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Brief Note on Drug Discovery and Development

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Perspective

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DESCRIPTION

Drug discovery is the process of discovering novel candidate pharmaceuticals in the domains of medicine, biotechnology, and pharmacology. Drugs were previously found by finding the active ingredient in traditional treatments or by chance, as with penicillin. In a method known as classical pharmacology, chemical libraries of synthesised small molecules, natural products, or extracts were screened in intact cells or complete organisms to identify compounds that had a desired therapeutic effect. After the human genome's sequencing enabled quick cloning and synthesis of vast quantities of purified proteins, reverse pharmacology (high throughput screening of massive chemical libraries against isolated biological targets thought to be diseasemodifying) has become routine practise. Modern drug development entails identifying screening hits, medicinal chemistry, and optimising those hits to improve affinity, selectivity (to lower the risk of adverse effects), efficacy/potency, metabolic stability (to extend the half-life), and oral bioavailability. The drug development process can resume after a molecule that meets all of these criteria has been identified. Clinical trials are developed if the experiment is successful.

As a result, modern drug discovery is typically a capital-intensive process involving considerable investments from both pharmaceutical companies and national governments (who provide grants and loan guarantees). Despite advances in technology and knowledge of biological systems, drug development remains a lengthy, "expensive, demanding, and inefficient process" with a low rate of new therapeutic discovery. Each new molecular entity cost roughly US$1.8 billion in research and development in 2010. Basic discovery research is generally supported by governments and philanthropic groups in the twenty-first century, but late-stage development is primarily funded by pharmaceutical firms or venture capitalists. High-Throughput Screening (HTS) is a method of identifying new drugs against a specific target for a disease, in which enormous libraries of compounds are screened for their capacity to change the target. If the target is a novel GPCR, for example, compounds will be examined to see if they can inhibit or stimulate that receptor (see antagonist and agonist). If the target is a protein kinase, chemicals will be investigated to see if they can block that kinase. Another significant use of HTS is to indicate how selective the compounds are for the target of interest, as the goal is to find a molecule that will only interfere with the target of interest and not with other, related targets. Other screening runs will be performed to examine if the "hits" against the specified target may interfere with other related targets—this is the cross-screening process. Because the more unrelated targets a chemical hits, the

more probable it is to induce off-target toxicity once it reaches the clinic, cross-screening is critical. Drugs must successfully complete multiple phases of clinical trials and pass through a new drug approval procedure in the United States, known as the New Drug Application.

Drug discovery that has the potential to be a commercial or public-health success necessitates a complicated interaction between investors, industry, academia, patent laws, regulatory exclusivity, marketing, and the need to strike a balance between secrecy and communication. Meanwhile, the orphan drug funding process assures that those who suffer from rare conditions have some hope of pharmacotherapeutic advancements, even if no substantial commercial success or public health benefit is envisaged. De novo drug design is another essential strategy for drug discovery, in which a prediction is produced about the types of molecules that might (for example) fit into an active site of the target enzyme. Virtual screening and computer-aided drug creation, for example, are frequently employed to find new chemical moieties that could interact with a target protein. To increase the efficacy and characteristics of potential therapeutic leads, molecular modelling and molecular dynamics simulations can be utilised as guidance. Natural products continue to serve an important role as a starting material for drug development, despite the rise of combinatorial chemistry as an integral part of the lead discovery process. According to 2007 report, natural derived or semisynthetic derivatives of natural sources accounted for 63% of the 974 small molecule novel chemical entities created between 1981 and 2006. The numbers were larger in some therapy categories, such as antimicrobials, antineoplastic, antihypertensive, and anti-inflammatory medications. In many cases, these goods have been in use for a long time. When a medicine is developed with data from previous studies proving that it is safe and effective for its intended purpose in the United States, the company can file a New Medicine Application (NDA) to have it marketed and available for clinical use. The FDA can look at all of the information about the medication candidate and decide whether or not to approve it based on its safety, specificity of action, and dose efficacy.