ECONOMICS

Conservation in the red

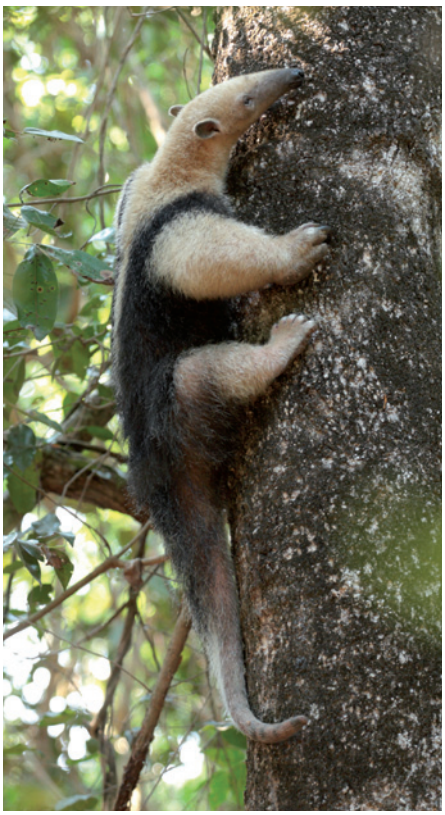
The Convention on Biological Diversity has pledged to reduce species-extinction threats around the globe by 2020. Analysis shows that this goal is achievable but requires a significant increase in the current rate of investment.

STEPHEN POLASKY

International environmental agreements often contain lofty goals, but gathering the necessary resources and commitment to implement such agreements has proven far more difficult than signing them. Over recent decades, numerous target dates have passed with little or no progress made. Writing in *Science*, McCarthy *et al.*[1] provide a financial assessment of the prospects for meeting the targets of the international Convention on Biological Diversity. The good news is that meeting the convention's goals for 2020 is achievable without breaking the bank — the authors' estimated costs to reduce the extinction risk for all globally threatened species is only about 0.1% of global gross domestic product. The bad news, however, is that this level of spending far outstrips the amount currently spent. If this financing gap continues, then these conservation targets will also remain unmet.

The Convention on Biological Diversity (CBD) was signed at the United Nations Conference on Environment and Development (also known as the Earth Summit) in Rio de Janeiro in 1992. After a decade of little progress, the CBD member states agreed to set a target of achieving a significant reduction in the rate of biodiversity loss by 2010. But 2010 came and went and biodiversity loss continued unabated. Towards the end of 2010, the member states agreed to a new strategic plan, which included targets to prevent the extinction of all threatened species and to improve their conservation status, as well as protect 17% of terrestrial ecosystems, by 2020. McCarthy and colleagues sought to assess what these goals mean in dollar terms, and how likely it is that they will be achieved from a financial perspective.

The evidence base from which one can estimate the cost of reducing extinction risk is relatively poor, and the methods McCarthy *et al.* used are 'back-of-the-envelope' calculations. The authors surveyed 236 experts in bird conservation, who supplied estimates of the cost of improving the conservation status of a species about which they were knowledgeable. The survey covered 211 globally threatened bird species, and McCarthy and collaborators extrapolated these per-species estimates to cover all 1,115 threatened bird species. They then determined an upper-bound cost estimate, based on the assumption that expenditure for each species is independent (in other words, that expenditure on one species would not help any other species), and a lower-bound estimate determined from a degree of shared expenditure. To further extrapolate these estimates to costs for non-bird species, the authors used data from New Zealand showing that birds are on average 4.2 times more expensive to conserve per species, and they factored in that there are approximately 12 times more threatened non-bird species than threatened bird species.



JAMES LOWEN/FLPA

Figure 1 | Dollars for diversity. McCarthy *et al.*[1] have estimated that the international community will have to spend US$76.1 billion each year to protect and manage all terrestrial sites of global conservation significance, such as regions of the Mato Grosso state of Brazil, home to this collared anteater (*Tamandua tetradactyla*).

There is somewhat more evidence on which to base estimates for the costs of protecting terrestrial sites of biodiversity significance. We have global maps for 'Important Bird Areas' that are thought to contain habitat for threatened, restricted-range or migratory birds[2], and maps of areas that are already protected[3]. McCarthy *et al.* combined these maps with information on management costs and rough estimates of land-purchase costs[4] to work out the money required to protect important bird habitat. They then used these values, together with estimates of the land needed for habitat to conserve non-bird threatened species, to derive a total amount.

