of the virus and are therefore safe, but their development has been hindered by the limited identification of antigens. Attempts to use either recombinant proteins or DNA vaccination have induced only partial protection or no protection.

In the 1960s, it was observed that recovery from infection with less virulent ASFV isolates protected pigs against subsequent challenge with related virulent ASFV. This is because almost all virus proteins are expressed in infected cells, thus inducing a cellular immune response against a range of virus epitopes in addition to antibody responses to the native virus particle. This demonstrated the potential for LAVs as vaccines. The introduction of ASFV to Portugal and Spain in 1960 provided impetus to produce LAVs for vaccination. LAVs are produced by selecting attenuated ASFV resulting from passage in cells, which results in genome modifications. Vaccines derived by this procedure were used for an extensive vaccination campaign (*13*). However, these vaccines were insufficiently tested and caused a debilitating chronic disease in many vaccinated pigs, resulting in vaccine withdrawal. Other naturally attenuated ASFV strains have conferred different levels of protection but also caused unacceptable postvaccination reactions (*1*).

The current status of ASFV vaccine development shows some encouraging results. The most advanced vaccine candidates are LAVs in which virulence genes are deleted, resulting in a weakened virus that still replicates (so it can trigger immunity) and can be amplified in cell culture for vaccine production. However, a licensed cell line in which a LAV can be stably grown and produced on a large scale is still required. Deletion of ASFV genes that inhibit host antiviral type I interferon responses has been an effective strategy to attenuate the virus and induce protection. These interferon inhibitory proteins include members of multigene family (MGF) 360 and MGF 505. Genetic modification allows for fine-tuning of safety and efficacy and the introduction of markers to distinguish infected from vaccinated animals (DIVA). This is needed to monitor vaccine efficacy and to confirm disease eradication. Several gene-deleted genotype I and genotype II LAV vaccine candidates have shown promising results in preliminary testing (*1*). However, these require further testing and scale-up of production before completing larger-scale safety and efficacy testing in vivo (see the figure).

Although LAVs have the potential to be effective vaccines and have been used for the eradication of smallpox and rinderpest, there are safety concerns. These include induction of ASF-like symptoms and dispersal of the vaccine virus. The vaccine may not protect enough animals to stop the epidemic. Moreover, vaccinated animals may spread the virulent virus to uninfected animals. These safety issues were also observed using a naturally attenuated ASFV strain from Latvia (Lv17/WB/Rie1) (*14*). This virus caused clinical signs of ASF in pigs, including joint swelling, which is associated with a chronic form of ASF (*15*). In addition, the vaccine replicated to high concentrations in blood and spread to pigs on contact. Replication of the virulent virus was not sufficiently controlled, and the pigs shed the virulent virus sporadically and could therefore spread ASF to other animals (*14*), potentially failing to stop the epidemic. Such safety issues should be considered during animal testing of vaccine candidates.

The race to develop an ASFV vaccine may overshadow comprehensive efficacy and safety testing, thus potentially investing in the wrong vaccine development strategy and in unnecessary use of animals for experiments. Additional caution should be taken when developing LAV vaccines to be spread in nature in oral baits. The challenge of ASFV vaccine development, including vaccination of wild boar, should not be underestimated and requires the cooperation of many disciplines in the early stages of vaccine development. ■

REFERENCES AND NOTES

1. M. Arias *et al.*, *Vaccines (Basel)* **5**, 35 (2017).
2. R. E. Montgomery, *J. Comp. Pathol. Ther.* **34**, 159 (1921).
3. D. Beltrán-Alcrudo *et al.*, *FAO EMPRES Watch* **2008**, 1 (2008).
4. European Food Safety Authority (EFSA) et al, *EFSA J.* **16**, 5494 (2018).
5. D. Smith, T. Cooper, A. Pereira, J. B. D. C. Jong, *One Health* **8**, 100109 (2019).
6. Food and Agriculture Organization of the United Nations (FAO), "One year on, close to 5 million pigs lost to Asia's swine fever outbreak," 9 August 2019; www.fao.org/news/story/en/item/1204563/icode/.
7. N. Pitts *et al.*, "Agricultural commodities report" (Australian Government Department of Agriculture, 10 March 2019); www.agriculture.gov.au/abares/research-topics/agricultural-commodities/sep-2019/african-swine-fever.
8. E. Chenais, K. Ståhl, V. Guberti, K. Depner, *Emerg. Infect. Dis.* **24**, 810 (2018).
9. I. Nurmoja *et al.*, *Prev. Vet. Med.* 10.1016/j.prevetmed.2018.10.001 (2018).
10. EFSA et al, *EFSA J.* **12**, 3616 (2014).
11. World Organization for Animal Health, World Animal Health Information Database, "African swine fever"; www.oie.int/en/animal-health-in-the-world/information-on-aquatic-and-terrestrial-animal-diseases/african-swine-fever/reports-on-asf/.
12. C. Alonso *et al.*, *J. Gen. Virol.* **99**, 613 (2018).
13. J. Manso Ribeiro *et al.*, *Bull. Off. Int. Epizoot.* **60**, 921 (1963).
14. C. Gallardo *et al.*, *Transbound. Emerg. Dis.* **66**, 1399 (2019).
15. P. J. Sánchez-Cordón, M. Montoya, A. L. Reis, L. K. Dixon, *Vet. J.* **233**, 41 (2018).

