

files between “helped” and “unhelped” memory CD8 T cells to better understand how memory CD8 T cell differentiation proceeds.

How “fixed” are memory CD8 T cell qualities? In other words, are the qualities instilled during the initial priming of naïve CD8 T cells permanently embedded, or are they amenable to change every time the T cells are activated? Current data favor the former model, because the presence of CD4 help during “unhelped” memory CD8 T cell recall responses could not remedy their proliferative defects; and vice versa, the lack of CD4 help during “helped” memory CD8 T cell recall responses did not impair their expansion (3, 4). However, these experiments raise two concerns. First, the CD4 help that was supplied to “unhelped” memory CD8 T cells arose from primary effector CD4 T cells, rather than from memory CD4 T cells, and therefore, may not have been robust enough. Second, these studies did not examine whether the secondary memory CD8 T cell population that arose from the “helped” then “unhelped” situation had any qualitative defects. Perhaps, like the primary response, short-lived secondary effector cells are generated normally without CD4 help, but the secondary memory

population will be suboptimal. Janssen *et al.* (4) showed that addition of IL-2 could correct the proliferative defect of the unhelped CD8 T cells in vitro, but this has not been verified in vivo. Furthermore, Bourgeois *et al.* (3) demonstrated that the memory CD8 T cells generated without CD4 help produced less IL-2. Therefore, one might speculate whether the autocrine production of IL-2 determines optimal memory CD8 T cell proliferative responses. In support of this idea, Wherry *et al.* (15) show that the subset of memory CD8 T cells that produces IL-2 has greater proliferative responses than the subset that cannot. Together, these findings suggest that the developmental program instilled in the absence of CD4 T cells may lack instructions to produce IL-2 autonomously and that this is an important function for enhanced recall responses.

This interesting group of papers (1–4) clearly identify that multiple signals, both intrinsic and extrinsic, are integrated into the CD8 T cell developmental program and drive the formation of superior protective responses. Signals from CD4 T cells, perhaps both direct and indirect, help to mold the functional responsiveness of memory CD8 T cells and in particular their ability to acquire a high proliferative potential. It

will be imperative to implement this concept into the design of CD8 T cell-oriented vaccines in order to generate the most long-lasting and efficacious CD8 T cell protection possible. Greater clarification of how CD4 help influences memory CD8 T cell responsiveness will also yield important therapeutic insights into diseases such as AIDS, where CD4 T cell help is reduced or obliterated.

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PLANETARY SCIENCE

An Isotopic View of the Early Solar System

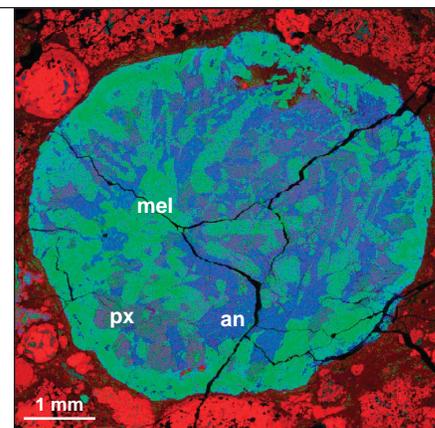
Ernst Zinner

The isotopic composition of ancient meteorites indicates that short-lived, now extinct radioisotopes existed in the early solar system. Recent measurements on meteorites provide evidence that several of these short-lived isotopes came from a stellar source shortly before our solar system formed. It is thus likely that a stellar event triggered the formation of the solar system, and recent evidence points to a supernova explosion.

Short-lived nuclides can potentially shed light on a variety of processes in the early solar system (1). Some of them may have been formed in stellar sources, connecting the birth of the solar system to the presence of nearby stars. Others may have been produced in the solar system, provid-

ing information about the early Sun. The nuclides may also serve as chronometers with a resolution of less than a million years (2). And two nuclides—²⁶Al and ⁶⁰Fe—may have been powerful heat sources for the melting of early planetary bodies.

