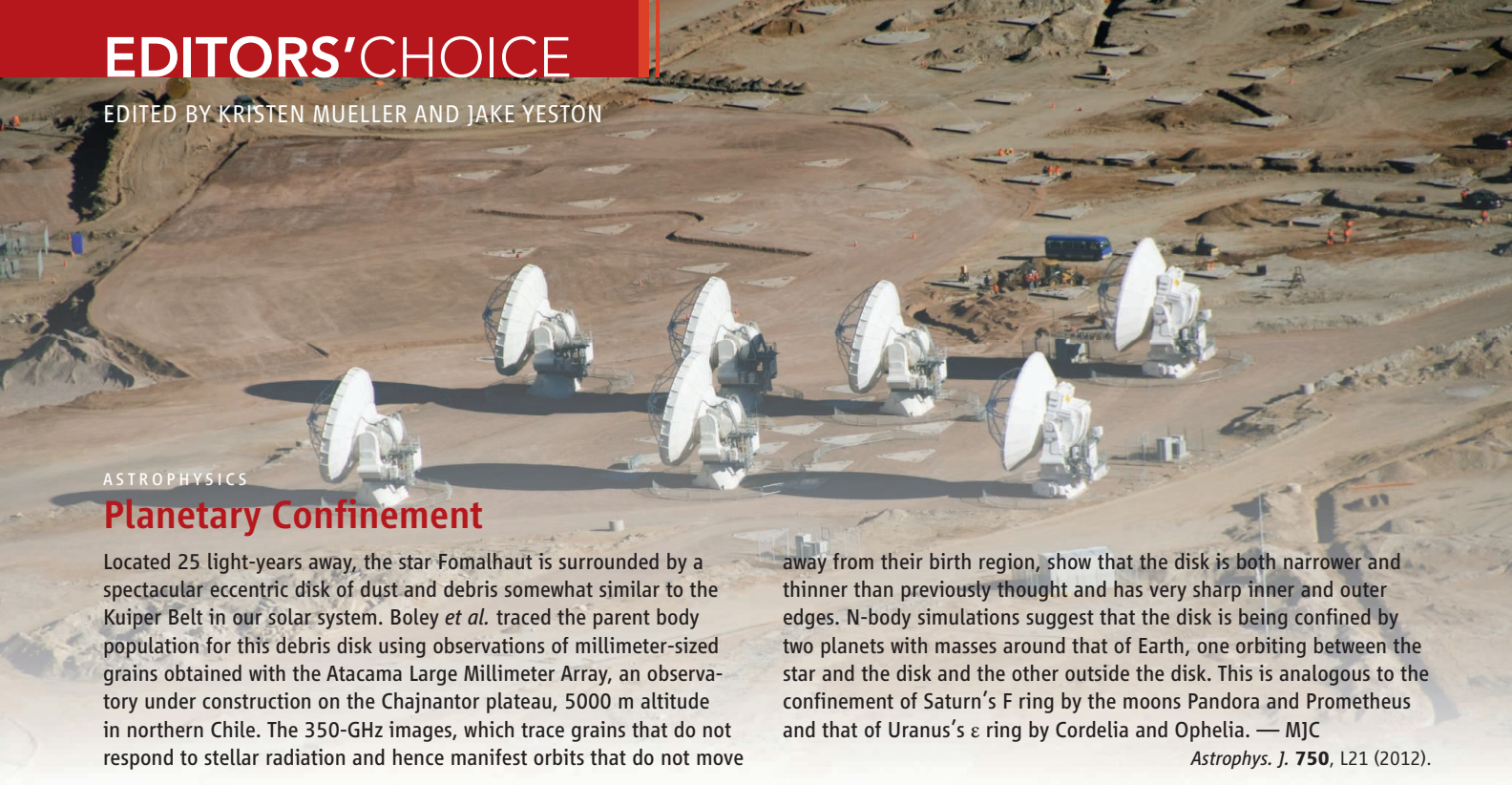
EDITORS' CHOICE

EDITED BY KRISTEN MUELLER AND JAKE YESTON



ASTROPHYSICS

Planetary Confinement

Located 25 light-years away, the star Fomalhaut is surrounded by a spectacular eccentric disk of dust and debris somewhat similar to the Kuiper Belt in our solar system. Boley *et al.* traced the parent body population for this debris disk using observations of millimeter-sized grains obtained with the Atacama Large Millimeter Array, an observatory under construction on the Chajnantor plateau, 5000 m altitude in northern Chile. The 350-GHz images, which trace grains that do not respond to stellar radiation and hence manifest orbits that do not move away from their birth region, show that the disk is both narrower and thinner than previously thought and has very sharp inner and outer edges. N-body simulations suggest that the disk is being confined by two planets with masses around that of Earth, one orbiting between the star and the disk and the other outside the disk. This is analogous to the confinement of Saturn's F ring by the moons Pandora and Prometheus and that of Uranus's ε ring by Cordelia and Ophelia. — MJC

Astrophys. J. **750**, L21 (2012).

MOLECULAR BIOLOGY

Prions: A New Part to Play

MicroRNAs (miRNAs) are small noncoding RNAs that, when part of a miRNA-induced silencing complex (miRISC), repress the expression of fully or partially complementary mRNAs. Argonaute (Ago) proteins bind miRNAs and form the heart of the silencing machinery. Intriguingly, plasma membrane–associated forms of the human prion protein (PrP^C), which is associated with neurodegenerative diseases in humans, also interact with components of the miRNA pathway.

Gibbings *et al.* show that a transmembrane form of PrP^C exposes an AGO anchor sequence in the cytoplasm and that this repeat binds AGO1 and AGO2. These PrPC-AGO complexes are found on vesicles in cells that resemble multivesicular bodies (MVBs). During miRNA maturation, AGO protein bound to miRNA must be transferred from the RISC-loading