

## Impact of Pharmacogenomics and other Drug Development Technologies on Modern Pharmacology and Therapeutics

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During the last 2-3 decades of the past century, health professionals were confronted with an expanding body of information as well as an impressive number of technological advances related to drug development, therapy and clinical practice. Recombinant DNA (rDNA) technology have provided several new methods, revealed novel molecular targets and DNA-based diagnostics to pharmaceutical research that can be utilized in assays for screening and developing potential biopharmaceutical drugs. Pharmacogenomics aims the selection of the proper drug therapy in clinical practice to certain individuals. These genomic technologies are changing the process of developing new therapeutic agents and helping us to understand the drug actions at the molecular level. Among the most exciting developments are:

- a) The emergence of Pharmacogenomics as a discipline that links drug efficacy and safety (drug response) with genetic variations of the individuals.
- b) The DNA microarray (DNA chip) technology which allows rapid analysis of the expression for thousands of genes of an organism, thus identifying genes involved in several human disorders.
- c) The availability of bioinformatic tools to analyze the load of genomic data and identify novel drug targets and unique structural characteristics.
- d) The application of new genetic approaches for gene and protein therapy protocols and the development of fascinating site-specific drug delivery systems.

e) The advantage of Combinatorial Chemistry that allows the synthesis of large libraries of low molecular weight compounds for High-Throughput Screening for pharmacodynamically active agents.

f) Finally, Proteomics, Functional and Structural Genomics, Expression Genetics, and Genome Mapping are emerged for the analysis of gene products (proteins) serving as drug receptors, or other biological functions.

All these advances have changed the pharmaceutical sciences into a more biology- and biotechnology-oriented direction. Pharmacogenomics is a major development that is taking place in pharmaceutical sciences today with the progressive transition from genetics to genomics and the attempt of analyzing the whole genome of an organism and correlating genotyping with specific drug actions. The combined use of DNA microarray technology and automated DNA sequencing permitted the detection of specific Single Nucleotide Polymorphisms (SNPs) in several genes involved in drug actions. Correlation of such genetic variations with altered drug efficacy or toxicity in certain individuals, indicates that personalized medicine in drug therapy can be applied to some if not all people. Exploitation of genomic information related to genes that encode either drug metabolizing enzymes, drug-specific receptors, or drug-transporters is now well accepted by modern therapeutics. Moreover, detailed analysis of molecular drug actions has clearly shown in some cases that "drugs" may exert their effects

via specific "molecular networks" involving several genes and proteins. This fact stresses even more the complexity that already exists in Modern Pharmacology, and makes the possibility of applying personalized medicine into clinical practice a very difficult task. As a matter of fact, the identification of functional SNPs in several genes related to drug actions, is a huge challenge for the pharmaceutical industry, especially after the completion of several genome-sequencing projects from different organisms. The advantage for pharmacologists to apply the principles of personalized medicine seems to go in parallel with the application of pharmacogenomics, and by taking into account the serious moral issues raised by the application of genomic technologies into clinical practice. Thus, the role of future pharmacologists in these new concepts of drug therapy will be an increasing demand in pharmaceutical care in order to ensure effective and safe drug delivery to each individual patient. More interestingly, all these achievements and challenges in pharmaceutical research that have added new knowledge in pharmacology have already stressed the need for appropriate adjustments in both teaching curriculum and research areas of pharmacology in medical and pharmacy faculties. It is obvious, that the better training of future medical and pharmacy students in pharmacology will clearly depend on the development of new curriculums by integrating the new drug-related genomic and bioinformatic technologies into the teaching process. This is a very difficult task, since this means development and introduction of new interactive computer-assisted learning methods into the teaching process and in

a very strict timetable for completing both theory and practice in pharmacology. Finally, another challenging issue in the design of new pharmacology curriculums will be instruct the students to keep pace with new scientific knowledge rapidly entering the drug-related industry even after their graduation.

## REFERENCES

- Drews J.: Drug discovery: A historical perspective. *Science* 287: 1960-1964 (2000)
- Emilien G., et al.: Impact of genomics on drug discovery and clinical medicine. *Q. J. Med.* 93: 391-423 (2000)
- Housman D., Ledley F.D.: Why pharmacogenomics? Why now? *Nature Biotechnology* 16: 2-3 (1998)
- Hughes I., et al.: Knowledge and skills needs of pharmacology graduates in first employment: how do pharmacology courses measure up? *Trends Pharmacol. Sci.* 18: 111-116 (1997)
- Jazwinska E.C.: Exploiting human genetic variation in drug discovery and development. *Drug Discovery Today* 6: 198-205 (2001)
- Landro J.A., et al.: HTS in the new millenium: The role of pharmacology and flexibility. *J. Pharmacol. Toxicol. Methods* 44: 273-289 (2000)
- Lee K.H.: Proteomics: a technology-driven and technology-limited discovery science. *Trends Biotechnol.* 19: 217-222 (2001)
- McCarthy J.J., Hilfiker R.: The use of single-nucleotide polymorphism in pharmacogenomics. *Nature Biotechnol.* 18: 505-508 (2000)
- McLeod H.L., Evans W.E.: Pharmacogenomics: unlocking the human genome for better drug therapy. *Annu. Rev. Pharmacol. Toxicol.* 41: 101-121 (2001)
- Phillips K.A., et al.: Potential role of pharmacogenomics in reducing adverse drug reactions: a systematic review. *JAMA* 286: 2270-2279 (2001)
- Ramstrom O., Lehr J.-M.: Drug discovery by dynamic combinatorial libraries. *Nature Rev. Drug Discovery* 1: 26-36 (2002)
- Rodriguez R., et al.: Changing the countenance of pharmacology courses in medical schools. *Trends Pharmacol. Sci.* 18: 314-318 (1997)