its terminus blocked germ cell adhesion to Sertoli cells. Furthermore, there was a 50% decrease in this oligosaccharide in testis tissue from the mutant mice. The newly identified oligosaccharide carried three exposed GlcNAc residues as well as a fucose residue attached to the core of the sugar chain (see the figure). Intriguingly, this oligosaccharide did not have an unusual linkage, but rather was produced by arrest of the biosynthetic pathway before the addition of galactose.

There are two obvious anomalies. First, although GlcNAc-terminal oligosaccharides decreased in the mutant mice, Gal-terminal oligosaccharides did not, even though the former are precursors of the latter. As the authors point out, one possibility is that α-mannosidase II may predominate in non-germ cells and process Gal-terminal oligosaccharide precursors. Alternatively, both α-mannosidase II and α-mannosidase IIx may exist in germ cells, each processing carbohydrate attached to different sets of target glycoproteins (with Gal-terminal carbohydrate presumably still processed by α-mannosidase II).

Second, the newly identified GlcNAc-terminal oligosaccharide decreased by only 50%, yet male germ cell survival was almost completely suppressed. The authors propose that this could be due to a dosage effect: Below a certain concentration of the oligosaccharide, the binding of germ cells to Sertoli cells is negligible. Another possibility is that this oligosaccharide is attached to a specific target glycoprotein whose sugar chains must be processed by α-mannosidase IIx. It is known that carbohydrates attached to glycolipids, such as seminolipid (*8*) and gangliosides (*9*), are crucial for spermatogenesis, although carbohydrate recognition was not investigated.

Germ cells must adhere to Sertoli cells to survive, and the Akama *et al.* work has now identified the key molecule involved in binding. Their finding opens up new avenues that may benefit research into the cause of human male sterility. The Akama *et al.* study illustrates the importance of cell-specific or even protein-specific glycosylation machinery for cellular recognition. An interesting subject for future research will be identification of the germ cell target glycoprotein to which the new oligosaccharide is attached. One candidate is basigin (CD147) (*10*), a highly glycosylated member of the immunoglobulin superfamily, the absence of which results in sterility in mice. Equally interesting is the nature of the molecule on Sertoli cells that recognizes the germ cell oligosaccharide. In carbohydrate-dependent cell adhesion, the specific carbohydrate sequence is usually recognized by lectins, which are classified into several groups, for example C-type lectins, galectins, and siglecs. Discovering whether a Sertoli cell lectin binds to the unique germ-cell oligosaccharide will be the next step.

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PERSPECTIVES: AGING

Dietary Advice on Q

Marc Tatar and David M. Rand

How much you eat, not what you eat, seems to make a difference in the aging process. It is well established that reduced calorie consumption robustly extends adult life expectancy in a variety of animal models. Now, on page 120 of this issue, Larsen and Clarke show that diet quality also affects aging (*1*). In the worm *Caenorhabditis elegans*, reduced consumption of coenzyme Q (Q) dramatically extends longevity.

Among other chores, Q carries electrons and protons across the inner mitochondrial membrane to maintain the proton gradient that drives ATP synthesis (see the figure). *C. elegans* is able to synthesize the most prevalent isoform, Q_9, from a demethoxy-Q_9 (DMQ_9) intermediate. But worms carrying mutations in the *clock* gene (*clk-1*) lack the di-iron carboxylate enzyme required for the final hydroxylase step and so accumulate DMQ_9 instead of Q_9 (*2*, *3*). To obtain Q, *clk-1* mutants depend solely on their primary diet of bacteria, which synthesize the Q_8 isoform. The balance of Q isoforms in the worm is determined by both endogenous synthesis and dietary intake. Earlier work showed that worm *clk-1* mutants fail to develop or become sterile if fed *Escherichia coli* bacteria lacking Q, and that these effects could be rescued by feeding worms wild-type *E. coli* that synthesized Q (*4*). Given the importance of Q in mitochondrial electron transport, and the importance of electron transport in the production of reactive oxygen species in aging (*5*, *6*), do the quantity and quality of Q isoforms impact worm longevity?

