Thus, adult rats that were not licked and groomed adequately as pups by their mothers display increased anxiety, and this may reflect serotonin-dependent mechanisms[7]. Assuming that we can equate developmental stages in mice and humans, these findings might be relevant to brain development and the genesis of anxiety in people, too.

Serotonin appears to be an all-purpose neurotransmitter; it has been implicated in many aspects of brain function and in the effects of many important drugs that are used to treat anxiety, depression, migraine headaches, nausea, pain and irritable bowel syndrome. Gross *et al.*'s discovery[1] — that anxiety is linked to the need for serotonin$_{1A}$ receptors in a specific brain region, at a particular period of development — adds a new layer of understanding of serotonin's function. More generally, the authors' technique lends greater precision and flexibility to gene-knockout approaches for understanding neurotransmitter function, and will hopefully soon be extended to many other neurotransmitters and behaviours. ■

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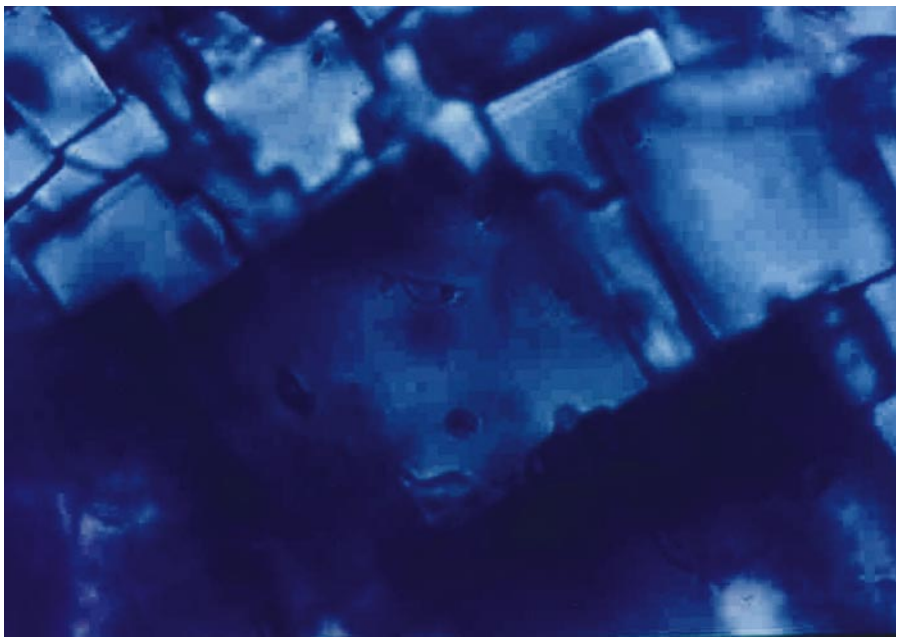
Astrobiology

Seeds of life?

Everett L. Shock

Amino acids, a basic constituent of life, can form in dust grains that are similar to those found in the space between stars. But how much does this tell us about the origins of life on Earth?

Organic compounds in meteorites and interplanetary dust particles are thought by some to hold the key to the origin of life. Increasingly, investigations are revealing a complex history of chemical processes in the Solar System — processes by which the chemicals that are the basis of life may have been synthesized from the gas and dust that make up the interstellar medium. From page 401 of this issue, Bernstein *et al.*[1] and Muñoz Caro *et al.*[2] add another convolution to the plot: their experiments suggest that the conditions that are believed to exist on ice-coated grains in the interstellar medium may be suitable for the synthesis of amino acids, the building-blocks of proteins.



