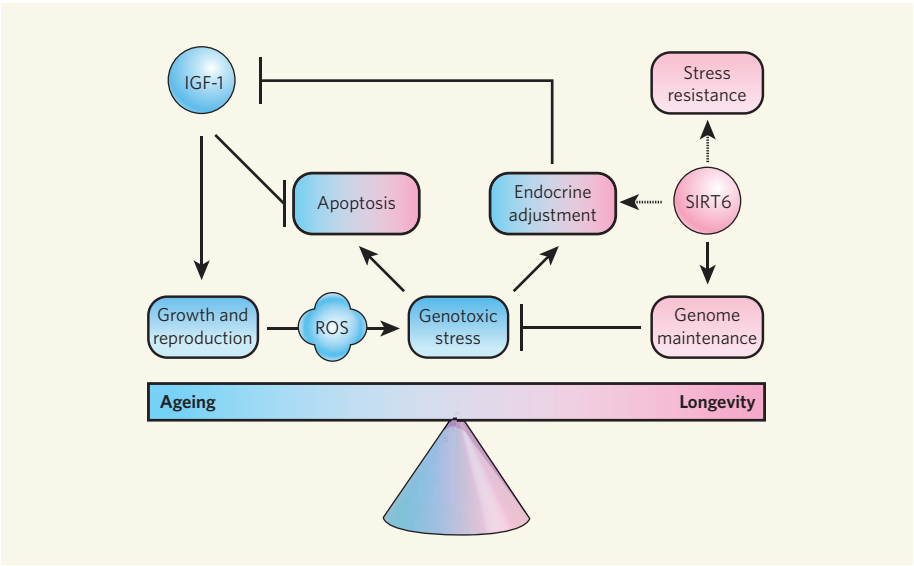

Figure 1 | Balancing act. The possible role of SIRT6 and genome maintenance in balancing ageing (blue) and longevity (pink). Although a mechanism is as yet unclear, SIRT6 may act in its pro-longevity role by promoting DNA repair, increasing stress resistance and maintaining metabolic homeostasis. The genotoxic stress resulting from its absence may cause a compensatory metabolic shift towards reduced insulin-like growth factor (IGF-1) signalling, thereby lowering the production of reactive oxygen species (ROS). The resulting increase in apoptosis could be a cause of the premature ageing symptoms observed by Mostoslavsky *et al.*[1] in mice lacking SIRT6.

the lymphocyte depletion was not cell-intrinsic but rather a response to a systemic defect. Analysis of the blood serum of SIRT6-deficient mice revealed extremely low levels of IGF-1, as compared with normal, control animals. IGF-1 strongly inhibits apoptosis in lymphocytes, and the age-related reduction in lymphocyte production by the thymus has been ascribed to a decline in IGF-1 levels with age[8]. This finding presents us with a paradox, because reduction of IGF-1 signalling is linked with a longer, not a shorter lifespan. How can these results be reconciled?

Life extension conferred by dampening IGF-1 signalling is likely to represent a metabolic switch in the use of resources, away from growth and reproduction with the inevitable side effect of DNA damage, towards increased maintenance and repair[5]. Although defects in insulin signalling in mammals cause diabetes, reduced IGF-1 signalling extends life in mice[9]. The attenuation of IGF-1 signalling in the SIRT6-deficient mice may indicate that this switch has been activated as a means to limit the onslaught of spontaneous DNA damage and to upregulate the apoptosis of severely damaged cells. Indeed, modulating IGF-1 signalling, possibly through members of the Sir2 family, may be a general mechanism for coping with environmental stress, including nutrient limitation and genotoxic stress. Interestingly, Xpd^{TTD} mutant mice, which harbour a defect in another form of DNA repair known as nucleotide excision repair, display characteristics of accelerated ageing and caloric restriction, suggesting that metabolism adjustment might be a general mechanism to deal with genotoxic stress (Fig. 1)[10].

So does SIRT6 connect BER to the IGF-1 signalling pathway? As yet, this is far from clear. For example, neither the nature of the SIRT6 enzymatic activity, nor its potential substrates, is known. Indeed, Mostoslavsky and colleagues' results only indirectly implicate SIRT6 in BER, so although it is reasonable to assume that SIRT6 promotes the access of repair enzymes through chromatin remodelling, there is no direct evidence for this. Also, it is not apparent if and how SIRT6 is involved in regulating the IGF-1 response. Finally, not all degenerative symptoms associated with reduced lifespan necessarily involve the causes that underlie natural ageing. Indeed, the degenerative symptoms observed in SIRT6-deficient mice are far from comprehensive and may well result from developmental defects.

Nonetheless, Mostoslavsky *et al.*[1] provide a potential link in the chain connecting genome instability, metabolic effects and ageing. Ultimately, this may lead to ways of exploiting the role of Sir2 family members in genome maintenance to silence senescence. ■

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CONSERVATION BIOLOGY

Roads and genetic connectivity

Jared L. Strasburg

The Ventura Freeway slices through wildlife habitat near Los Angeles. A case study shows how large highways such as this can seriously impede genetic exchange in large vertebrates.

Roads are bad news for wildlife. Vehicles kill animals attempting to cross them, sometimes in large numbers. Conservation biologists have recognized for many years that roads also split up populations, and they continue to explore the degree and consequences of this fragmentation. Techniques such as radiotelemetry and motion-triggered photography can be used to observe animals crossing highways, but not whether the animals mate on the other side. In a seven-year study published in *Molecular Ecology*[1], Riley *et al.* compare direct observations with genetic estimates of the disruptive effects of a busy highway in southern California. They show that the highway acts as a social barrier to gene flow in two large and mobile carnivores, and that it does so to a much greater extent than would seem to be the case from observations of animal dispersal.

