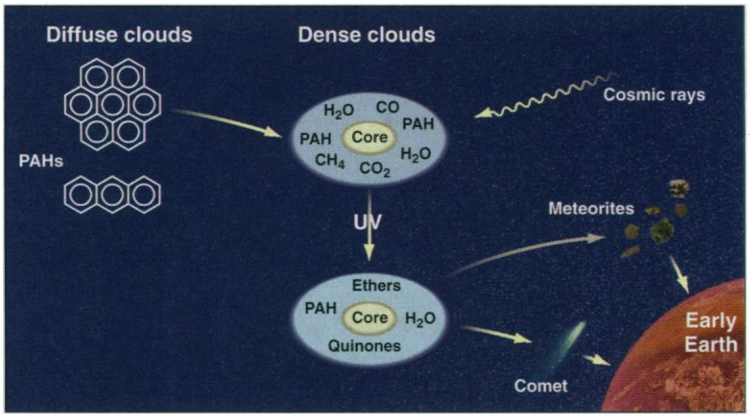
PERSPECTIVES: ASTROPHYSICAL CHEMISTRY

Molecules on a Space Odyssey

Pascale Ehrenfreund

Aromatic molecules have been identified in extraterrestrial matter such as meteorites, and their fingerprints have been observed in astronomical spectra. Their ubiquitous presence has been confirmed by recent measurements of the Unidentified Infrared Emission bands (UIRs) between 3 and 15 μm made by the Infrared Space Observatory (ISO) (*1*). Polycyclic aromatic hydrocarbons (PAHs) may be the most abundant organic molecules in space, making up 20% of the total cosmic carbon (*2*). Could these molecules hold clues for the origin of life? PAHs themselves are not one of the key molecules forming the basis of life. Nevertheless, laboratory experiments reported by Bernstein *et al.* on page 1135 of this issue (*3*) lend support to the idea that PAHs may have been important intermediates in the chemical pathways that led from space to the origin of life on Earth.



Did life's building blocks come from space? PAHs are thought to form in circumstellar outflows or by processing of carbon dust in the diffuse interstellar medium. They may then be accreted on icy grains in dense clouds. Alternatively, PAHs may be formed directly in icy grains by energetic processing with cosmic rays. Ultraviolet light can lead to chemical reactions of the PAHs in the icy grain mantle, resulting in possible precursors for biogenic molecules (*3*). Organics incorporated in comets or meteorites may have been delivered to the early Earth.

Aromatic compounds have been observed widely in many different regions of space (*1*). The UIR bands observed in these regions have been attributed to various aromatic species such as PAH molecules, hydrogenated amorphous carbon, quenched carbonaceous composites, or coals. Of these, all except the PAHs are in the condensed phase. ISO showed the presence of UIR bands in regions with low UV irradiation, indicating that the responsible carriers are transiently heated through the absorption of a single UV photon (*4*). This is a strong argument in favor of the gaseous nature of PAHs in such environments, although their presence in other regions has to be further investigated.

PAHs are not only found in interstellar space. A wide variety of PAHs is found in the terrestrial environment, for example, as air pollutants resulting from incomplete combustion (*5*). Traces of PAHs are found in the solar system, where they have been identified in carbonaceous and ordinary chondrites (granules in meteorites), interplanetary dust particles and comets. The origin of PAHs (martian or terrestrial contamination) in the martian meteorite ALH84001 is still hotly debated.

It is assumed that PAH molecules are produced in the outer atmospheres of carbon stars. Shock fragmentation of carbonaceous solid material can also be an important source of aromatic molecules. A recent analysis of the UIR bands indicates that interstellar PAH molecules typically contain several hundred atoms (*6*), although molecules responsible for many narrow Diffuse Interstellar Bands (DIBs) in absorption could be PAHs with 30 to 70 carbon atoms (*7*). PAHs are very stable, which can be attributed to the delocalization of electrons over their carbon skeleton. The strength of the local ultraviolet radiation field in the interstellar space determines their degree of ionization, dehydrogenation, fragmentation, and destruction. It can be hypothesized that once formed, PAH molecules are accreted on interstellar grains in dense molecular clouds. Recent laboratory experiments have shown that PAHs may also be produced by bombardment of interstellar ices with galactic cosmic ray particles (*8*).

PAHs may react further to form a variety of compounds. Interstellar icy grains act as an important catalyst in the interstellar medium. Processes such as ultraviolet irradiation, cosmic ray bombardment, and temperature variations determine the growth and chemical evolution of interstellar icy grains (see the figure). Such processes become important when molecular clouds evolve from an initial cold quiescent phase to warm, dense, and active protostellar regions. Ices (consisting of water, methane, methanol, or carbon dioxide) that are detected in the vicinity of protostars are orders of magnitude more abundant than their gas-phase counterparts. It is therefore likely that most of the chemical evolution toward complex molecules takes place in the solid phase. Fortunately, the solid phase is particularly accessible to laboratory experiments simulating an astrophysical environment (*9*).

Bernstein *et al.* show that irradiation of PAHs in water ice with ultraviolet light results in the formation of a diverse mixture of organic molecules, including ethers, quinones, and alcohols. These may then react further to form amino acids and other biochemical molecules. A limiting factor for the formation of complex organics via the mechanism proposed by Bernstein *et al.* (*3*) is the uncertain strength of the UV field, which is attenuated efficiently in dense clouds. Recent ISO results show strong evidence for thermal processing of ices and a surprising lack of evidence for radiative processing (*10*).

The incorporation of interstellar matter in meteorites and comets in the presolar nebula provides the basis of the "cosmic dust connection," which proposes that the building blocks of life originate in cosmic dust and are transported to Earth. Many building blocks or precursor molecules for life, such as hydrogen cyanide, formaldehyde, purines, and amino acids, have been identified in astronomical observations of the interstellar gas, in comets, and in laboratory measurements of extraterrestrial material. The anomalous isotopic composition of certain compounds (such as PAHs) as well as deuterium enrichments in meteoritic samples are an important tool for reconstructing the extrasolar origin of such compounds. An important finding by Bernstein *et al.* is that hydrogen and deuterium exchange rapidly between the PAHs and the ice. This may explain the deuterium enrichment observed in some meteorites. However, recent chemical models also indicate that PAH cations can

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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

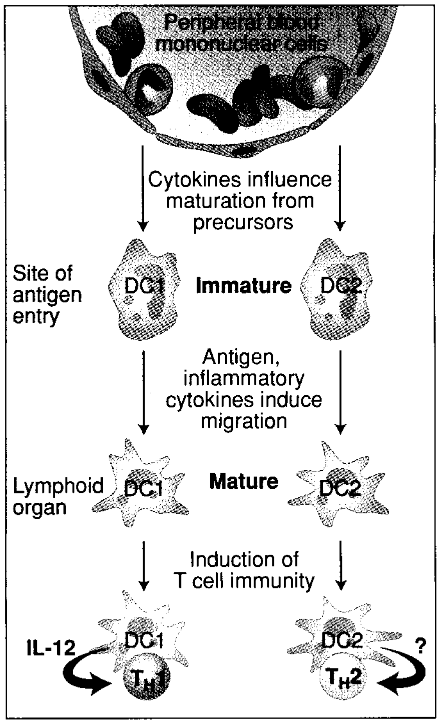
Kim Bottomly

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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