The authors' final estimates are that between US$3.41 billion and $4.76 billion would need to be spent annually to reduce the threat of species extinctions, and that the cost of protecting and managing all terrestrial sites of global conservation significance would be $76.1 billion annually (Fig. 1). This might sound like a lot of money, until one considers that the value of the global economy is roughly $70 trillion per year. But, according to the present paper, the estimates are still ten times larger than the amount currently being invested in conservation.

The actual costs of protecting biodiversity could easily be higher (or lower) than these values. For example, the recent rise in food and commodity prices has increased land prices around the globe; in the United States, the average price of farmland in real terms roughly doubled between 1990 and 2010 (ref. 5). Furthermore, many additional threats that will variably affect species, including climate change, introduced pests and pathogens, pollution, poaching, or many of these combined, could make it much harder and more costly to conserve species. On the other hand, species protection will bring with it other ecosystem services that could significantly reduce the net cost of conservation. For example, some areas that are targeted for protection also supply drinking water for major cities — here, the benefits of improved ecosystem-service provision alone are surely enough to justify conservation.

Although the data and methods used in this paper are simple and subject to potentially significant error, they still probably get the big picture right. McCarthy and colleagues show that the costs of providing adequate protection for biodiversity are substantial yet clearly affordable, but that they are much larger than the sums currently being devoted to conservation. Obtaining more refined estimates might be desirable, but will require better data and more detailed methods — and more exact numbers are unlikely to alter either of these two main conclusions.

In the end, whether or not the 2020 CBD targets will be met rests primarily on making the political and economic argument that the benefits of conserving biodiversity outweigh the costs. This point may be self-evident to most biologists, but it is not to many politicians. McCarthy *et al.* have supplied a piece of useful evidence on the costs of conserving biodiversity and have shown that they are

affordable. What is needed now is compelling evidence that conserving biodiversity is essential for human well-being[6], in the hope that this will convince decision-makers that conservation is well worth the investment. ■

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CELL BIOLOGY

Death by deacetylation

Necrosis is associated with various diseases, yet it is arguably the least-understood form of programmed cell death. It emerges that a sirtuin protein regulates one form of necrosis through a deacetylation reaction. SEE ARTICLE P.199

WEN ZHOU & JUNYING YUAN

It has long been thought that necrotic cell death is simply a passive process resulting from severe stress on a cell, due to infection or trauma, rather than a regulated mechanism. But there is increasing evidence that at least one form of necrosis is mediated by a cellular program called necroptosis[1]. In this issue (page 199), Narayan *et al.*[2] add to this body of evidence by showing that necroptosis is regulated by the deacetylase enzyme sirtuin-2. Deciphering the molecular basis of this process is an exciting prospect, not least because dying cells showing characteristics of necrosis are found in various diseases. Mechanistic insight into necroptosis might therefore provide opportunities for developing inhibitors that block disease-related cell death*.

Necroptosis is activated by TNF-α, an immune-mediator protein that is associated with diseases such as rheumatoid arthritis[3] and inflammatory bowel disease[4]. When this protein interacts with its receptor TNFR1 on the cell membrane, a cytoplasmic complex called complex I rapidly forms, binding to the receptor's intracellular domain. Among the proteins that make up complex I, RIP1 is involved in activating the transcription factor NF-κB and thereby counteracting another form of programmed cell death called apoptosis (Fig. 1a).

RIP1 is a kinase enzyme, which modifies the activity of its substrates by adding phosphate groups to them. Its amino-terminal domain is essential for mediating necroptosis. If caspase-8, a key enzyme in apoptosis, is inhibited, RIP1 leaves complex I. It then interacts with RIP3 — another member of the RIP enzyme family — to form complex IIb. The formation of complex IIb is essential for necroptosis[5–7], and so the biochemical mechanisms that regulate it are under intense investigation.

Narayan *et al.* present intriguing data that implicate sirtuin-2 in mediating the formation of complex IIb. Sirtuin-2 belongs to the sirtuin family of enzymes, which are deacetylases, removing acetyl groups from their substrates. Notably, deacetylases have been linked to the regulation of transcription, apoptosis, stress resistance and ageing[8]. While searching for binding partners of sirtuin-2, the authors came upon RIP3. They also found that, in cells lacking sirtuin-2 or in the presence of pharmacological inhibitors of this protein, TNF-α-mediated necroptosis is blocked. This finding suggests that sirtuin-2-mediated protein deacetylation is involved in controlling necrosis.

