molecular pharmaceutics

editorial

The "Site of Action"

Drug discovery paradigms for the past 50 years have focused on the "site of action" with high affinity ligands for receptor proteins as the drug targeting approach, with a more or less detailed pharmacological mechanism of action that, hopefully, has some relevance to human clinical response. The complexity of the response in the human in vivo system makes this risky, with many more failures than successes. While successes have been of obvious enormous benefit, the success rate has not improved over the past decade or more. This has been attributed to such factors as increasing regulatory requirements or difficulty in finding new targets. A factor that is of prime importance, generally recognized but not deeply thought about or investigated, is the ability to get the drug to the right target. While drug targeting and drug delivery are at least superficially recognized as important, the general lack of in-depth understanding is due to the complex processes involved in distribution of drugs in the body, both whole body and cellular and subcellular distribution. The drug development process often goes from a high affinity ligand, to candidate selection, directly into a much more empirical safety and biopharmaceutical and pharmaceutical development approach. We have biopharmaceutical screening today, but in cell systems that, at best, only partially reflect the in vivo processes. The complexity of this biodistribution process is being unraveled today with advances in cellular transporters and metabolizing enzymes, rapidly bringing a molecular basis to biopharmaceutics, pharmacokinetics, and biodistribution. We have been looking too long under the street light. It's time to shine the light into the darker corners of in vivo human response: distribution to the site of action.

Molecular Pharmaceutics finishes its second year of publication with outstanding progress in publishing in this new era of multidisciplinary molecular science. Manuscript flow continues to increase at an excellent pace, we are available worldwide as part of the ACS journal packages, and we are indexed in a number of high profile databases, including Medline and PubMed. The theme issue on dendrimers was a huge success. We have several theme issues in process for 2006, and guest editors have been very enthusiastic in responding to our suggestions for additional theme issues. *Molecular Pharmaceutics* topical areas, based on the most frequently used key words the authors have cited in their articles, include drug delivery, P-glycoprotein, prodrugs, cancer, dendrimer, biodistribution, drug resistance, and targeting. The choice of key words is indicative of the focus of the manuscripts on molecular mechanistic drug delivery: "the site(s) of action". We look forward to continued rapid growth of *Molecular Pharmaceutics* in these rapidly advancing fields. We are well on our way to establishing *Molecular Pharmaceutics* as the preeminent journal in the molecular pharmaceutics and drug delivery fields.

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Editor-in-Chief

MP058083J

10.1021/mp058083j CCC: $30.25
Published on Web 12/05/2005