ECOLOGY

Foraging further

ANTOINE JORIS

King penguins on the Crozet archipelago in the southern Indian Ocean travel south to forage for food around the Antarctic Polar Front, where cold Antarctic waters meet warmer sub-Antarctic seas (pictured, a king penguin diving). Writing in *Nature Communications*, Bost *et al.* report that climatic variability can alter the birds' foraging behaviour and population dynamics (C. A. Bost *et al. Nature Commun.* http://dx.doi.org/10.1038/ncomms9220; 2015).

By tracking king penguins (*Aptenodytes patagonicus*) for 16 years, Bost *et al.* found that changes associated with an increased sea surface temperature of just 1 °C pushed the polar front southward, and increased both the distances penguins travelled to forage and the depths to which they dived for food. After large-scale climatic anomalies, their population size also fell. Climate models predict that the front will continue to shift southward, which may threaten penguins and their prey. **Jennifer R. Gardiner**

CHEMICAL BIOLOGY

Protein modification in a trice

Organometallic reagents have been developed that chemically modify proteins and peptides specifically at cysteine amino-acid residues — potentially offering a general route to making therapeutically useful compounds. SEE LETTER P.687

HEATHER MAYNARD

Proteins are valuable therapeutic and imaging agents, but they often need to be chemically modified to work optimally in these roles. If a protein is to remain fully biologically active after a chemical group has been attached, the modification must often take place at a specific, predetermined amino-acid side chain. On page 687 of this issue, Vinogradova *et al.*[1] report palladium-containing organometallic reagents that not only modify proteins and peptides at selective sites, but also do so quickly and without being heated, to generate high yields of products.

Chemically modified proteins can have several advantages over their naturally occurring counterparts. For example, attaching polymers to a protein can increase the time that the protein spends in the body, leading to fewer injections for patients[2,3]. Proteins that target certain cancerous tissues can be visualized *in vivo* if radioactive labels are attached, facilitating identification of prognosis and treatment monitoring[4]. And anticancer drugs attached to protein antibodies can be as effective as the unmodified drugs, but have fewer side effects[5].

Therapeutic proteins have conventionally been modified non-selectively, but this sometimes leads to large reductions in biological activity — as much as 93% when polymers are attached[6]. However, site-specific modifications can be crucial for the modified product to retain full biological activity. Many organic reagents have been used to modify proteins at specific sites, with varying success. By contrast, the use of organometallic reagents has lagged behind that of their wholly organic counterparts because of the difficulty of finding reaction conditions that are compatible with the use of both proteins and organometallic reagents. Furthermore, it is hard to achieve selectivity in the presence of the many reactive chemical groups found in proteins[7].

One approach to achieving site selectivity is to exploit either naturally occurring or non-natural amino acids that have unique reactivity, by judiciously placing them at protein sites at which the attachment of a chemical group will not alter the protein's function or structure. Cysteine is commonly used for this purpose, because the thiol group (SH) in this natural amino acid's side chain can be targeted selectively depending on the reagent or the pH used in the modification reaction. Many proteins do not have 'free' cysteines that contain thiols, because these groups often react with other cysteine residues in the same protein to form disulfide bonds (S–S). But modern biochemical techniques now allow a free cysteine to be placed in any position in a protein's amino-acid sequence, thereby pre-directing the site of attachment.

Organometallic approaches to modifying proteins[7,8] have most often targeted non-natural amino-acid residues or certain natural ones (lysine, tyrosine or tryptophan residues), but rarely free cysteines. In Vinogradova and colleagues' method, the organometallic reagent reacts specifically with the thiol groups of free cysteines across a broad pH range (5.5–8.5). The reactions are complete within minutes, and can be performed using low