elements capable of responding to the same stereotyped signals de novo (see the figure). The de novo origination model, for example, would require the independent evolution of the same transcription factor binding site(s) in many genes distributed across the genome, whereas TEs can donate the same sets of transcription factor binding sites to nearby genes upon their integration into the genome.

Although TE-mediated rewiring of GRNs provides a simple and straightforward model of gene regulatory evolution, and numerous cis-regulatory elements for individual genes in mammalian genomes are derived from TEs (*10*), few studies have demonstrated that TEs actually have globally rewired GRNs (*11*). Among the most notable barriers to developing mechanistic explanations for the role of TEs in the origin and diversification of GRNs is a lack of model networks that are both amenable to detailed functional studies and that evolve rapidly enough that TEs can be caught in the act of remodeling the regulatory landscape. The mammalian immune system is an ideal model in which to explore the molecular mechanisms that underlie GRN evolution because numerous genomic and experimental resources have been developed for mammals. In addition, immune responses evolve fast enough that evolutionary changes can occur between relatively closely related species, yet slow enough that the functional significance of TE-derived regulatory elements can be inferred and experimentally validated.

> ***"TEs provide a mechanism to rapidly distribute nearly identical copies of regulatory elements..."***

Proinflammatory cytokines, such as interferon-γ (IFNG), are essential signaling molecules in the innate immune response that are released upon infection and that regulate a battery of downstream immunity factors called IFN-stimulated genes (ISGs). ISGs are regulated by cis-regulatory elements containing binding sites for interferon regulatory factor (IRF) and signal transducer and activator of transcription (STAT) transcription factors that are activated by IFN signaling. Although the innate immune response is conserved as a process, the specific genes activated by IFNG signaling have diverged within mammals, potentially reflecting lineage-specific adaptations to host-pathogen interactions. Chuong *et al.* found that 27 TE families were enriched within IFNG-responsive cis-regulatory elements. Remarkably, 20 of these TE families originated from long terminal repeat (LTR) promoter regions of ERVs. These data suggest that many TE-derived IFNG-responsive cis-regulatory elements arose from ancient retroviral infections.

Previous studies have implicated ERVs in the genesis of cis-regulatory elements important for the evolution of mammalian pregnancy (*12*), placentation (*13*), and most notably the core regulatory networks in embryonic stem cells (*14*). ERVs are normally repressed in somatic cells by histone modifications and methylation, suggesting that ERVs escape silencing in some contexts, such as the placenta and embryonic stem cells, which appear to have pervasive expression of ERVs. Chuong *et al.*, for example, speculate that IFNG-responsive cis-regulatory elements in LTRs are remnants of ancient retroviral enhancers that used host signaling to promote viral transcription and replication; thus, ERVs may have evolved to be derepressed upon IFNG stimulation. This conjecture suggests an answer to a nagging question: What is it about TEs that predisposes them to act as tissue-specific regulatory elements? In this case, ERVs may be predisposed to act as regulatory elements in IFNG-responsive cells because they already possess functional IRF and STAT binding sites. More generally, TEs may be biased in the kinds of transcription factor binding sites they contain because of their own biology, leading to domestication as regulatory elements in cell types that already express those transcription factors. Although more detailed experimental approaches will be required to reconstruct the exact mechanisms by which TEs rewire gene regulatory networks, the experimental framework provided by Chuong *et al.* will lead the way. ■

Department of Human Genetics, The University of Chicago, 920 East 58th Street, CLSC 319C, Chicago, IL 60637, USA. E-mail: vjlynch@uchicago.edu

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CHEMISTRY

Surprised by selectivity

A bifunctional catalyst enables olefin synthesis from carbon monoxide and hydrogen at high selectivity

By **Krijn P. de Jong**

Lower olefins, particularly ethylene (C_2H_4), propylene (C_3H_6), and butylenes (C_4H_8), are important intermediates in the manufacture of products such as plastics, solvents, paints, and medicines. They are produced worldwide in amounts exceeding 200 million tons per year (see the photo) (*1*), mostly from crude oil. More recent approaches use methanol or synthesis gas (syngas; a mixture of carbon monoxide and hydrogen) as feedstocks, but capital investments are high and/or selectivities to lower olefins limited. A bifunctional catalyst reported by Jiao *et al.* on page 1065 of this issue (*2*) enables the direct conversion of synthesis gas to lower olefins with a surprisingly high selectivity.

Synthesis gas is an important intermediate in the chemical industry for the production of ammonia, hydrogen, and methanol. Any carbon-containing feedstock such as coal, natural gas, or biomass can be converted via steam reforming or gasification into a mixture of carbon monoxide and hydrogen. In previous studies, lower olefins have been produced in one step from synthesis gas with selectivities of 50 to 60% (*1*, *3*), a process referred to as FTO (Fischer-Tropsch to olefins).