Larsen and Clarke show that reliance upon the endogenous isoform Q_9 without a dietary source of Q_8 dramatically extends survival of the adult worm. The investigators raised worms on a diet of wild-type *E. coli* during the larval phase, and then switched them to a diet of *E. coli* lacking Q just before the worms emerged from the last larval stage as adults. Convincingly, extension of longevity was observed in both wild-type and mutant strains of *C. elegans*, as well as with mutant strains of *E. coli* in which different steps in Q biosynthesis were disrupted.

The authors uncover some important connections among *clk-1* mutants, dietary Q, and aging. The extended life-span of *clk-1* mutants lacking Q_9 is partly due to a general delay in larval development (*7*). The new study shows that adult life expectancy is not altered by *clk-1* mutations. Rather, young adult mutants suffer higher mortality compared with control worms, but mortality rates are reduced at later ages. In the presence of DMQ_9, juvenile reliance on dietary Q_8 may debilitate adults in an age-independent manner, which could counter any positive benefits of slower aging on mean life-span.

By shifting the dietary intake of Q between the larval and adult phases, the study reveals important age-specific characteristics. It is known that trade-offs across ages can foster the evolution of senescence (*8*). The ability to assimilate dietary Q and to synthesize endogenous Q supports growth and development, and clearly increases components of fitness expressed at young ages. This physiological capacity, however, reduces adult survival. Senescence can evolve under these conditions because the strength of natural selection is greatest upon traits expressed early in the life cycle.

Larsen and Clarke also unveil some important interactions between Q and the insulin signaling pathway that may intersect at the mitochondrion. Mutations in the insulin receptor homolog *daf-2* extend the longevity of *C. elegans* (*9*, *10*). The new study shows that a Q-less diet further extends the longevity of these *daf-2* mutants. *Daf-12* mutants, on the other hand, show slightly reduced longevity relative to controls at 25°C, and do not respond

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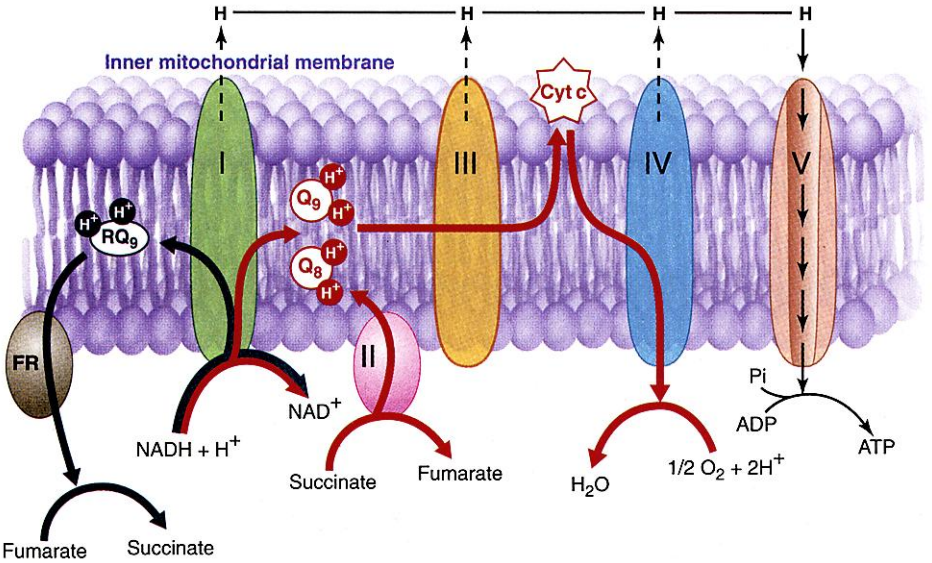

