Drug Discovery Informatics: Targets, Leads, Drugs, and the “Black Swan”

Pharma R&D totaled $55.2 billion in 2006 for the development of new medicines and vaccines; at the same time, the top 50 pharma companies grossed $643 billion in global sales. We examine this business from a scientific aspect, by highlighting some of the issues related to drug discovery: “Targets” - macromolecular structures that, when manipulated therapeutically, lead to clinical effects; “Leads” - small molecule precursors that when modified result in clinical candidates; “Drugs“ – molecules that reach regulatory approval. When successful, the combination of “targets” and “leads” results in clinical candidates. This talk will provide an overview of the R&D process, with examples related to research at UNM and elsewhere. Examples related to CNS (central nervous system) drugs will be given. The “Black Swan”, a metaphor for the highly improbable, is also discussed in the context of drug discovery. Wall Street analysts and pharma management still view the discovery process akin to engineering airplanes. We argue that this is conceptually wrong, and that the pharmaceutical industry is subject to both positives and negative “Black Swans”. Familiar negative “Black Swans” such as the all-markets withdrawal of Vioxx will be discussed in contrast to positive ones, such as Lipitor. The role of informatics in drug discovery will be emphasized.