

Germ-line stem cells call the shots

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In the nematode *Caenorhabditis elegans*, developmental biologists find that tissues derived from embryonic germ-line progenitor cells regulate reproductive costs. New work from the laboratory of Cynthia Kenyon demonstrates that signals that reduce adult survival are mediated by a small set of progenitor descendants, the germ-line stem cells, and by their interaction with components of the endocrine system. *Caenorhabditis elegans* is now providing a new way of understanding the mechanisms of tradeoffs between reproduction and ageing.

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Studies of the tradeoff between reproduction and adult survival date back to at least 1958, when Maynard-Smith showed that reproductive mutants of *Drosophila subobscura* were long lived [1]. Many workers have since validated the generality of this tradeoff with the use of genetic and phenotypic analysis and have helped to establish it as a cornerstone in the evolutionary theory of life history. At the same time, a powerful mechanistic metaphor has been developed to explain this constraint: resource allocation occurs between reproduction and soma (the *Loi de Balancement* [2]). But, although many observations are consistent with the allocation model, few studies have demonstrated how reproduction actually modulates ageing [3]. Remarkable progress is now being made on this front, and from a very unlikely quarter. Developmental biologists are uncovering how gonad tissue mediates ageing in the roundworm *Caenorhabditis elegans*. In a recent report, Arantes-Oliveira *et al.* [4] show that adult germ-line stem cells (GSC) regulate life span. This research opens up new avenues with which to explore the fundamental mechanistic relationship between reproduction and survival.

Caenorhabditis elegans that are mutated at *daf-2*, the gene that encodes the insulin-like growth factor (IGF) receptor protein, are long lived [5]. Paradoxically (to evolutionary biologists), this lifespan extension relative to controls is retained

even when the potential for reproduction is eliminated by surgical ablation of the gonad in both mutant and control strains. Is this a case of longevity extension without reproductive tradeoffs? Apparently not. First, fitness studies with mutants of the insulin-IGF signal transduction pathway show an environment-dependent disadvantage [6]. Second, elimination of one specific part of reproduction does reveal tradeoffs, because ablation of the embryonic germ-line precursor cells is sufficient to increase adult lifespan [7]. Finally, extended longevity is produced through mutation of *daf-2* in a limited set of neuronal cells [8]; insulin signals appear to mediate a secondary hormonal signal that, in turn, systemically modulates longevity. Endocrine mediation of reproductive costs is implicated in this model, because extended lifespan with ablation of the germ-line precursors requires the function of two genes of the insulin-IGF signal system: *daf-16* (a transcription factor downstream of DAF-2) and *daf-12* (a nuclear hormone receptor) (Table 1). Why, then, does ablation of the whole gonad not extend longevity or

abrogate the effect of *daf-2* mutation upon ageing? Current interpretations suggest that the gonad balances pro-ageing and anti-ageing endocrine signals [7]. Therefore, total gonad removal is neutral with respect to lifespan, and some descendants of the germ-line progenitor cells must encourage ageing, because their removal extends lifespan in a *daf-16*- and *daf-12*-dependent manner.

These initial findings are refined by Arantes-Oliveira and colleagues [4]. Adult GSC, oocytes and spermatozoa derive from the germ-line progenitor cells. Which component of this cell lineage accelerates ageing, and at what stage of development? Arantes-Oliveira *et al.* used collections of constitutive and temperature-sensitive mutants to show that GSC are the sole culprit (Table 1). For instance, *glp-1* encodes a receptor that maintains GSC mitotic proliferation, without which GSC enter meiosis, differentiate and abandon their stem-cell mode. The allele *glp-1 (e2141)* is temperature sensitive, and hermaphroditic adults were allowed to develop full complements of sperm and eggs at the permissive temperature before

Table 1. Mutants of *Caenorhabditis elegans* discussed in [4]^{a,b}

Gene (allele)	Mutant phenotype	Impact on life span
Reproductive mutants		
<i>mes-1 (bn7)</i>	Lacks GSC	–
<i>glp-1 (qu158)</i>	Few GSC	–
<i>glp-1, e2141</i>	Temperature sensitive, GSC differentiate	–
<i>glp-1 (oz112gf)</i>	Overproliferate GSC	↓
<i>gld-1 (q485)</i>	Overproliferate GSC	↓
<i>fem-3 (e1996)</i>	Feminize, no sperm	No effect
<i>fez-1 (q186)</i>	Feminize, no sperm	No effect
<i>fog-1 (q180)</i>	Feminize, no sperm	No effect
<i>fog-2 (q71)</i>	Feminize, no sperm	No effect
<i>fog-3 (q470)</i>	Feminize, no sperm	No effect
<i>daz-1 (tj3)</i>	Oocyte precursor cells undergo apoptosis	No effect
Insulin/IGF signal mutants		
Gene	Gene product and function	Impact on life span
<i>daf-2</i>	Insulin-like receptor protein	Increased in hypomorphs
<i>daf-16</i>	Forkhead family transcription factor, downstream of <i>daf-2</i> signal transduction	Required for <i>daf-2</i> longevity
<i>daf-12</i>	Nuclear hormone receptor	Required for <i>daf-2</i> longevity

^aFor information on additional genes, see supplemental material of [4] at <http://www.sciencemag.org/cgi/content/full/295/5554/502/DC1>.

