IN THE NEWS

Max Perutz 1914–2002

Max Perutz, one of the great figures in molecular biology, died of cancer on 6 February 2002 at the age of 87. The importance of his work in the development of molecular biology can never be overestimated and his discoveries still remain the foundation of current research.

Perutz pioneered the use of X-ray crystallography to study the structure of proteins, and he shared the Nobel Prize for Chemistry in 1962 with John Kendrew for his work on identifying the structure of haemoglobin. He was Chairman of the Laboratory of Molecular Biology in Cambridge, which has been home to nine Nobel prize-winners since the 1950s, perhaps the most famous being James Watson and Francis Crick.

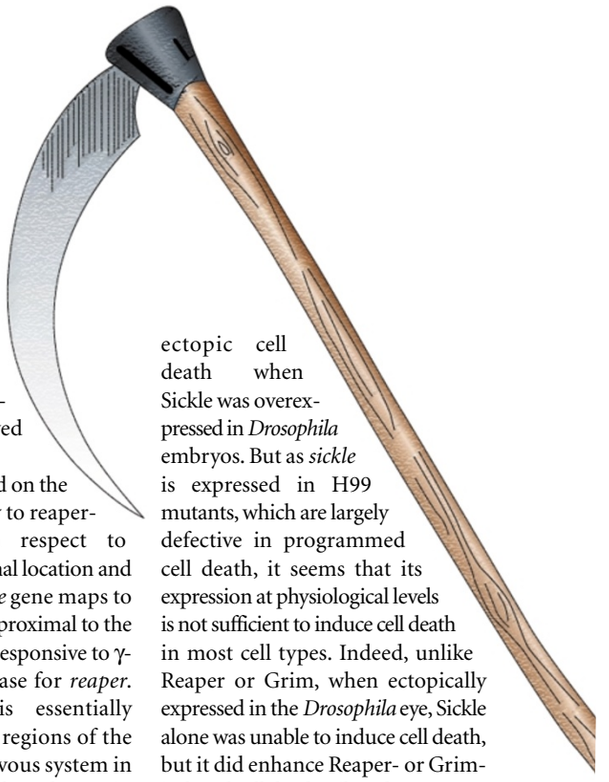
"Not only have his colleagues lost a great co-worker and friend, but Britain and the world will be mourning the loss of one of the 20th Century's scientific giants", said Professor Sir George Radda, Chief Executive of the UK's Medical Research Council (*BBC News Online*, 7 February 2002). "He has inspired countless young scientists. He will be sorely missed, but his life and work will continue to shape science", Radda added. (*The New York Times*, 7 February 2002).

Although he officially retired in 1979, Perutz's appetite for research never waned. He still worked almost every day in the lab, and submitted his last scientific paper for publication just before Christmas 2001. This work, on the structure of the glutamine repeats in Huntington's disease, is now in press in the *Proceedings of the National Academy of Sciences*.

Simon Frantz

APOPTOSIS

Grim, reaper and the sickle of death



In 1994, a fly strain was discovered that is essentially defective in developmental cell death. This strain bears a homozygous genomic deletion (called H99). Three genes — *reaper*, *hid* and *grim* — were subsequently identified that map to this deletion, and regulate programmed cell death by similar mechanisms. Now, reporting in *Current Biology*, three laboratories have identified Sickle, a fourth homologue in *Drosophila melanogaster*, that seems to acts in parallel with Reaper and Grim.

Reaper, Hid and Grim not only map close together, but they are also structurally related. The homology is limited to the amino-terminal 10–15 amino acids, and to a 30-amino-acid region called the 'Trp block'. The three proteins also function by a similar mechanism — they regulate the activity of caspases, the effector enzymes of cell death, by relieving the repression of caspases by the 'inhibitor of apoptosis' (IAP) proteins. It seems that Reaper, Hid and Grim compete with caspases for binding to IAPs; a function that requires the presence of the conserved amino terminus.

sickle was identified on the basis of its homology to reaper-family genes with respect to sequence, chromosomal location and expression. The *sickle* gene maps to chromosome 3L, just proximal to the *reaper* gene, and it is responsive to γ-radiation, as is the case for *reaper*. *sickle* expression is essentially restricted to specific regions of the head and central nervous system in developing *Drosophila* embryos, in areas where *reaper* and *grim* have been reported to be expressed. This suggests that Sickle might functionally interact with Reaper and Grim to regulate cell death in the central nervous system.

All three groups found that Sickle can induce cell death when overexpressed in mammalian or insect cells, and the Alnemri lab saw ectopic cell death when Sickle was overexpressed in *Drosophila* embryos. But as *sickle* is expressed in H99 mutants, which are largely defective in programmed cell death, it seems that its expression at physiological levels is not sufficient to induce cell death in most cell types. Indeed, unlike Reaper or Grim, when ectopically expressed in the *Drosophila* eye, Sickle alone was unable to induce cell death, but it did enhance Reaper- or Grim-induced cell death. Like other Reaper-family proteins, however, the Sickle gene product has a conserved amino-terminal end and a Trp block. Induction of apoptosis by Sickle is dependent on this conserved amino terminus, and it is inhibited by caspase inhibitors and IAPs.

How does Sickle regulate Reaper- and Grim-induced death? Does it simply contribute to titrating out

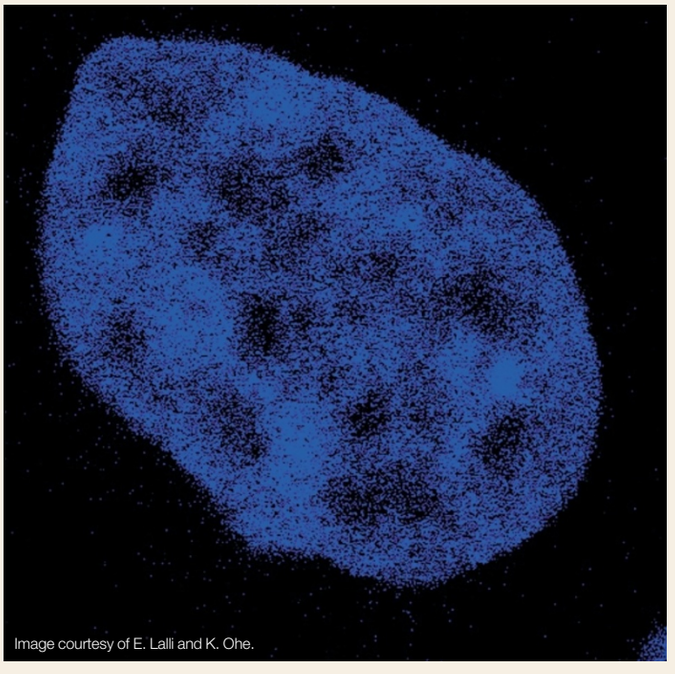


Image courtesy of E. Lalli and K. Ohe.

RNA SPLICING

New feat for Sox

DNA-binding Sox (SRY box) proteins are important during development; many are expressed in a tissue-specific manner. Sassone-Corsi and colleagues now report that Sox proteins are also involved in pre-messenger RNA (pre-mRNA) splicing.

The authors showed that SOX6 is expressed diffusely in the nucleoplasm, but is concentrated in nuclear speckles. Such localization resembles that of components of the pre-mRNA splicing machinery. Moreover, the authors showed that SOX6 co-localizes with splicing factors and U small nuclear RNAs in the speckles, and that blocking splicing caused SOX6 and SRY to redistribute in the