complex (RLC) to the miRISC silencing complex. PrP^C binds components of both the RLC and the miRISC but seems to do so in distinct cellular locations. PrP^C promotes the association of AGO with the miRISC and/or the stability of this complex. Indeed, PrP^C is required for effective miRNA silencing of a number of target mRNAs. PrP^C may do this through subcellular trafficking, as it seems to increase the interaction between MVBs and AGO-rich structures, such as P or GW bodies, thence promoting shuttling of AGO between the RISC-loading complex and the miRNA-induced silencing complex. — GR

Nat. Struct. Mol. Biol. **19**, 10.1038/nsmb.2273 (2012).

CHEMISTRY

Making Methanol

If chemistry worked like Tinkertoys, it would be rather straightforward to make methanol from methane: You'd simply pull off a hydrogen atom and stick on an OH group. Alas, it's not that simple, and most scalable implementations of this reaction tend toward overoxidation; the primary industrial route circuitously oxidizes the carbon to CO before reducing it back down to the alcohol. Hammond *et al.* explored one means of taming the direct oxidation, so as to stop at the desired product. Specifically, they sought to optimize zeolite-catalyzed oxidation of methane by hydrogen peroxide. They first discovered that trace iron is essential to the catalytic activity and went on to map out a preliminary diiron-centered mechanism using a combination of spectroscopic probes and density functional theory simulations. Next, the authors observed that OH radicals underlie overoxidation processes and that the introduction of copper ions stems this activity. A combination of iron and copper additives to the zeolites offered >90% methanol selectivity at ~10% methane conversion. Although hydrogen peroxide is currently an expensive oxidant to apply to commodity-scale methanol synthesis, the selectivity principles uncovered in the study may enhance selective hydrocarbon oxidation processes more broadly. — JSY

Angew. Chem. Int. Ed. **51**, 10.1002/anie.201108706 (2012).

