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## PHARMACOLOGICAL REVIEWS

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About the cover: The UPS. Ubiquitin (Ub) is activated in an ATP-dependent reaction by the E1 ubiquitin-activating enzyme and appended to target proteins by the successive action of E2 ubiquitin-conjugating enzymes, E3 ubiquitin ligases, and E4 chain elongation factors. See the article by Yi and Ehlers on page 14 of this issue.