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MEMBRANES

Porous crystals as membranes

Microporous crystalline membranes are designed for gas separation and potential scale-up

By **Moises A. Carreon**

Chemical separations account for about half of the United States' industrial energy use and as much as 15% of total U.S. energy consumption (*1*). Most of these industrially employed separations, including distillation, evaporation, and drying, are thermally driven. Energy-efficient separation technologies require reducing heat consumption. Non–thermally driven membrane technology could play a key role in gas separations that are less energy-intensive, making them potentially economically feasible. On page 667 of this issue, Li *et al.* (*2*) illustrate a powerful example using a microporous crystalline membrane to separate water from light gases, with subsequent carbon dioxide conversion to liquid fuels by hydrogenation.

Porous crystals grown as membranes with equally sized micropores or with limiting pore apertures are highly appealing materials to effectively separate gas molecules by size exclusion. Li *et al.* designed a sodium aluminosilicate microporous crystalline molecular sieve NaA zeolite membrane displaying precise water conduction nanochannels that allow water to effectively permeate through a continuous crystalline membrane and restrict the diffusion of gas molecules. This strategy may be useful for many industrially important processes where water is present.

The precise gate effect of the membrane can be exploited for the separation of other industrially relevant gas mixtures, including ammonia separation from light gases. For instance, this zeolite composition has a pore entrance size that should be ideal to effectively sieve ammonia from hydrogen and nitrogen. Furthermore, the pore entrance of NaA zeolite promotes favorable charge-dipole interaction with polar molecules. The higher polarizability of ammo-

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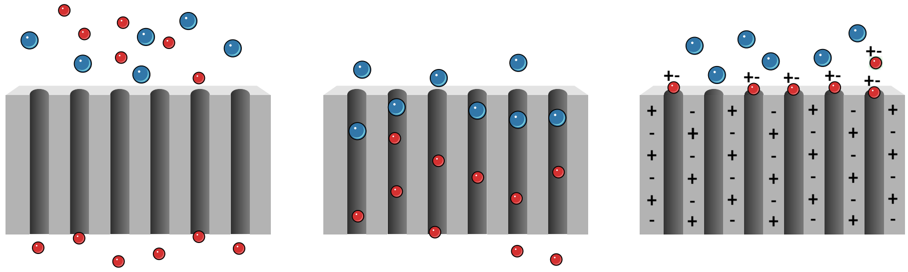
Different strategies to separate gases

Porous crystalline membranes are designed to use several different mechanisms to separate out different types of gases.



Molecular sieving: Changing the effective pore diameter will separate out the smaller gas molecules from larger ones.

Diffusivity differences: The pore size and shape can affect how quickly large and small molecules move through the porous crystal membrane.

Competitive adsorption: Tailoring membrane surface charge can change the relative adsorption of different molecules depending on their polarity.

GRAPHIC: KELLIE HOLOSKI/*SCIENCE*

nia should favor adsorption over the zeolite surface, resulting in highly selective ammonia membranes.

Microporous crystal sieves suitable for gas separations can be inorganic, organic, or a hybrid material. Zeolites are the prime example of porous inorganic crystalline molecular sieves that have been effectively used in gas separations (*3*). Metal-organic frameworks are microporous crystalline materials composed of transition metal ions linked together by organic ligands (*4*) that have shown an ability to separate gas mixtures. Covalently bonded porous organic cages can be assembled into crystalline microporous materials with three-dimensional connectivity. These materials combine highly desirable properties, such as uniform micropores, high surface area, and thermal and chemical stability. This makes them highly appealing candidates for challenging molecular gas separations (*5*).

