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Senescence in a Bacterium with Asymmetric Division

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Senescence (or aging) is a deterioration of function with age manifested as a drop in survival and reproduction (*1*). A fundamental question about senescence has not been settled: Which organisms should be senescent, and which should be potentially immortal? We present evidence for senescence in a bacterium with asymmetric division, supporting the notion that asymmetry is the key condition for senescence to evolve (*2*).

The molecular processes underlying senescence are genetically determined. Why then is senescence—which imposes a cost on the individual—not eliminated by natural selection? For most organisms, selection against senescence is weak. Because of external insults to survival and reproduction, even in the absence of senescence, only a few individuals reach advanced age while continuing to reproduce. Mutations causing senescence can become frequent, either because they have beneficial pleiotropic effects early in life (*3*) or because deleterious mutations acting only in older age classes are selected against in a limited fashion (*4*). This argument assumes that reproduction is rejuvenating, so that progeny are born with the full life potential. Consistent with this, senescence has been observed in multicellular eukaryotes in which the negative effects of age are confined to the parent (*1*) and in unicellular eukaryotes with asymmetric division like *Saccharomyces cerevisiae* (*5*) in which structural changes that potentially contribute to senescence segregate to one of the products of division (*6*). Prokaryotes, which typically produce two apparently identical cells during division, are considered to be nonsenescent and potentially immortal (*1*, *3*).

However, rejuvenating reproduction might occur in bacteria if division is asymmetric and the characters that change with age are reset in one of the emerging cells. The paradigmatic example of an asymmetrically dividing bacterium is *Caulobacter crescentus* (*7*) (Fig. 1A). The life cycle of *C. crescentus* begins with a swarmer cell. After an episode of free swimming, the nonreproductive swarmer cell differentiates into a sessile and reproductive stalked cell. The stalked cell starts to produce progeny swarmer cells while remaining attached to a solid substrate through a polar stalk with an adhesive holdfast. If the stalked pole or any of the structures segregating with it deteriorate

many divisions after differentiation, this would affect only the few stalked cells that had managed to survive external mortality. Thus, such changes would not be opposed by strong selection and could be the basis for senescence.

We tested stalked cells of *C. crescentus* for senescence. We used microscopy flow chambers to observe stalked cells attached with their holdfast to the walls of the chamber; most progeny were removed by the medium flowing through the chamber (*8*). In three independent experiments, we followed a group of cells of the same age for about 300 hours and monitored their reproductive events. We calculated the number of progeny produced per individual as a function of its age. This quantity represents the age-specific reproductive output, combingboth survival and division. Although some cells produced up to 130 progeny in 300 hours, many stopped dividing or divided more slowly with increasing age, resulting in a decrease in reproductive output with age (Fig. 1B). The
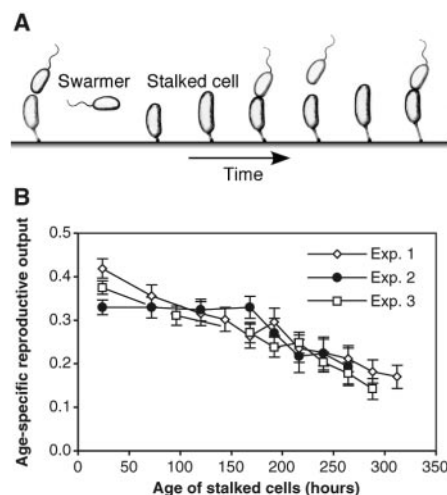

Fig. 1. (**A**) Life cycle of *C. crescentus*. (**B**) Reproductive output (progeny produced per stalked cell and hour) as a function of age from three independent experiments with sample size 53 (exp. 1), 17 (exp. 2), and 72 cells (exp. 3). Each point represents measurements over a period of 8 to 10 hours (mean and standard error). Quadratic regression of the log-transformed rate of reproduction on cell age indicated that reproductive output decreased with age (combined probability for the linear term $P < 0.001$) and that the rate of decrease accelerated with age (probabilities for the quadratic term exp. 1: $P = 0.180$; exp. 2: $P = 0.023$; exp. 3: $P = 0.03$; combined probability $P = 0.006$).

results were not caused by a change in the experimental conditions over time; young cells born in the chamber after 250 hours were indistinguishable in terms of cell division time from young cells measured at the beginning of the experiment (a difference of 9% or greater would have been detected with $P = 0.95$). Furthermore, the reproductive output of stalked cells decreased at an accelerating rate with increasing age, indicating that this decrease was not caused by damage accumulating at a constant rate in the course of the experiment.

These results indicate that senescence can indeed evolve in bacteria if there are systematic differences between the two cells emerging from division. This condition might potentially be met in many bacterial species; even bacteria that are generally thought to be symmetrical often localize subcellular structures to their poles (*9*). As a consequence, division gives rise to two cells that differ with respect to the age of their poles. *C. crescentus* stands out because cells with old and new poles can readily be distinguished by their morphological appendages. This organism could serve as a model system to provide new insights into fundamental aspects of senescence.

References and Notes
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10. We thank M. Doebeli and M. Riek for helpful discussions and F. Zoller, R. Wyss, and P. Jäggi for technical assistance. Supported by the Swiss National Science Foundation grants 31-59050.99 (to U.J.) and 31-28511.90 (to S.C.S.).

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