^bAbbreviations: GSC, germ-line stem cells; IGF, insulin-like growth factor.

being transferred to a temperature that extinguished GSC. Lifespan after the switch was increased relative to controls even whilst oocytes continued to grow and eggs accumulated yolk. Endocrine interactions are implicated because longevity was not extended when GSC were deactivated in *daf-16* mutants. Interference RNA was used in further studies to show that the requirement for DAF-16 occurs exclusively in the adult stage. These results demonstrate that only the GSC descendants of germ-line progenitors have the capacity to mediate lifespan, and that these cells influence an adult-specific, *daf-16*-dependent signal.

These details provide new insights to the mechanism of the tradeoff between reproduction and ageing. Overall, the data are inconsistent with the notion of resource allocation toward reproduction at the expense of somatic function. Treatments that fully eliminate reproductive investment (gonad ablation) do not extend life [5], and lifespan is extended in treatments in which GSC are terminated even whilst adults continue to invest in eggs [4]. Alternatively, loss of the GSC reduces gonad mass, and this itself might enhance longevity. However, the gonads of *daz-1* are small and this genotype has no impact on lifespan, although the *daz-1* gonads might still produce a large number of germ cells. Arantes-Oliveira *et al.* suggest that GSC have a direct negative impact upon longevity that is mediated through the endocrine state. Direct costs of reproduction, for instance, can be

produced by hormone suppression of stress response systems during active reproduction (an inhibitory direct cost [3]). Many longevity-extending mutants of *C. elegans* have elevated resistance to oxidative, thermal and UV stress, and stress-resistance proteins, such as superoxide dismutase and heat shock protein 16, are overexpressed in these genotypes [9]. Consistent with this pattern, adults with extinguished germ-line stem cells have elevated resistance to oxidative stress. The data support a model in which active GSC normally suppress this resistance and thereby incur a direct cost of reproduction.

Where, then, is the *Loi de Balancement*? That is, can reproductive costs be mediated indirectly through the competitive allocation of resources between somatic and gonad function? To assess this mechanism requires experiments that are designed to test the interaction of resource level and reproductive investment upon survival [10]. Such studies have yet to be conducted with either *Drosophila* or *C. elegans*; however, the potential to understand such tradeoffs is now at hand. With *C. elegans*, developmental biologists have discovered which cells are responsible for signals that 'call' for accelerated ageing whilst they contribute positively to reproduction – these are GSC. Such a system of call and response, the basic stuff of systemic endocrine feedback, could provide a way in which to coordinate plasticity of ageing and reproduction across gradients of

resource and seasonality. Dissection of this signal and its downstream effects will provide insight to the mechanistic constraints between reproduction and survival.

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Shedding new light on nature's brightest signals

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Most colour in nature arises from pigments, but the most brilliant, deeply saturated visual signals have structural origins. These colours are generated from nanoscale structural arrays that interact with incident light to produce specific optical effects. Perhaps the most dazzling of nature's signals, the iridescent colours of tropical butterflies, have long been known to originate from such structures. However, new research by Vukusic and colleagues reveals the true depths to which evolution has crafted these fascinating optical devices.

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Butterflies are among the most beautifully emblazoned creatures on the planet and, as a consequence, have earned intense admiration from biologists and nonbiologists alike. Although gaudy colour patterns abound in this group, the pinnacle of visual brilliance is attained by many species whose wings appear to 'sparkle' with iridescence. The iridescent blue flash of a South American *Morpho*, for example, is famous for being spotted against the rainforest canopy from low-flying aircraft. Equally notable is the intense (yet invisible to us) ultraviolet colouration of

male pierids, and the strikingly metallic greens, azures and blues of the wings of many tropical swallowtails. This visual brilliance has long been understood to originate from nanostructures on the surface of wing scales that interact with incident light in a very specific manner [1]. However, until very recently, our understanding of the optical mechanisms at play was incomplete and based upon flagship examples from a limited number of butterfly families. New work [2–4] by an enterprising group of optical physicists has greatly increased the number of studied species, and has