NOVEL SCENARIOS IN DRUG DISCOVERY

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Regardless of the exact cost, the process of developing a new drug is an activity of high long-term risk that has few equals in the business world, but the potential benefits for the millions of patients with serious diseases provide a constant driving force for everyone involved in the process. In this perspective, the search for new structures that have a significant therapeutic activity remains a primary objective in pharmaceutical chemistry. Currently, drug discovery depends critically on in silico assays and in vitro carried out on large collections of molecules, called high throughput screening (HTS), in which the ability of small molecules is tested to interact with biological targets preselected. Unfortunately, most approaches used to create new compounds are based on the use of known substrates or commercial building blocks. Thus, the development of small molecules that are poorly represented in the collections of commercial detection is a source of suitable fragments for the development of potential new molecular entities (NMEs).

The development of synthetic methods in organic chemistry has created new tools to the organic chemist who has provided the means to generate not only individual molecules or collections of such compounds, but also preparing collections of structurally divergent compounds. Essentially, the discovery of new drugs can be categorized into three approaches covering chemical space differently. The first approach uses a target-oriented or target (Target-oriented synthesis, TOS) synthesis. Since the pioneering synthesis of urea Wohler in 1828, this focused strategy has been enriched with great strides, and is now possible to synthesize highly complex structures. This approach is mainly based on nature to discover molecules with useful properties. The second approach makes use of synthetic chemistry to explore the chemical space next to a specific region. The origin of the starting compounds or may be different leads and include natural products, known drugs or rational designed from a crystal structure of a macromolecule of interest. The objective of this approach is to access some diversity using various building blocks and usually involves the synthesis of analogs of a target structure using a retrosynthetic plan. Finally, the approach based on a divergent strategy (Diversity-oriented synthesis, DOS), aims to create a broad distribution of compounds in the chemical space, including sparsely populated regions. The synthetic routes used in DOS are branched and divergent, and are planned in a direct synthetic sense, in counterpoint to the retrosynthesis.

This increase in the number of possible targets of therapeutic interest has not been the only chapter in the drug discovery process that has been invaded and surpassed some way by the big numbers. The development of biological in vitro, and miniaturized robotic assays makes it possible in many cases and in a few hours, testing the activity of hundreds or thousands of chemical compounds. The pharmaceutical industry applies this procedure work, leaving aside for more advanced, i.e. when already selected products called "seeded" (lead compounds), animal research models stadiums.

Such scenarios have a number of important consequences, as the priority concern of most of the multinationals is focused on diseases affecting mainly the first world, while others, who come to decimate poor countries of resources, do not wake the necessary attention. The problem is real and complex, and not fit simplistic speeches, but the solutions, it is necessary that there should come from the involvement of all stakeholders worldwide. Another consequence of the figures cited is the need to reduce costs and development time, not only thinking about the possible industrial profitability but on the ill.