M. E. ZOLENSKY/NASA

Figure 1 **Is it possible that the amino acids found in meteorites originated in the interstellar medium, as recent laboratory experiments suggest? Or were they synthesized on the asteroid parent bodies of the meteorites by the action of aqueous fluids? This picture shows a fluid inclusion in salt crystals found in a meteorite that fell in Monahans, Texas, in 1998, and may be a rare sample of water from an asteroid.**

A wide range of conditions and reaction mechanisms can generate the spectrum of compounds observed in meteorites and dust particles. Isotopic evidence (especially enrichments in ^{15}N and deuterium) supports the idea that at least half of the insoluble organic matter in carbonaceous meteorites originated from sources that existed before the Solar System formed[3,4]. In contrast, soluble organic compounds in these meteorites, including amino acids, are generally thought to have been produced soon after the formation of the Solar System, by the action of aqueous fluids on the asteroids that gave rise to the meteorites (Fig. 1)[5]. In this scenario, the carbon, nitrogen and hydrogen that went into forming the amino acids found in the well-studied Murchison meteorite[6–8] would have been carried by reactive precursors from the interstellar medium, but the amino acids themselves would have formed on the meteorite's parent body.

Results from the Tagish Lake meteorite[9], which fell to Earth in 2000, make the picture more complicated still. Although it contains evidence of aqueous alteration, and although the bulk abundance of organic carbon is similar to that of the Murchison meteorite, concentrations of amino acids in the Tagish Lake meteorite are around a thousand times lower than those in Murchison.

Now two groups[1,2] report amino-acid synthesis in experiments in which ice mixtures thought to be representative of the interstellar medium were subjected to ultraviolet radiation at temperatures below 15 K. Bernstein *et al.*[1] (page 401) report the synthesis of three amino acids (glycine, serine and alanine) in a mixture of water, methanol, ammonia and hydrogen cyanide, where the ratio of the components was 20:2:1:1, respectively. Muñoz Caro *et al.*[2] (page 403) report the synthesis of 16 amino acids and several other compounds in their 2:1:1:1:1 mixture of water, methanol, ammonia, carbon monoxide and carbon dioxide.

Assuming that conditions are comparable between the two experiments, the difference in their results demonstrates the profound effect that bulk composition can have on chemical synthesis. The water-rich experiment reported by Bernstein *et al.* produced only a few compounds. But the water-poor experiment of Muñoz Caro *et al.* generated a host of amino acids, some carrying not just one but two amino groups. The relative yields of mono-amino acids in this latter experiment show a reasonable correlation with the relative abundances found in extracts[10] from the Murchison meteorite. But the meteorite shows no evidence of

di-amino acids such as those seen by Muñoz Caro and colleagues.

Of course, precisely matching meteorite compositions is not the goal of these experiments. Nor has it been the goal of dozens of other successful synthesis experiments, be they gas-phase reactions driven by spark discharges, ultraviolet radiation, shock waves, γ-rays or heat, or aqueous synthesis from a variety of starting materials, including hydrogen cyanide, formaldehyde, methane, carbon monoxide, oxalic acid, carbides or mixtures of these compounds. It appears that nearly every experimental scenario produces organic compounds of some form, which could hardly be more frustrating when trying to unravel what actually produced the organic inventory of the Solar System. Perhaps it is time to stop this seemingly endless series of phenomenological experiments and to concentrate instead on quantifying reaction rates, the relative stabilities of synthesized compounds and the effects of variables such as temperature and pressure.

What about the big picture? Given the truly diverse array of energy sources that may initiate synthesis, complex organic compounds should be expected in any sector of the Solar System that is rich in volatile elements. This is especially true for the outer parts of the Solar System, which host most of the light elements that did not go into making the Sun. On Earth, the hydrosphere (water, including ice and water vapour) accounts for 0.0013% of the planetary volume. But water makes up more than 15% of the volume of Europa, and more than 65% of that of Ganymede — two of Jupiter's largest moons. Even the drier carbonaceous meteorites show evidence of a water-rich past on their parent bodies; some have organic carbon contents that rival those of petroleum source rocks on Earth. So it is plausible to suggest that most organic compounds in our Solar System are extraterrestrial — and abiological — in origin.

