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Journal club

MYSTERIOUS MODIFICATION OF TUBULIN

When biologists today start to work on a particular protein, their first instinct is to clone the gene that encodes it. Although genome projects were not completed when I entered research in the 1990s, molecular cloning by PCR was widely used. Therefore, reading papers from the 1960s and 1970s, describing how proteins and their properties were studied before the discovery of their genes, was very insightful.

Tracing back the discovery of microtubules, their building block tubulin and its post-translational modifications, I found how the first post-translational modification of tubulin was identified in 1975. The group of Ranwel Caputto, from the University of Córdoba in Argentina, had shown that several amino acids, including Tyr, could be incorporated into brain proteins without ribosomes. After narrowing down the candidate proteins that might be modified by this astonishing mechanism, they identified α-tubulin as a substrate of enzymatic tyrosination. In a follow-up study in 1977, they demonstrated that Tyr can also be selectively cleaved from α-tubulin in a process that is now known as detyrosination. Together with the ligation of Tyr (tyrosination), this biochemical process forms the tyrosination–detyrosination cycle of tubulin that is well known today.

> “the primary modification of the protein is the removal, and not the addition, of a functional group”

However, the greatest surprise came when Valenzuela *et al.* cloned the tubulin genes in 1981, revealing that the Tyr residue is in fact encoded by the α-tubulin genes. Thus, the striking feature of this particular post-translational modification is that the primary event is the removal, and not the addition, of a functional group. Explaining this modification to students and peers, I still notice some bewilderedness in their eyes; the thought that a removal reaction is in fact ‘the modification’ seems counter-intuitive to most of us.

The detyrosination–tyrosination cycle has since fascinated the microtubule field, although functional and structural insights into its biological roles were only provided in recent years.

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