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Sommario/riassunto	In the genomic era of 1990s-2000s, pharmaceutical research moved to target-based drug discovery which enabled development of a number of small molecule drugs against a wide range of diseases. In many cases however, drugs that arose from genomics failed, questioning the validity of the targets and the suitability of target-based drug discovery as an optimal strategy for all disease states. For monogenic diseases, target-based approaches may be well-suited to the identification of novel therapies. Most diseases, however, are caused by a combination of several genetic and environmental factors and are likely to require simultaneous modulation of multiple molecular targets/pathways for successful treatment. For such diseases, reductionist approaches focusing on individual targets rather than biological networks are unlikely to succeed and new drug development strategies are required. In search of more successful approaches, the pharmaceutical industry is moving towards phenotypic screening beyond individual genes/targets. However, this requires rethinking of diseases and drug discovery approaches from a network and systems biology perspective. Since returning to the pre-genomics era of screening drug candidates

in laborious animal models is not a feasible solution, the industry needs to evolve a new paradigm of phenotypic drug discovery within the context of systems biology. Such a paradigm must combine physiologically and disease relevant biological substrates with sufficient throughput, operational simplicity and statistical vigour. Biomarker strategies for translational medicine, as well as preclinical safety and selectivity assessments, would also need to be revised to adapt to the target agnostic style. This focused issue aims to discuss strategies, key concepts and technologies related to systems-based approaches in drug development. Design and implementation of innovative biological assays, featuring multiple target strategies, and rational drug design in the absence of target knowledge during the early drug discovery are illustrated with examples.