 pair per 16–44 km² of suitable habitat. This characteristic, combined with the degraded condition of the current habitat and the paucity of sightings, suggests that any breeding population must be extremely small, perhaps only a few pairs. Such a tiny population would be highly vulnerable to stochastic extinction processes. Other North American birds, however, have rebounded from remarkably low numbers. The whooping crane (Grus americana) population was down to 14 adult individuals in 1938 (4); today, it exceeds 200. No more than 7 Laysan ducks (Anas laysanensis) survived in 1912 (5); the current population is ~500. Also, given the ivorybill’s apparent dependence on old forests (3) (see photo), the passage of time should result in more and better habitat for the woodpeckers, as second-growth forests age.

Events preceding and following the ivorybill’s rediscovery illustrate the relative benefits of two different approaches to conservation. The Cache River National Wildlife Refuge, where Fitzpatrick et al. made their discovery, was established in 1986 with the transfer of 154 ha from The Nature Conservancy, a private nonprofit conservation organization, to the U.S. Fish and Wildlife Service. Subsequent land-acquisition efforts by The Nature Conservancy and...