Because the short-lived isotopes no longer exist, they can only be traced through their daughter isotopes (see the table). The ratios of short-lived isotopes relative to stable isotopes of the same elements in early solar system objects change with time, because different radioisotopes decay at different rates. The ratios for different isotopes should therefore ideally be measured at the same time, but this is not always possible. The reason is that the original presence of a short-lived isotope is indicated by excesses in the daughter isotope in samples from various meteorites. Measurements of such excesses require a large parent/daughter ratio. There are no



As old as the solar system. X-ray map of a coarse-grained Ca-Al-rich inclusion (CAI) from the carbonaceous chondrite Efremovka. Elemental compositions are reflected in the color (Mg, red; Al, blue; Ca, green). The major phases are anorthite (an), melilite (mel), and pyroxene (px). CAIs show excesses in ¹⁰B, ²⁶Mg, and ⁴¹K, indicating the initial presence of ¹⁰Be, ²⁶Al, and ⁴¹Ca at the time of their formation.

samples where this is the case for many different short-lived nuclides.

The best samples available are calcium-aluminum-rich inclusions (CAIs), which contain evidence and reliable initial ratios (at the time of CAI formation, inferred from daughter isotope excesses) for three

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**SHORT-LIVED, NOW EXTINCT RADIOISOTOPES
FOR WHICH EVIDENCE HAS BEEN FOUND IN METEORITES**

Radioisotope	Half-life (million years)	Daughter isotope	Reference isotope	Initial ratio
⁴¹ Ca	0.10	⁴¹ K	⁴⁰ Ca	1.5×10^{-8}
²⁶ Al	0.74	²⁶ Mg	²⁷ Al	5×10^{-5}
¹⁰ Be	1.5	¹⁰ B	⁹ Be	$\sim 5 \times 10^{-4}$
⁶⁰ Fe	1.5	⁶⁰ Ni	⁵⁶ Fe	$\sim 10^{-6}$
⁵³ Mn	3.7	⁵³ Cr	⁵⁵ Mn	$\sim 10^{-5}$
¹⁰⁷ Pd	6.5	¹⁰⁷ Ag	¹⁰⁸ Pd	4.5×10^{-5}
¹⁸² Hf	9	¹⁸² W	¹⁸⁰ Hf	10^{-4}
¹²⁹ I	16	¹²⁹ Xe	¹²⁷ I	10^{-4}
²⁴⁴ Pu	81	Fission Xe	²³⁸ U	$(4 - 7) \times 10^{-3}$
¹⁴⁶ Sm	103	¹⁴² Nd	¹⁴⁴ Sm	$(5 - 15) \times 10^{-3}$

isotopes: ⁴¹Ca, ²⁶Al, and ¹⁰Be (see the figure) (1, 3, 4). CAIs are found in primitive meteorites and are believed to represent the oldest samples from the solar system. Their absolute age can be determined from the U-Pb “chronometer,” which has a 1-million-year resolution (5).

The abundances of ²⁴⁴Pu, ¹⁴⁶Sm, ¹⁸²Hf, and ¹²⁹I (and possibly ⁵³Mn) in the early solar system can be explained by continuous equilibrium production of these nuclides by supernovae in the Galaxy. In contrast, the other short-lived nuclides listed in the table require either a stellar source closely preceding the formation of the solar system or energetic particle production by the early Sun.

Until recently, the consensus of the astrophysical community seemed to favor a stellar source. Scenarios for the triggered formation of the solar system were of particular interest. In these models, a supernova (6) or an asymptotic giant branch star (7) led to the collapse of the presolar cloud and injected newly synthesized nuclides.

This consensus has been challenged by the X-wind model of Shu and co-workers (8, 9). According to this model, the short-lived isotopes—specifically ²⁶Al, ⁴¹Ca, and ⁵³Mn—are produced by local irradiation from solar energetic particles in the X-wind (the outflow from a region close to a young star) region of the early Sun. The model postulates that CAIs and chondrules are produced in this region, but at different distances and therefore with different abundances of the short-lived nuclides. This would explain why initial ²⁶Al/²⁷Al ratios in chondrules are systematically lower than in CAIs (10).

Support for the X-wind model has come from the discovery in CAIs of ¹⁰Be (3), which is only produced by energetic particle irradiation and not by stellar nucleosynthesis. Some authors have argued that irradiation in the early solar system could not

yield the observed ratios (11). Others have claimed that the ¹⁰Be/⁹Be, ²⁶Al/²⁷Al, ⁴¹Ca/⁴⁰Ca, and ⁵³Mn/⁵⁵Mn ratios can be reproduced, albeit with special assumptions about target composition and spectral shape of the energetic particles (9, 12).

