catalyze the recombination of hydrogen in the gas phase and can enhance the degree of deuterium enrichment in PAHs (*11*).

It is possible that extraterrestrial organic matter was delivered to the early Earth during the heavy bombardment phase. Possible annual delivery rates from 4.4 to 3 billion years ago have been calculated for carbon originating from interplanetary dust particles, comets, and meteorites (*12*). This possible delivery of significant amounts of life's building blocks or their precursors does not, however, explain how living organisms evolved from them.

Despite some caveats, the results presented by Bernstein *et al.* lend support to the possible conversion of PAHs into biogenic molecules on instellar icy grains in dense molecular clouds. These results provide important constraints for the chemistry of the solar system and the origin of life. Future experiments with PAHs in water ices including other major ice components, such as carbon dioxide and methanol, may lead to a great variety of additional products and may provide further insights into the possible astrophysical origin of life's building blocks.

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PERSPECTIVES: IMMUNOLOGY

T Cells and Dendritic Cells Get Intimate

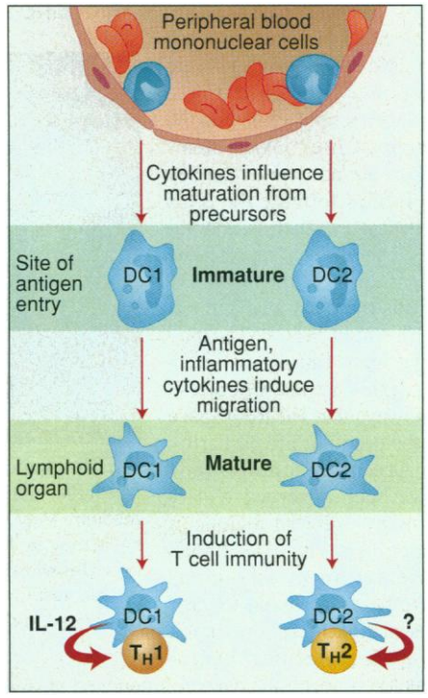
Kim Bottomly

T cells and dendritic cells (DCs) must interact to initiate immune responses against invading pathogens. Immature DCs, located at sites of antigen entry such as the gut mucosa, are specialized for antigen capture but lack the ability to activate T cells. As they mature, DCs migrate to peripheral lymphoid organs where they lose the ability to capture antigen but acquire the capacity to activate naïve T cells carrying receptors for that antigen (*1*). Thus, DCs have all of the features that are essential for the initiation of T cell immunity.

Newly activated CD4 T cells commit early to a pathway of differentiation that results in the formation of two functionally distinct T cell subsets: T helper 1 (T_H1) and T_H2. T_H1 and T_H2 cells differ in the cytokines they secrete (*2*) and the type of response (*3*) they elicit in target cells expressing cytokine-specific receptors. The activation of the appropriate T cell subset is critical for providing protective immunity against a variety of pathogens: T_H1 immunity protects against intracellular parasites such as *Leishmania*, and T_H2 immunity protects against extracellular pathogens such as helminths. The current theory to explain the selectivity of T cell responses postulates that cytokines secreted by neighboring cells drive resting naïve T cells down a particular differentiation pathway. However, a study by Rissoan and colleagues on page 1183 of this issue (*4*) challenges aspects of this model by suggesting that DCs not only provide a common set of signals to initiate clonal expansion of T cells but also provide T cells with selective signals leading to either T_H1 or T_H2 immunity (see the figure).

Why has it taken so long to understand how DCs influence T cell differentiation? Up until 10 years ago, these cells were virtually impossible to study because the low numbers of DCs in lymphoid organs made them difficult to isolate and analyze. Their obvious lack of endocytic capabilities, necessary for efficient antigen uptake and processing, made them unlikely candidates for inducing T cell immunity. Initially identified in 1973 (*5*), their importance as antigen-presenting cells was firmly established through the pioneering work of Steinman and Inaba (*6*). Now it is widely accepted that DCs are antigen-presenting cells that specialize in the initiation of T cell responses in vivo. They provide not only an array of antigenic peptides needed to activate the appropriate antigen-specific T cells, but also produce potent costimulatory signals that drive quiescent T cells into the cell cycle and along the differentiation pathway. Immature DCs located outside the lymphoid organs specialize in antigen capture, whereas mature DCs lose this ability as they acquire the capacity to activate T cells.

How do DCs elicit the appropriate T cell response? One means to induce predominantly either a T_H1 or T_H2 response is to manipulate the cytokine milieu during CD4 T cell activation: Interleukin-12 (IL-12) skews differentiation toward a T_H1 response, and IL-4 toward a T_H2 response. The influence of these cytokines during T cell activation can be readily determined in vitro, but it has been more difficult to determine the primary source of these cytokines in vivo. Recently, DCs were shown to produce IL-12. This raises the question that if DCs are required for the activation of all CD4 T cells and if DCs produce IL-12 upon interaction with the CD4 T cell, then how is a T_H2 response ever elicited? Furthermore, if IL-4



Regulating T cell immunity. Dendritic cells (DCs) are antigen-presenting cells that specialize in initiating T cell activation. There are two categories of DCs: DC1 secretes IL-12, which skews CD4 T cell differentiation toward the production of T_H1 cells, whereas DC2 favors production of T_H2 cells. T helper cells may regulate T_H1 or T_H2 responses by determining the survival of the appropriate dendritic cell subset.

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is required for the generation of a T_H2 response, which cells located in the vicinity of DC-dependent T cell activation produce the IL-4?