GENETICS

Isoform Identification

The differential reconnection of transcribed exons, termed alternative splicing, has the potential to result in one gene encoding multiple protein isoforms. The degree to which alternatively spliced transcripts are translated into functional proteins, however, is not well understood. Ezkurdia *et al.* used data across multiple mass spectrometry experiments to investigate the degree to which genes with alternative transcripts gave rise to protein isoforms. Comparison of the predicted proteins from the gene and genetic variant database of ENCODE (GENCODE) to the Swiss-Prot database allowed for the identification of 150 human genes that encoded at least one protein isoform and 13 with three or more, with the caveat that identification was biased toward those most likely to be detected. Heterogeneous nuclear ribonucleoproteins, which are involved in the regulation of alternative splicing, showed enrichment in alternative isoforms. Furthermore, the majority of differences detected among all predicted isoforms differed

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in sequence by the insertion/deletion of a single amino acid. Investigations into the *Drosophila* and mouse proteomes revealed similar patterns. Together, these results suggest that alternative splicing is under selective constraint. — LMZ

Mol. Biol. Evol. **29**, 10.1093/molbev/mss100 (2012).

BIOMEDICINE

Aiming Even Lower

The use of statins to lower plasma levels of LDL (low-density lipoprotein) cholesterol can reduce the risk of cardiovascular disease by an estimated 30 to 40%. Yet some experts have argued that lowering LDL cholesterol to levels below current recommendations—by coadministering drugs that act by a complementary mechanism, for example—may confer even more health benefits than statins alone. PCSK9 (proprotein convertase subtilisin/kexin type 9) is an appealing new drug target because it keeps plasma cholesterol levels high by promoting degradation of the receptor on liver cells that removes cholesterol from the blood. Interestingly, a small percentage of humans carry mutations in PCSK9 that reduce its activity and these individuals have a lower risk of heart disease, suggesting that therapeutic inhibition of PCSK9 will be safe. Stein *et al.* conducted small phase-1 trials of a human PCSK9 monoclonal antibody (REGN727) given to healthy volunteers and to individuals with familial and nonfamilial hypercholesterolemia. Injection of REGN727 induced no serious adverse effects in these short-duration trials, and in all groups the antibody significantly reduced LDL cholesterol levels as compared with placebo. — PAK

N. Engl. J. Med. **366**, 1108 (2012).

ENTOMOLOGY

A Toast to Fruitfly Health

A propensity for rotting fruit puts the fruit fly *Drosophila melanogaster* in contact with fermented material that can contain substantial amounts of alcohol. Milan *et al.* tested whether alcohol consumption by fly larvae might actually serve to protect them from nasty wasps that attack and lay their eggs in the fruit fly larvae. Indeed, the wasps appeared to be more sensitive to the toxic effects of alcohol than were the flies. The wasps laid fewer eggs on flies that were consuming ethanol and when they did, those eggs had disrupted development and were less likely to prevent proper development of the fly larvae. Furthermore, the flies seem to know what's good for them. When given a choice of food with or without alcohol, flies that were infected were more likely than control flies to seek out and consume the ethanol-spiked food. Whether humans might derive benefits from such a defense against parasites remains to be determined. — LBR

Curr. Biol. **22**, 488 (2012).

ECOLOGY

Fluctuating Forests

In the current era of rapidly changing climate, the past can provide useful lessons about the responses of ecological communities to climate fluctuations. Increased or repeated drought is a plausible scenario in some currently humid environments under climate change, although where and when this might occur is still hard to predict. The kinds of ecological change that might be expected, however, are illustrated in a study of historical ecological change in the humid western Great Lakes area of North America in response to the Medieval Climate Anomaly (MCA). The MCA began approximately 1050 years ago, lasted for 450 years, and was characterized by a warmer climate in north temperate regions and a series of droughts in the Great Lakes region. Booth *et al.* used pollen analyses and subfossil testate amoebae (which are sensitive indicators of water table depth in peatlands) to trace the population changes in drought-sensitive beech trees during this period. They show that beech declined in abundance sharply wherever drought and increased moisture fluctuations occurred, with associated effects on fire incidence and other components of the ecological community. These findings illustrate how currently moist regions could experience rapid ecological change as a result of increased climatic fluctuations in a warming world. — AMS

Ecology **93**, 219 (2012).

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