Recent measurements of Be-B, Al-Mg, and Ca-K ratios in CAIs containing the mineral hibonite have shed new light on this issue. The chemical and isotopic features of these special CAIs indicate that they are the first solids to form in the solar nebula (13). The measurements provided evidence for the initial presence of ¹⁰Be (with inferred ¹⁰Be/⁹Be ratios comparable to those in other CAIs), but no evidence for ²⁶Al and ⁴¹Ca. Hence, the production of ¹⁰Be appears to be decoupled from that of the other two short-lived isotopes (14).

The X-wind model explains the difference in ²⁶Al/²⁷Al ratios between CAIs and chondrules by assuming that the two types of objects were formed at the same time at different distances from the early Sun and therefore received different amounts of irradiation from solar energetic particles. Alternatively, the difference in ²⁶Al/²⁷Al ratio can be explained by assuming that CAIs and chondrules formed from a reservoir with uniform ²⁶Al/²⁷Al ratio, but that chondrules are younger than CAIs. Several recent studies show agreement between the Al-Mg clock and other independent chronometers (5, 15), providing evidence for the second scenario—and hence an additional argument against the production of ²⁶Al by energetic particles from an early Sun.

The finding of ¹⁰Be in samples without ²⁶Al and ⁴¹Ca and the agreement between the Al-Mg clock and other chronometers leave stellar sources as the most likely production sites for the short-lived isotopes other than ¹⁰Be (and possibly ⁵³Mn). For ²⁶Al, ⁴¹Ca, ⁶⁰Fe, and ¹⁰⁷Pd, it has to be a

nearby star because continuous galactic nucleosynthesis is insufficient. Recent ion microprobe measurements of the Fe-Ni system in troilite grains from two unequilibrated ordinary chondrites (meteorites that never experienced high temperatures) (16, 17) provide further support for a stellar source closely predating solar system formation. ⁶⁰Fe cannot be produced by energetic particles, which excludes irradiation from an early Sun. Earlier measurements on differentiated meteorites (from larger asteroids that experienced geological activity) gave low ⁶⁰Fe/⁵⁶Fe ratios that can be explained by continuous galactic production. However, the newly measured ratios are much too high (up to 10^{-6}) for such an explanation and require a recent stellar source.

The prime stellar candidates—core-collapse supernovae and asymptotic giant branch stars—have been previously discussed in detail (1, 6, 7), but each scenario had its problems. For example, a core-collapse supernova produces large amounts of ⁵³Mn, and ad hoc fine-tuning of the models is required to achieve a fit to the observed ratio. Low-mass asymptotic giant branch stars can produce ²⁶Al, ⁴¹Ca, and ¹⁰⁷Pd with the correct abundances, but fail to produce enough ⁶⁰Fe to fit the newly reported high ⁶⁰Fe/⁵⁶Fe ratios.

Thus, if the high ⁶⁰Fe/⁵⁶Fe ratio of 10^{-6} (16) is confirmed, it eliminates an asymptotic giant branch source and provides a smoking gun in favor of a supernova explosion preceding (and most likely triggering) solar system formation. This scenario has the added advantage that it could also produce the required amount of ¹⁸²Hf by nucleosynthesis in a shell of the exploding massive star (18), eliminating the need for galactic production by the r-process (rapid neutron capture at very high neutron densities).

Identification of a supernova trigger, however, does not mean that all the work is done. For example, in addition to obtaining confirming evidence for production of ¹⁰Be by energetic particles from the early Sun it will be of interest to find out what other short-lived nuclides were produced in this way; there are some hints for production of ⁷Be (19).