A different explanation for the initiation of CD4 T cell responses is provided by the study of Rissoan *et al.* The investigators (*4*) report that DCs exist in at least two forms: myeloid-like cells (DC1) produce abundant IL-12 and induce a T_H1 response, and lymphoid-like cells (DC2) induce a T_H2 response (see the figure). Not surprisingly, the lymphoid-like DCs secrete very low levels of IL-12, providing a permissive environment for T_H2 generation. Yet intriguingly, these DC2 cells fail to secrete IL-4. In this model, the CD4 T cell cytokines induced by DCs differ because the two types of DCs themselves differ in the inductive signals they provide to newly activated CD4 T cells. Most importantly, the induction of T_H2 responses described in this report is not only independent of IL-12 but also of IL-4, suggesting that there is a unique signal provided by DC2 that induces naïve T cells to become T_H2 cells.

These studies suggest a new function for DCs: determining which type of T cell immune response is generated. To do this, DCs must exist as functionally distinct subsets that are distinguished through morphology and the expression of cell surface glycoproteins. Both DC subsets retain the ability to activate naïve T cells, but differ in the delivery of cytokines or signals influencing CD4 T cell differentiation and functional commitment. The differences between the DC subsets appear to be a consequence of early maturation events. What is not known from the Rissoan study is whether the two types of DCs originate from the same precursor cells or whether the same precursor is influenced by its microenviroment to give rise to distinct subsets. (In this study, DC1 and DC2 were generated in vitro in the presence of distinct maturing cytokines.)

Selective T_H1 or T_H2 activation is crucial to the outcome of many immune responses. The findings of Rissoan and co-workers (*4*) now suggest that the responsibility for this decision be shifted from the T cell to the antigen-presenting cell. This, in turn, raises more questions: Which molecules induce T_H2 responses during contact between T cells and DCs? What distinguishes DC1 from DC2? Is it their microenvironment, as suggested by the recent study of Stumbles *et al.* (*7*), or is it the distinct invariant receptors used to ingest antigen by immature DCs in peripheral tissues? The focus of future research will now shift from the control of T cell activation to the control of DC1 and DC2 production. Intriguingly, the results of Rissoan *et al.* also indicate that T helper cells themselves may regulate T_H1 and T_H2 responses by determining the survival of the appropriate dendritic cell subset.

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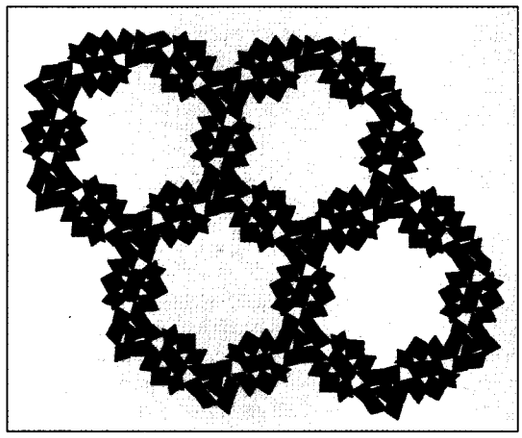
PERSPECTIVES: POROUS MATERIALS

Prospects for Giant Pores

Gérard Férey and Anthony K. Cheetham

The world of crystalline porous materials has long been dominated by aluminosilicate zeolites, which are used widely in catalysis, separations, and ion-exchange processes (*1*). The discovery of new families of porous materials, including new crystalline systems as well as amorphous mesoporous materials, has raised hopes that such materials could be tailored for new applications, for example, in sensors and nanotechnology. Consequently, there has been tremendous interest in novel porous solids, both inorganic and organic (*2*).

To date, more than 40 elements have been incorporated as major components in crystalline porous materials. Researchers seek even further diversity by increasing the size of their pores. Zeolites typically have pore diameters of less than 10 Å. Larger, "giant" pores might be used, for example, as nanoreactors, and may allow attachment of different chemical groups to their walls. An elegant natural material of this class is the iron phosphate mineral cacoxenite, which has channels 14 Å in diameter (see the figure) (*3*). Two eye-catching reports in this issue on pages 1145 and 1148 illustrate exciting synthetic design strategies being used for creating large-pore inorganic (*4*) and metallo-organic systems (*5*).



Ahead of the game? Cacoxenite, a natural iron phosphate mineral, has one of the largest pore sizes of the known crystalline nanoporous materials, but recent synthetic materials are surpassing its pore size (*4*).

It has been said that "Nature hates vacuum". This is certainly true in many solids with potentially very large cavities: The empty space is often filled by guest species or by interpenetration of identical sublattices. Different strategies can be used to circumvent this problem. Li *et al.* (*4*) use the templated "secondary building unit" (SBU) strategy to build up porous solids based on indium sulfide. SBUs are the structural components that create the architecture of the open framework. Large SBUs can be constructed from smaller units, for example, by assembling 4 or 10 tetrahedral units into supertetrahedral units, which then replace the single tetrahedra of the parent structures, resulting in much larger pores. Li *et al.* obtain open frameworks with a wall composition of $In_{10}S_{18}^{6-}$. The cavities are filled with charge-compensating organic cations and water molecules (*4*). Depending on the organic cation, two different architectures are found, named ASU-31 and ASU-32. The strategy is not new, but its use by Li *et al.* leads to structures with remarkably large cavities, with diameters of 25.6 and 14.7 Å for ASU-31 cages and ASU-32 tunnels, respectively. In both phases, the framework corresponds to only ~20% of the total volume, far below the ~40% found in other solids with large pores, such as cacoxenite and the zeolite faujasite.

Chui *et al.* (*5*) use metallo-organic polymers (*6*) to synthesize a material with large pores, which they name HKUST-1. In this

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