Many animals, especially vertebrates, alter their behaviour to avoid roads, shifting home ranges, feeding sites and nesting areas away from them[2]. But most animal groups still attempt to cross these barriers with some frequency, often by making use of culverts and other potential crossing points[3–5]. These crossing points may be specifically designed for animal dispersal, such as large vegetated overpasses or underpasses; or they may be unintentional dispersal corridors where highways cross rivers, canyons or other roads.

Direct estimates of dispersal rates across

roadways are often high enough to lead researchers to conclude that habitat connectivity is adequate to maintain genetic connections between populations. But although these estimates may seem encouraging, the studies concerned (refs 4 and 6, for example) generally don't include data on levels of gene flow. Combining information from radiotelemetry and genetics, Riley and colleagues[1] have measured both dispersal and successful gene exchange in bobcats (*Lynx rufus*) and coyotes (*Canis latrans*) across the Ventura Freeway. They conclude that, for these species, relatively high rates of dispersal across the freeway do not translate into genetic connectivity.

The Ventura Freeway is one of the largest and busiest highways in the United States: it is 10–12 lanes wide and carries 150,000 vehicles every day. It divides a crucial habitat corridor between the Santa Monica Mountains to the south and areas of more extensive undisturbed habitat to the north. Riley *et al.* captured 110 coyotes and 87 bobcats within dispersal distance of the highway, fitted them with radio-collars, tracked their movements for seven years, and genotyped most of them at seven microsatellite loci. These loci are highly variable DNA markers, distributed throughout the genome, that can be used to identify individual animals and infer genetic relationships among populations.

The authors found that 4.5% of coyotes and 11.5% of bobcats crossed the highway at some point during their study period. Assuming two-year generation times for each species, these numbers translate into respective migration rates of 1.3% and 3.3% per generation. But based on genetic variation at the microsatellite loci, they found significant differentiation between populations on either side of the highway; estimates of effective migration rates based on these genetic data were 3–18 times lower than direct estimates of dispersal.

J.-P. LAHALL/STILL PICTURES

Figure 1 | A coyote on the verge. Roads act as artificial territorial boundaries for wildlife.

A likely explanation for this discrepancy is 'home-range pile-up' — the radiotelemetry data indicate that home ranges abut the highway but do not cross it, so that it acts as an artificial territorial boundary (Fig. 1). Animals with home ranges bordering the highway show much higher range overlap with other individuals than do those farther away, and ranges adjacent to the highway are also much smaller. Migrants, especially young migrants, entering into this situation will find it more difficult to establish and defend a territory, and find mates. This in turn probably results in fewer individuals remaining and lower reproductive success of those that do. The sample sizes of migrants are small, but Riley *et al.* note that six of the ten bobcats that crossed the highway soon returned, and neither of the two females that did remain on the other side produced litters the following spring. Only one of five coyotes that crossed the highway stayed on the other side during the mating season, and most dispersers were under two years old and so were probably less able to establish a territory.

Road ecology has been described as a 'sleeping giant' among environmental biologists[7]: there are indeed very few data concerning genetic fragmentation in animal populations separated by roadways, and what data are available are not encouraging[8,9]. Not all highways are as busy as the Ventura Freeway, and not all animals will behave like the bobcats and coyotes studied by Riley and colleagues[1]. But if the discrepancy between dispersal and gene flow that Riley *et al.* have found is widespread, as seems likely, the effectiveness of highway dispersal corridors needs to be tested to see how well they meet their goal of ensuring genetic connections among populations. There is evidently also a great deal to learn about how widespread the phenomenon of home-range pile-up is, the degree to which territorial and non-territorial animals may be differently affected by barriers such as highways and railways, and the extent to which corridor strategies thereby need to be adapted. ■

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CHEMISTRY

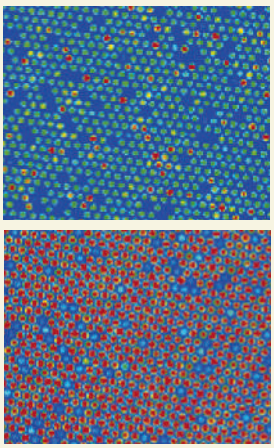
A nose for sarin

The gas attack on the Tokyo subway in 1995 demonstrated the need to rapidly detect and identify sarin and similar substances used in chemical warfare. David R. Walt and colleagues have devised a system to do just that (*J. Am. Chem. Soc.* doi:10.1021/ja057057b; 2006).

The authors attached a fluorescent indicator to polymeric, micrometre-sized beads. The indicator, fluoresceinamine, reacts with nerve agents such as sarin and soman that contain chemical groups known as phosphoryl halides. This causes the beads to fluoresce within seconds of a vapour burst (see lower image; red indicates fluorescence). As the reaction also generates acid, which reduces the intensity of the fluorescence, the authors coated the beads with another polymer that included units of the organic compound pyridine. This basic layer neutralized the acid, maximizing the beads' shine.

The fluoresceinamine reaction is specific to a certain class of chemical, so the microbeads don't respond to other, chemically distinct warfare agents such as mustard gas. Crucially, everyday vapours such as ethanol, toluene and water also fail to stimulate fluorescence, allowing the unambiguous detection of sarin-like chemicals.

The beads can be easily integrated into current 'electronic nose' technology



ACS

used to detect and respond to many different vapours. Incorporated into the sensor array of such a nose, the sarin-detecting beads could react to small amounts of toxin in high concentrations of background vapours. Rapid-response nerve-agent detectors for public areas may soon be a reality.

Andrew Mitchinson