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EVOLUTION

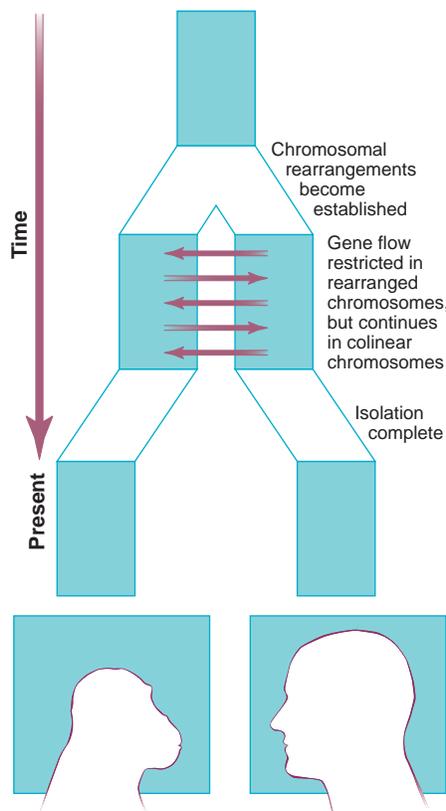
Chromosomal Speciation in Primates

Loren H. Rieseberg and Kevin Livingstone

The divergence of humans from the great apes highlights two of the most debated issues in speciation theory. First, modern humans and their closest relative, the chimpanzee, differ in both gene sequence and chromosome structure, and it is not clear which kind of change was the initial cause of reproductive isolation. Second, early humans and chimpanzees are likely to have lived in the same part of Africa, which bears on the larger question of whether speciation often occurs in the absence of geographic isolation. In a report on page 321 of this issue, Navarro and Barton (1) address both questions. They compare rates of protein evolution for genes on chromosomes that are colinear between humans and chimpanzees with genes from chromosomes that have undergone large structural rearrangements. They show that, on average, proteins from rearranged chromosomes evolved more than twice as fast as those from colinear chromosomes (that is, chromosomes with the same gene order). The most plausible interpretation of this pattern is that the chromosomal rearrangements “triggered” speciation by allowing differences under selection to accumulate in genes linked to the rearrangements, despite continued interbreeding between the two lineages for up to 3 million years after their initial divergence (see the figure).

So, why would chromosomal rearrangements affect rates of protein evolution? A simple solution to this puzzle is provided by a new model of chromosomal speciation (2–4). In traditional models, recombination between rearranged chromosomes is assumed to generate gametes carrying

chromosomal duplications or deficiencies. The unbalanced gametes or offspring produced from them may be nonviable, thereby creating a reproductive barrier. These models are unconvincing, however, because rearrangements that cause large reductions in the fitness of heterozygotes (that is, underdominant rearrangements)



Human origins. Chromosomal rearrangements appear to have triggered the separation of humans from the great apes by providing a barrier to gene flow in rearranged chromosomes. In contrast, gene flow continued for genes on colinear chromosomes.

can only be established in small inbred populations. Rearrangements that are neutral or weakly underdominant are more easily fixed in populations, but they will be ineffective as isolating barriers. Also, rearrangements that act solely to reduce hybrid fitness are unlikely to affect rates of protein evolution in loosely linked genes—the pattern reported by Navarro and Barton.

In the new model of chromosomal speciation, recombination is reduced in chromosomes heterozygous for the rearrangements (2–4), thereby minimizing the fitness effects of these rearrangements. Because recombination is required for gene flow, the rearrangements create a semipermeable reproductive barrier, where gene flow is reduced for rearranged chromosomes but continues across colinear chromosomes. As a consequence, selected differences are predicted to accumulate more readily in rearranged than in colinear chromosomes. Some of the accumulated differences are likely to cause incompatibilities in hybrids, ultimately sealing off the entire genome from gene flow and enabling completion of speciation, although this may take a very long time.

The origin of the human lineage represents a particularly appropriate test of this hypothesis for two reasons. First, biogeographic and anthropological evidence suggests that early forms of humans and chimpanzees are likely to have co-inhabited the same region of East Africa. Although it is possible that physical barriers such as rift valleys, rivers, and mountains might have provided the necessary isolation to initiate divergence among groups of apes, it seems unlikely that the different forms would have remained isolated long enough for speciation to be completed. Thus, the human-chimpanzee split may represent a kind of speciation with gene flow or “parapatric” speciation, where the effects of chromosomal barriers would be most pronounced. Second, humans and chimpanzees are known to differ in major chromosomal rearrangements involving 10 of 22 human autosomal chromosomes. The large number of chromosomes affected by rearrangements greatly increases the statis-

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