

nature cell biology

A Nobel Prize for cell biology

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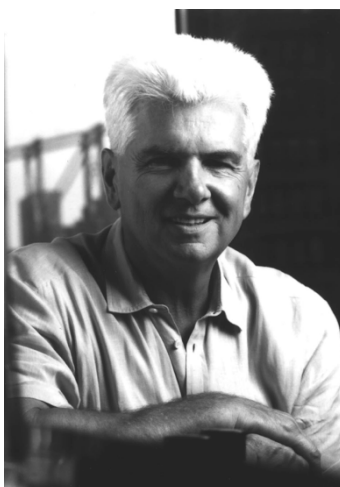
This year’s Nobel Prize in Physiology or Medicine has been awarded to Günter Blobel, of the Rockefeller University, for “the discovery that proteins have intrinsic signals that govern their transport and localisation in the cell”. Angus Lamond of the University of Dundee says that the prize is “a landmark in its recognition of the fundamental importance of basic research in molecular cell biology for modern medicine and the fight against disease”.

The idea that proteins contain targeting zip codes originated in 1971, when Blobel and his colleague David Sabatini postulated that the information needed to direct a nascent peptide to the membrane of the endoplasmic reticulum is contained within the peptide itself. A year later, César Milstein and colleagues provided experimental evidence for a transient signal sequence at the amino-terminal end of a secretory protein. Building on this important discovery and work from his own laboratory, Blobel, together with Bernhard Dobberstein, formulated the ‘signal hypothesis’. In a 1975 paper — which has since become a citation classic — they predicted that newly synthesized proteins have a built-in signal which directs them to the endoplasmic reticulum and through a channel in the membrane. This principle has turned out to be a common mechanism, operating in a variety of intracellular pathways in all organisms, from bacteria to yeast to man. According to Peter Walter of the University of San Francisco, “Günter’s accomplishment is not defined by a single paper or even a set of papers, but rather is the fruit of his casting a wide net over a fundamentally important problem in biology. Many firsts came out of his lab, but it’s the sum of the individual pieces that adds up to the big picture”.

As well as his proposal of the signal hypothesis, it is Blobel’s imaginative approach towards the *in vitro* reconstitution of protein transport that has revolutionized the field of cell biology. “The early realisation that many, perhaps most, reactions that occur in the cell could ultimately be recapitulated *in vitro*,” says Hidde Ploegh of Harvard University, “is in no small measure due to Blobel’s work in this area”. According to Randy Schekman of the University of California, Berkeley, it was the first time that “a cell-free system was developed to dissect the process of intracellular transport using the tools of the enzymologist. Before this landmark event, the field had relied essentially exclusively on morphology and cell fractionation, techniques that by themselves had little prospect of elucidating the machinery required to move proteins from one place to another in the cell”. Blobel’s *in vitro* experimental system inspired other cell biologists and, according to Graham Warren of Yale University, it “made people believe that any cellular function, no matter how complicated, can be mimicked in the test tube”.

Founder of a distinguished scientific lineage

Like any high-profile award, this Nobel Prize has sparked some controversy and speculation. It is, however, undeniable that Blobel has played a pivotal part in training an impressive group of cell biologists, including Bernhard Dobberstein, Peter Walter, Reid Gilmore, Larry Gerace, Vishwanath Lingappa, Gerry Waters, David Anderson, Sandy Simon and Mary Moore, to name just a few. These scientists are now shaping the field of molecular cell biology. Blobel himself was trained by the 1974 Nobel laureate George Palade, who fondly remembers him as a “young, impetuous and highly promising postdoctoral fellow”. Palade, who is well known for his dedication to his students and postdoctoral fellows, no doubt provided an excellent role model in this regard. Waters, who was a graduate student with Blobel, says that he “was always available to discuss science, and was an extraordinarily supportive and enthusiastic graduate advisor”. Lingappa “is, and always has been, immensely proud to be one of his scientific offsprings”. It seems that Blobel’s extraordinary track record as a mentor reflects his ability to bring out the best in people by making them believe in themselves. Perhaps it is this, and not the Nobel Prize, that is his greatest achievement.



Günter Blobel, this year’s winner of the Nobel Prize for Physiology or Medicine