The preparation of continuous porous crystalline membranes for molecular gas separations is not a trivial issue. Porous crystals displaying particular separation properties in powder or particle form may not be suitable for membrane preparation because limited adhesion to the support can lead to delamination, induced stresses at the membrane-support interface, or poor crystal intergrowth. Nonetheless, several examples of the successful synthesis of microporous crystalline membranes for gas separations are well documented. ZSM-5 (Zeolite Socony Mobil-5 with MFI topology) membranes are one example; they effectively separate gas molecules, including isomers, with very small differences in size and shape (*6*).

Over the past two decades, considerable effort has gone into developing zeolite membranes for gas separations (*7*). The successful synthesis of any metal-organic framework membrane demonstrated the feasibility for using porous crystalline compositions for hydrogen separation (*8*). This motivated the development of continuous metal-organic framework membranes (*9*) and continuous porous organic cage membranes for gas separation (*10*).

> **"Porous crystals grown as membranes with… limiting pore apertures are highly appealing materials to effectively separate gas molecules by size exclusion."**

Three main separation mechanisms—molecular sieving, differences in diffusivities or kinetic contribution, and competitive adsorption or thermodynamic contribution—are observed for gas mixtures over microporous crystalline membranes (see the figure). When the effective pore aperture of the microporous crystal lies between the kinetic diameters of the molecules to be separated, molecular sieving may be possible (*11*). However, strictly speaking, true molecular sieving takes place only when molecules diffuse selectively through crystal micropores or through a single crystal. When comparing zeolites to metal-organic frameworks, we expect sharper molecular sieving for zeolites, as they have rigid pore sizes when compared to metal-organic frameworks. Smaller and lighter molecules should diffuse faster than larger and heavier molecules, promoting separation on the basis of differences in diffusivities. Preferential adsorption occurs through a variety of surface forces between the membrane and molecules with high dipole moments (*11*). Li *et al.* demonstrate that exploiting the kinetic and thermodynamic contributions could lead to highly selective water membranes.

A different separation mechanism for gases over porous organic cages was shown to effectively separate hydrogen isotopes by kinetic quantum sieving (*12*). The structure and distinctive solid-state molecular packing of porous organic cages differentiate them from other porous crystals, resulting in special transport and adsorption properties, and therefore unusual separation mechanisms.

The study by Li *et al.* represents a path toward the rational design of zeolite membranes for a highly relevant industrial separation focused on water removal from light gases, and subsequent conversion of carbon dioxide into liquid fuels. An outstanding issue is whether these high-performance NaA zeolite membranes can be scaled up. Demonstrating zeolite membranes at scale requires a testing facility; one in the United States is currently under construction. This oil field facility will allow testing of a scaled-up zeolite membrane, denoted as DDR, having uniform limiting pore apertures of 0.36 nm for carbon dioxide recovery from natural and associated gases. This field demonstration test is an exciting step toward the potential deployment of porous crystalline membranes for gas mixture separations. This should motivate focusing membrane development around cheaper supports amenable to scale-up, the assessment of membrane performance under industrial-like conditions, and stability studies. Promising membrane compositions from laboratory studies can then be scaled up and tested in the presence of impurities and the effects of pressure and temperature. This requires a true but difficult integrative connection among academia, national laboratories, and industry. ■

REFERENCES AND NOTES

1. D. S. Sholl, R. P. Lively, *Nature* **532**, 435 (2016).
2. H. Li *et al.*, *Science* **367**, 667 (2020).
3. M. E. Davis, *Nature* **417**, 813 (2002).
4. M. Eddaoudi *et al.*, *Science* **295**, 469 (2002).
5. T. Tozawa *et al.*, *Nat. Mater.* **8**, 973 (2009).
6. Z. Lai *et al.*, *Science* **300**, 456 (2003).
7. N. Kosinov *et al.*, *J. Membr. Sci.* **499**, 65 (2016).
8. R. Ranjan, M. Tsapatsis, *Chem. Mater.* **21**, 4920 (2009).
9. S. Qiu, M. Xue, G. Zhu, *Chem. Soc. Rev.* **43**, 6116 (2014).
10. Q. Song *et al.*, *Adv. Mater.* **28**, 2629 (2016).
11. X. Feng *et al.*, *J. Am. Chem. Soc.* **138**, 9791 (2016).
12. M. Liu *et al.*, *Science* **366**, 613 (2019).

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