Indeed, Narayan and colleagues show that, as well as binding to RIP3, sirtuin-2 deacetylates RIP1 at a specific lysine amino-acid residue; this deacetylation seems to be required for the direct interaction between RIP1 and RIP3. Moreover, in the absence of sirtuin-2, the formation of complex IIb — defined as the interaction between RIP1 and RIP3 following TNF-α stimulation — does not occur (Fig. 1b).

Consistent with the importance of RIP1 deacetylation in necrosis, the researchers show that, on activation of necroptosis in cultured mouse cells, RIP1 acetylation markedly declines. This was also observed in a mouse model of a disorder known as heart ischaemia reperfusion, in which the heart tissue is damaged when the blood supply to it is re-established after a period of limited supply. Inhibition of sirtuin-2 activity prevented RIP1 deacetylation and protected the heart from injury. Because necroptosis also mediates ischaemic brain injury[1], and given that sirtuin-2 is abundantly present in the central nervous system, it is possible that this protein also contributes to necroptosis in neurodegenerative diseases by deacetylating RIP1.

Deacetylation of RIP1 by RIP3-bound sirtuin-2 suggests that at least one reason for the formation of RIP1–RIP3 in complex IIb is to allow this deacetylation. A recent study[9] suggests that RIP1–RIP3, as part of complex IIb, might be present in insoluble filamentous protein clusters called amyloid structures, which are linked to various neurodegenerative disorders. It is possible, therefore, that protein deacetylation is involved in amyloid formation — and thus in these diseases — where it serves as a platform to maintain a stable RIP1–RIP3 complex in the amyloid state.

The enzymatic activity of sirtuin-2 depends on the level of its cofactor NAD^+, a metabolic intermediate. Reduced activity of NAD^+ is associated with energy deficiency and oxidative stress in cells. This indicates that deacetylation — and, by inference, necroptosis — is subject to metabolic regulation. Although NAD^+ levels and sirtuin-2 activity are not altered during necroptosis, NAD^+ depletion

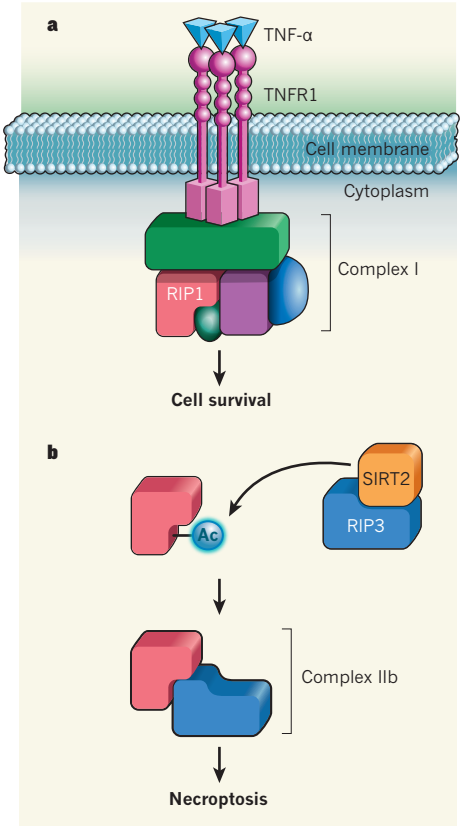

Figure 1 | Evolution of a death complex. a, When TNF-α binds to its receptor TNFR1, which is a protein that straddles the cell membrane, the receptor is activated and a group of proteins — collectively known as complex I — assembles on its cytoplasmic side. As part of complex I, RIP1 mediates NF-κB activation and so promotes cell survival. **b**, RIP1 that dissociates from complex I is in the acetylated form, and this prevents a stable interaction between RIP1 and RIP3. Narayan *et al.*[2] show that the deacetylase enzyme sirtuin-2 (SIRT2) interacts with RIP3 and is required to deacetylate RIP1. Deacetylated RIP1 forms another stable complex with RIP (complex IIb), leading to necroptosis.

*This article and the paper under discussion[2] were published online on 28 November 2012.