Methanol can also be converted to olefins with the help of zeolite catalysts (*4*). Using this MTO (methanol to olefins) process, high yields of ethylene and propylene have been obtained, but catalyst deactivation poses challenges. Recently, the MTO technology was implemented at industrial scale in China, using coal as feedstock for the production of methanol. Since the shale-gas revolution in the United States, methanol production has become economically much more attractive. In the coming decade, transport of an additional 30 million tons per annum of methanol from the United States to China for use in MTO technology in Asia is foreseen (*5*). How-

Inorganic Chemistry and Catalysis, Debye Institute for Nanomaterials Science, Utrecht University, Utrecht, Netherlands. E-mail: k.p.dejong@uu.nl

Large-scale olefin production. At this chemical plant in Ludwigshafen, Germany, steam cracking is used to make olefins from crude oil.

ever, methanol needs to be produced from methane, making olefin production more complex and expensive. Direct conversion of methane to chemicals (including lower olefins) seems attractive, but product yields have been limited (*6*) or process conditions harsh (*7*).

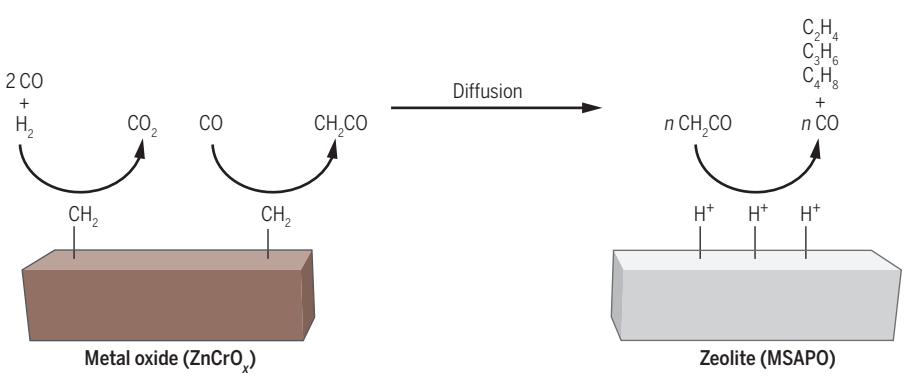
Jiao *et al.* now report selectivities for lower olefins of about 80% of total hydrocarbons, produced directly from synthesis gas at 17% CO conversion under industrially attractive conditions—400°C, 25 bar, and H_2/CO volume ratio of 1.5—and catalyst lifetimes exceeding 100 hours. Their bifunctional catalyst, OX-ZEO, consists of a metal oxide ($ZnCrO_x$) and a zeolite (MSAPO). CO and H_2 are activated on the metal oxide surface, leading to formation of CH_2 species and subsequently of ketene (CH_2CO). The latter diffuses via the gas phase to the zeolite and is converted to lower olefins (see the figure).

The authors provide extensive experimental and theoretical data in support of this mechanism for converting synthesis gas to hydrocarbons. On metal or metal carbide surfaces, CH_x species polymerize, resulting in a statistical distribution of hydrocarbon chain lengths called the Anderson-Schulz-Flory (ASF) distribution. This statistical distribution of products leads to a maximum lower-olefin yield of around 60% (*3*). By using a metal oxide catalyst to activate CO, the authors prevent polymerization of CH_x species, allowing CO insertion followed by ketene formation. Mass spectrometry data show that ketene is indeed present in the gas phase. The authors use ketene from the decomposition of acetic acid anhydride to provide evidence for olefin formation over the zeolite from this intermediate. Well-known MTO catalysts (*8*) did not perform well as the second component of the bifunctional catalyst; the authors therefore tailored the acidity of the MSAPO zeolite, using temperature-programmed desorption of ammonia as an indicator for acid site strength.

The main components of the OX-ZEO catalyst resemble a methanol synthesis catalyst and an MTO catalyst. However, as noted by the authors, previous attempts to combine methanol synthesis and MTO catalysts mainly yielded paraffin and aromatics. Furthermore, they show that when methanol is fed to the MSAPO catalyst as an intermediate, catalyst stability does not reach the >100 hours found for the OX-ZEO catalyst.

Most important, by disconnecting CO activation and C-C bond formation in hydrocarbons, the authors circumvent ASF distribution in the FTO process. This leads to the surprisingly high 80% selectivity to lower olefins.

The research reported by Jiao *et al.* should be of interest to both academia and industry. It remains to be shown whether ketene or the thermodynamically more stable methanol is the key intermediate in the new process. The bifunctional nature of the catalyst invites structure performance studies including the effects of proximity of oxide and acid functions (*9*). The new process could become a serious competitor for industrial processes such as FTO (*3*) and MTO (*4*, *8*). ■



Two steps in one. Schematic representation of the OX-ZEO catalyst and the reaction scheme proposed by Jiao *et al.*

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