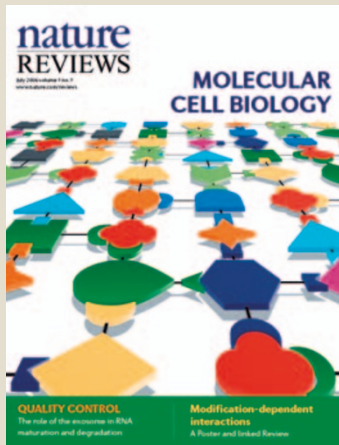




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► **COVER:** 'Modification-dependent interactions' by Vicky Askew; inspired by the Review on p473 and the linked Poster



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Cellular proteins are subject to a vast array of post-translational modifications (PTMs), which control many aspects of cellular function. Such modifications can regulate protein activity through allosteric effects, but can also provide binding sites for a number of interaction domains.

In their Review on page 473, Bruce T. Seet, Ivan Dikic, Ming-Ming Zhou and Tony Pawson explain how PTM-dependent protein–protein interactions represent a fundamental mechanism through which the state of the proteome is 'read' and interpreted. The specific recognition of modified protein sites by interaction domains can yield complex responses. For example, such interactions can mediate cooperative or switch-like effects, or can function in mutually exclusive or antagonistic modes. They also often function sequentially to create extended signalling pathways or networks.

The regulatory properties of PTMs and their interaction domains are also highlighted in the accompanying Poster by Bruce T. Seet, Caesar Lim and Tony Pawson (see <http://www.nature.com/nrm/poster/modifications>). The same protein can potentially be modified at several sites by different types of PTM, which allows complex forms of regulation. Generous support from Upstate and Chemicon International, Inc. means that the poster will be freely available online until the end of 2006.

The significance and timeliness of the topic of PTMs and their interaction domains is nicely illustrated on page 469. In a Research Highlight, we discuss a flurry of papers that report the identification of the plant-homeodomain, or PHD, finger as the interaction domain the trimethylated Lys4 residue of histone H3. This domain provides the crucial link between a physiologically important histone-tail modification and its effect on gene expression and chromatin function.

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