The electron transport chain. Coenzyme Q (Q) is a lipid-soluble factor that is crucial for transport of electrons and protons across the inner mitochondrial membrane, a process that maintains the proton gradient driving ATP synthesis. Q drives electron transport at complexes I, II, and III, and is essential for proton transport at complexes I and III. Worms endogenously synthesize the Q_9 isoform from a DMQ_9 intermediate. They can also obtain Q from feeding on bacteria that synthesize Q_8. Worms also produce RQ_9, an alternate quinone that is involved in anaerobic respiration (blue arrows) rather than aerobic respiration (red arrows). Restricting dietary Q in worms extends longevity perhaps because reduced Q results in the production of fewer oxygen radicals during electron transport.

strongly to a Q-less diet. Interestingly, *daf-2*; *daf-12* double-mutant worms have extended longevity, but do not respond to a Q-less diet. Analysis of these interactions should enable the intersection of insulin signaling with mitochondrial function to be elucidated.

How does Q impact aging? The worm shows an increased reliance on anaerobic respiration (fermentation) for energy production during the nonfeeding dauer larval stage, which occurs in place of larval stage three. Dauer larvae exhibit a number of traits known to slow aging when expressed in adults. Perhaps the balance of Q isoforms—by affecting signaling between mitochondria and the nucleus that results in altered gene transcription (*11*)—induces the longevity-assurance elements of the dauer stage. An attractive alternative is that an abundance of Q_8 and Q_9 may accelerate the rate of electron transport and thus the release of reactive oxygen species from mitochondria. Q is also a cofactor in the activity of uncoupling proteins, which pump protons across the inner mitochondrial membrane. Uncoupling may be an important mechanism to help modulate electron transport efficiency and proton leakage during aging (*12*). These hypotheses await decisive experimentation, and direct measurement of metabolic intermediates and reactive oxygen species. Ultimately, to establish the generality of Q's aging effects, we must also test its impact in organisms such as the fruit fly *Drosophila* and rodents, where the influence of fermentation pathways is likely to be different.

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PERSPECTIVES: GEOPHYSICS

Caught Offside

Tim Elliott

Eighty percent of global volcanism occurs out of sight, at submarine volcanoes along the 56,000 km of mid-ocean spreading centers that straddle Earth. This volcanic activity is confined to very narrow (~1 km) zones between two separating tectonic plates. This concentration of volcanic activity is particularly remarkable when the volume of the rock producing the magmatism is considered: a triangular melting region, with a base at least 60 km deep, extends 60 km on either side of the ridge axis (see the first figure).

Several fluid dynamic models have been developed to account for this strong focusing of melts beneath ridges (*1–3*). Yet it has also been noticed that the upper oceanic crust, which consists of the solidified remains of the erupted melts, continues to thicken away from the ridge axis (*4*, *5*). Is the architecture of oceanic crust governed by growth at the ridge crests alone, or is it embellished by off-axis additions?

To answer this fundamental question about the nature of oceanic crust, we require accurate chronometers that can tell us whether all off-axis lavas are older than their ridge crest counterparts, as in a classical plate-spreading model, or whether there are aberrant youngsters. This problem is beyond the resolution of commonly used isotopic dating systems, but is addressed in dramatic fashion by Zou *et al.* on page 107 of this issue (*6*).

The authors use high-precision uranium isotope series measurements to provide a new perspective on this problem. Melting is commonly believed to induce disequilibrium in the short-lived nuclide chains between U and Pb. After eruption, secular equilibrium (in which the decay rates of all intermediate nuclides are equal) is restored on the geologically short time scales of the half-lives of the intermediate nuclides; for example, ^{230}Th has a half-life of 75,000 years. For a fast-spreading ridge, with plates diverging at a rate of 10 cm/year, any melt-produced disequilibrium still present in lavas more than 20 km from the ridge clearly identifies off-axis volcanism.

A finer chronology is possible if the initial disequilibrium is known. Assuming that this has remained constant, Goldstein *et al.* (*7*) have inferred off-axis volcanism 1 to 4 km from the ridge crest. Zou *et al.* now show striking disequilibrium more than 20 km off axis. At these distances, few would have anticipated recent volcanism except at well-defined "seamounts." Yet the samples analyzed by Zou *et al.* are from normal oceanic crust on the flanks of the East Pacific Rise (*8, 9*).

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