Does this tell us much about the origin of life? Well, you can study geology for a living, but knowing how different rocks form doesn't tell you which lumps of rock will become Teotihuacán, the Taj Mahal or Tony's Tavern. Studying the chemical building-blocks of life shows that they are ubiquitous and can exist in the absence of life. Indeed, inferred cosmic abundances of these building-blocks from abiological sources greatly exceed those from living organisms. Accepting that fact, it follows that process-driven investigations into the emergence of life may need to be cast in a different way, which takes into account the materials involved but is not directly tied to them. This, I believe, is a major challenge for the fledgling field of astrobiology. ■

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Cell biology

The ubiquitin connection

Howard Riezman

The cellular world has some daunting problems for biologists. For example, cells use the ubiquitin molecule in different ways to achieve different effects. These tangled events come under the spotlight in new work.

The cells in our bodies need to interact with each other and with the environment around them. For example, they take up certain nutrients (such as cholesterol, vitamin B_{12} and iron) from their environment, and can signal to each other with messenger molecules that activate receptor proteins on the cell surface. Endocytosis — the process by which cells invaginate and then internalize portions of their own outer membrane — is central to these, and many other, cellular events. It allows cells to engulf and then take up nutrients, and to regulate cell-to-cell signalling by internalizing activated receptors.

Several proteins are involved in controlling endocytosis, and some of these are distinguished by the fact that they become labelled with a single copy of the ubiquitin molecule. On page 451 of this issue, Polo and colleagues[1] look at how this labelling comes about. Their results shed some light on the broader question of how cells differentiate between proteins that are to be tagged with just one or many copies of ubiquitin — events with very different outcomes. They also suggest how certain receptor proteins may be 'sorted' into invaginations, ready to be internalized.

The internalization step of endocytosis has been studied intensively, and the results have contributed greatly to our understanding of membrane-transport processes in general. An intracellular protein complex called clathrin is proposed to drive the formation of membrane invaginations ('pits') by coating portions of the membrane. Clathrin-coated pits are then pinched off to form clathrin-coated transport vesicles inside the cell[2]. To get into pits, many cell-surface proteins (such as receptors) in animal cells carry short peptide signals on their intracellular tails that interact directly with components of the clathrin coat.

But this is not universal. For example, many yeast plasma-membrane proteins are covalently modified on specific lysine amino acids by one (or at most two) ubiquitin molecules, and this seems to be the signal driving the proteins towards endocytosis. (Note that

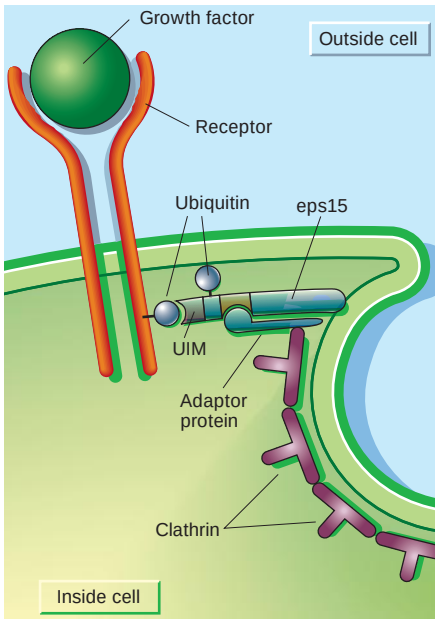

Figure 1 **The many uses of ubiquitin in endocytosis. Polo *et al.* looked at how various proteins that regulate endocytosis, including eps15, become modified with a single ubiquitin protein. They found that these proteins have a specific region that is necessary for such monoubiquitination, and that the previously identified ubiquitin-interacting motif (UIM) forms part of this region and is essential for monoubiquitination. They propose that this region, by binding to other ubiquitinated proteins such as activated growth-factor receptors, could recruit those proteins into membrane pits that are coated with the clathrin protein complex (these pits will later pinch off to form intracellular transport vesicles). Adaptor proteins link eps15 to clathrin.**