50 Years Ago

It has been reliably demonstrated that rats can discriminate between the presence or absence of X-rays … The process by which X-rays elicit arousal and orienting reactions in mammals has not yet been determined. However, for simplicity we assume this mechanism operates via a 'radiation receptor'. Attempts to locate this hypothetical radiation receptor have yielded conflicting results … We used a narrow 3/16-in. X-ray beam as a signal or conditioned stimulus to warn the animal of a subsequent shock to the paws. The beam was most effective when it was directed at the olfactory region of the head … In an attempt to clarify this issue, we conducted a study of the effectiveness of X-ray as an arousing stimulus in rats the olfactory bulbs of which had been removed … The results indicate a distinct loss of sensitivity when the olfactory bulbs are removed.
From *Nature* 6 February 1965

100 Years Ago

In *Popular Astronomy* Prof. E. C. Pickering quotes some interesting letters from Profs. Backlund, of Pulkovo, and Schwarzchild, of Potsdam, with reference to astronomers and the war. None of the Pulkovo astronomers have been called to serve, but Prof. Backlund's son is in the Russian ranks, and of French astronomers, M. Croze, astrophysicist of the Paris Observatory, has been summoned, as well as the son of the director, M. Baillaud, who has six sons and sons-in-law in the war. On the German side, many young astronomers are in the field. Dr. Zurhellen and Dr. Kühl, who were with the eclipse expedition, have been interned in Russia; Dr. Münch, of Potsdam, is wounded and a prisoner in France.
From *Nature* 4 February 1915

Finally, Zhao *et al.* tested the function of another enzyme in the lincomycin pathway, LmbT, which they thought might attach EGT to a biosynthetic intermediate. LmbT is a homologue of glycosyltransferase enzymes, which attach sugars to other molecules. The researchers performed a series of gene-disruption and *in vitro* biochemical experiments, establishing that LmbT must act before installation of the 4-propyl-L-proline (PPL) moiety, which forms part of the structure of lincomycin A. In the process, they also proved that three more enzymes — LmbC (ref. 8), LmbN and LmbD — collectively incorporate PPL into the antibiotic.

Zhao and colleagues went on to isolate the suspected product of LmbT and to demonstrate the enzyme's function using *in vitro* assays. They discovered that LmbT catalyses the transfer of lincomycin A's sugar (for which the biosynthetic pathway has previously been reported[9]) to EGT, thus chemically activating the sugar in readiness for its reaction with MSH later in the pathway. Such a role is completely unprecedented: EGT was known to exist as a metabolite, but not as a substrate for an enzyme-catalysed reaction.

A particularly impressive aspect of this work is the authors' use of an intricate series of *in vivo* and *in vitro* experiments that relied on intermediates obtained from mutant cultures and from both enzymatic and chemical syntheses, guided by comparative gene analysis and genome mining. More generally, the study demonstrates that integration of primary metabolites (those that are essential for an organism's survival, such as MSH and EGT) and secondary metabolites (non-essential compounds, such as the products of the Lmb enzymes) is crucial for the biosynthesis of complex molecules. It also highlights the ingenious ways in which nature repurposes enzymes — in this case, using homologues of MSH-dependent detoxification enzymes for biosynthesis. And the establishment of functions for LmbE, LmbV and LmbT will no doubt help researchers to work out the functions of the enzymes' numerous homologues in the ever-growing roster of sequenced genomes. ■

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This article was published online on 14 January 2015.

PALAEOCLIMATE

Climate sensitivity in a warmer world

Comparison of climate records from the Pliocene and Pleistocene geological epochs of the past five million years suggests that positive climate feedbacks are not strengthened during warm climate intervals. **See Article p.49**

DAVID W. LEA

A major concern in projecting future climate change using models is that positive climate feedbacks might become enhanced in a warm climate, accelerating future warming in response to rising greenhouse-gas levels. Climate feedbacks are changes in atmospheric or surface properties induced by climate change that magnify or diminish the overall temperature response. Their aggregate strength is represented by the climate sensitivity, which is the ratio of observed warming to climate forcing, such as increasing atmospheric carbon dioxide levels. Warm intervals of Earth's recent geological past, which can be studied through climate proxies, provide a basis for testing the response of climate sensitivity to warming. On page 49 of this issue, Martínez-Botí *et al.*[1] use improved proxy atmospheric CO_2 data to compare climate-sensitivity determinations from the warm Pliocene epoch, 5.3 million to 2.6 million years (Myr) ago, to those from the cold, extensively glaciated Pleistocene epoch, 2.6 to 0.012 Myr ago. They find that climate sensitivity differs little between these vastly dissimilar times, once the influence of ice sheets is removed.

Why should climate sensitivity be stronger in a warm world? A warmer world is likely to have less snow and ice, thereby reducing their