DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

Drug Discovery: Alternative Approaches to Lead Generation

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(ospite. Prof.ssa P. Hrelia)

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Biosketch

B.A. degree (1965, Biology) from Rockhurst University, Kansas City, Missouri, M.S. (1967, Pharmacology) and Ph.D. (1970, Pharmacology) degrees from the University of Missouri-Kansas City. Dr. Enna spent 10 years on the faculty at the University of Texas Medical School at Houston in the Departments of Pharmacology and Neurobiology. From 1986 1990, he was Senior Vice President and Scientific Director of Nova Pharmaceutical Corporation in Baltimore, and Executive Vice President. He is currently Associate Dean for Research and Graduate Education as well as Professor of Physiology and of Pharmacology at the University of Kansas Medical School. Dr. Enna served as editor of The Journal of Pharmacology and Experimental Therapeutics, and is currently co-editor of Current Protocols in Pharmacology, Editor-in-Chief of Biochemical Pharmacology, Executive Editor-in-Chief of Pharmacology and Therapeutics and Series Editor of Advances in Pharmacology. He has been the recipient of Research Career Development Awards from the National Institute of Mental Health and the National Institute for Neurological, Communicative Disorders and Stroke. Other awards include the John Jacob Abel Award and the Torald Sollmann Award from the American Society for Pharmacology and Experimental Therapeutics, the Daniel H. Efron Award from the American College of Neuropsychopharmacology, a PhARMA Foundation Excellence Award, the Paoletti Medal from the European Pharmacology Society, and appointment as an Honorary Fellow of the British Pharmacological. He has been President of the American Society for Pharmacology and Experimental Therapeutics (ASPET) and currently he is the President of the International Union of Basic and Clinical Pharmacology (IUPHAR). Dr. Enna's research interests include neuropharmacology, neurochemistry and neuropsychiatric disorders, described in 300 published research reports, reviews, and book chapters.

DRUG DISCOVERY: ALTERNATIVE APPROACHES TO LEAD GENERATION

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Historically, drug discovery was chiefly an empirical enterprise, with the shift to a more hypothesis-driven approach occurring in the 20th century. Whereas originally drug discovery was focused primarily on identifying therapeutically useful agents prior to defining their mechanisms of action, it is now more common to develop a target-selective compound before assessing its potential clinical utility. Too often this yields ligands that are useful as research tools, but worthless as therapeutics. Although the emphasis on target identification, or "targephilia", has yielded novel pharmaceuticals, it does not appear to have facilitated the drug discovery process overall, especially for compounds to treat central nervous system (CNS) disorders. In part, this is because the targephilic approach requires a keen understanding of the relationship between the target and organ system physiology, and the availability of in vivo and in vitro test systems that reliably predict human responses. The fact that the majority of CNS drugs have been identified empirically indicates the lack of knowledge about basic neurobiological processes and human behavior make drug discovery in this area less amenable to a target-based approach than for other types of therapeutics. Improving the success rate in CNS drug discovery requires a more pharmacometric-based strategy, with an emphasis on defining basic CNS function in intact animals and a more systematic in vivo behavioral analysis of novel chemical structures. Efforts should also be directed toward defining the sites of action of existing CNS drugs to aid in the design of second-generation agents and toward examining the CNS responses to drugs approved for other uses. Such a program requires a greater balance between, and integration of, pharmacometric and molecular techniques to maximize the contributions of both science and serendipity in drug discovery.