Cell sorting protein homologs reveal an unusual diversity in archaeal cell division

Isaac K. O. Cann

Departments of Animal Sciences and Microbiology, Energy Biosciences Institute, and Institute for Genomic Biology, University of Illinois at Urbana-Champaign, Urbana, IL 61801

In this issue of PNAS, Lindås et al. (1) report an interesting diversity in archaeal cell division, in contrast to those of bacterial and eukaryotic cells, which appear to be more uniform. The Archaea, Bacteria, and Eucarya constitute the 3 domains of life on our planet (2). Within the cell cycle of each lineage, DNA replication ensures faithful duplication of the chromosome, after which a copy of the genetic material from the mother cell segregates into 2 daughter cells. By this process, organisms generate progeny to ensure continuation of their lineage. In their seminal report, Woese et al. (2) subdivided Archaea into 2 major kingdoms, namely the Euryarchaeota and Crenarchaeota, although as discussed later, there appear to be more kingdoms within the Archaea.

Years of comprehensive studies have provided very good insights into cell division in bacteria and eukaryotes, and although the first genome sequence of an archaeon suggested that archaea share similar replication machinery with eukaryotes, it appeared that the archaeal cell division proteins were of the bacterial type (3). Thus, the Methanocaldococcus jannaschii genome encoded 2 FtsZ, 1 FtsJ, and 3 MinD proteins. In bacteria and eukaryotic organelles, such as chloroplasts, which are known to have bacterial origin, FtsZ serves as the hallmark of cell division. This protein is a structural homolog of tubulin (4) and is required for the septation that leads to cell division and 2 daughter cells. FtsZ functions by assembling into a ring that marks the future site of cell division (5), and the Min system, including MinD, functions as an inhibitor that allows assembly only at the right place and the right time (5, 6). In agreement with the report on M. jannaschii, an examination of the publicly available databases shows that the euryarchaeal genomes have at least a homolog of FtsZ, suggesting that the Euryarchaeota use an eukaryotic-like DNA replication apparatus for genome duplication (Fig. 1A) and a bacterial type mechanism for cell division (Fig. 1B).

Over the years, the absence of the bacterial type of cell division proteins in Crenarchaeota, the other archaeal subdomain, puzzled researchers interested in the stages of cell cycle in this group of organisms. Through the unyielding efforts of the members of Rolf Bernander’s laboratory in Sweden, the waiting is finally over. Their results, published in this issue of PNAS (1), provide evidence that the crenarchaeotes use a different set of proteins during septation, the process that finally leads to formation of 2 daughter cells. For more than a decade, it has been known that the archaeal DNA replication machinery is a simpler form of the more complex one found in eukaryotic cells (3). Thus, the members of archaea, including Sulfolobus acidocaldarius, used as models to decipher the mechanisms of archaeal DNA replication, have also provided critical insights to our understanding of the more complex eukaryotic DNA replication, especially in the studies on the replicative DNA helicase minichromosome maintenance (MCM) (7, 8) and translesion DNA synthesis (9). The report by Lindås et al. (1) will open new lines of research in the field of cell cycle as discussed below.

The clue to the interesting findings by Lindås et al. (1) derives from the investigators’ ability to synchronize the growth of a high proportion of S. acidocaldarius cells, so that the majority is at the same stage of the cell cycle. Having already deciphered the cell cycle of this crenarchaeon (10), Lindås et al. searched for the genes that were highly expressed concomitant to chromosome segregation and cell division. Of particular interest among the candidate genes were 3 that occurred in a cluster. The cluster was conserved in other members of the genus Sulfolobus, and its importance became more evident when Lindås et al. also found it in other members of the crenarchaeal family. They named the genes in the order of transcription as cdvA, cdvB, and cdvC.

Until recently, the crenarchaeotes were thought to be very unique, only being comprised of extreme thermophiles (11) that grow at temperatures >80 °C. However, it is now known that mesophilic crenarchaeotes abound in nature in agricultural lands playing yet unknown roles (12), and in the oceans where they are estimated to constitute 20% of all picoplankton and thought to play critical roles in ammonia oxidation and carbon fixation (13). These archaea are very intriguing.

Author contributions: I.K.O.C. wrote the paper.

The author declares no conflict of interest.

See companion article on page 18942.

1E-mail: icann@illinois.edu.

© 2008 by The National Academy of Sciences of the USA

www.pnas.org/cgi/doi/10.1073/pnas.0810505106

December 2, 2008 | vol. 105 | no. 48 | 18653–18654
morphic and are extremely difficult to culture. To date only 1 member, *Nitrosopumilus maritimus*, has been successfully cultured in the laboratory. A finding that is of particular evolutionary interest in ref. 1 is that the genome of *N. maritimus* and that of the uncultured mesophlic crenarchaeote, *Cenarchaeum symbiosum*, contain both ftsZ and the cdv genes. This finding suggests that these organisms use a “hybrid” of the 2 cell division systems found in the Euryarchaeota and the Crenarchaeota. The DNA replication machinery of the mesophilic crenarchaeotes, however, appears to be a mixture of those from the 2 subdomains of archaea, with the euryarchaeal ones being predominant. As a significant example, the 2-subunit family D DNA polymerase, hitherto considered a hallmark of the Euryarchaeota (14), is found in the mesophilic crenarchaeotes.

The evolutionary implication here is that either these mesophilic crenarchaeotes have acquired euryarchaeal genes or they portray the type of replication and cell division machineries indigenous to the ancestor of the Euryarchaeota and the hyperthermophilic crenarchaeotes. Surely, a greater thrust to reclassify the mesophilic crenarchaeotes into a new subdomain, as suggested by Forterre and co-workers (15), is anticipated.

**Diversity of Cell Division in Archaea**

From the above discussion, it is evident that the discovery made by Lindås et al. (1) suggests that a full understanding of archaean cell cycle will require several analyses, because several new and powerful tools are being brought to bear on the system was developed for the genus Sulfolobus (17) and a so-called “baby machine” has been developed for *S. acidocaldarius*, and the principles behind it have been elegantly demonstrated through synchronization of cells with little or no chemical perturbation (18). These new tools, together with the availability of microarrays and other biochemical approaches that determine protein/protein interactions, such as communoprecipitation and yeast 2-hybridization, will accelerate the assembly of the complete set of proteins required for cell division in *Sulfolobus*, and subsequently will provide a detailed mechanism of cell cycle in this archaean. Lindås et al. (1) also made an observation, based on previous microarray studies, that the damaging effects of UV radiation lead to attenuation of expression of all 3 cdv genes in Sulfolobus. As suggested by Lindås et al., this down-regulation of expression of the newly discovered cell cycle genes could reflect cell cycle arrest to allow the damage in the chromosome to be repaired and the chromosome to be completely segregated before cell division. This finding should not be too surprising, because eukaryotes and archaean have similar replication proteins, and it is known that DNA damage results in cell cycle checkpoint response to allow repair, replication, and chromosomal segregation in eukaryotic cells before cell cycle progression is reinitiated. Indeed, it has been clearly demonstrated that in eukaryotes there is a direct connection between DNA damage-induced phosphorylation of MCM subunits (Fig. 1B) and control of DNA replication (19), and the role of MCM is cell cycle-regulated to ensure that replication occurs only once per cell cycle. The *S. acidocaldarius* MCM has been reported as being produced at constant levels throughout the whole cell cycle (19). Thus, the archaenal replication fork factors that respond to DNA damage and trigger cell cycle arrest await discovery, and the report by Lindås et al. (1) will serve as a catalyst.

**ACKNOWLEDGMENTS.** My research is supported by National Science Foundation Grant MCB-0238451.