

## Teaching Molecular Medicine within Medical Education: No time to wait

A Rojas, R Silva, M Castro, E Mercadal, I González, H Figueroa

### *The birth of a new era in Medicine*

Individualization of therapy is not a new concept in medicine, considering it has been central to the practice of medicine since the writings of Hippocrates (1). Under this assumption, medicine is undergoing a very dynamic transformation towards a more predictive, selective and preventive medical practice.

During the twentieth century, physicians and researchers moved their attention from the organ to the cells and then to molecules. This new vision was a hallmark in the long and winding road to a more profound understanding of the basis of diseases. At present, a growing body of individual differences, in terms of susceptibility, diagnosis, prognosis and treatment of disease has arisen as a result of this change in approach.

We are at the beginning of an era of individualized, molecular and genomic medicine, where diagnosis, prognosis and treatment will be increasingly based on our understanding of human variability (2, 3).

Following the success of the Human Genome Project, many kinds of genetic maps are assisting to assign genetic components of disease phenotypes to specific chromosomal regions. For instance, microsatellite maps based on identification of tandem repeats of short nucleotide stretches can map traits or diseases that segregate in large families. Additionally, the number of identified human Single Nucleotide Polymorphisms (SNPs) has grown to more than 10 million; nearly 5 million of these have been validated, but fewer than 700 000 have been assigned population frequency estimates (3–6).

The SNP map provides a public resource for defining haplotype variation across the genome and should help researchers to identify multiple genes associated with complex diseases such as cancer, diabetes mellitus, cardiovascular diseases and mental illness. It may assist in identifying novel targets for diagnostic and therapeutic interventions. Some of the segments of the ancestral chromosomes occur as regions of DNA sequences that are shared by multiple individuals.

Genetic variants that are near each other tend to be inherited together (*ie* linked). These regions of linked variants are termed haplotypes. The SNPs are linked to regions coding for disease susceptibility, drug metabolizing enzymes *etc* so polymorphisms can be used to “map” disease genes.

The International HapMap Project was designed to identify common haplotypes in four populations with African, Asian and European ancestry. One of the objectives of this project is to identify the so-called “tag” SNPs that uniquely identify these haplotypes (5). By analyzing an individual’s tag SNPs, researchers will be able to identify the collection of haplotypes in a person’s DNA. The goal is to utilize the haplotype map of the human genome sequence for future genetic association studies of human diseases as well as drug efficacy and safety (7).

The description of physiology and illness in molecular terms and the capacity to explain individual susceptibilities to diseases and variations in response to treatments, due to bearing a particular set of genes or haplotypes, have emerged as an important and expanding field that should be increasingly incorporated into undergraduate medical curriculum (8). This is often viewed as a new medical “paradigm”, termed Molecular Medicine or Genomic Medicine, which emphasizes the importance of understanding the role of molecular mechanisms and genetic information in health and disease (9). This new paradigm has become a real challenge which must be addressed as an urgent task in medical academic settings (10–12), particularly in developing countries. The introduction of Molecular Medicine into curricula should be considered not only as simply teaching of the current molecular knowledge in diseases but also as learning activities to integrate both traditional and modern molecular approaches in clinical scenarios (13).

This new reform should be considered, not only in undergraduate curricula of medical students but in training programmes for residents and continuing professional development programmes for practising physicians. The development of new skills in future physicians and biomedical researchers will ensure proper diagnosis, more real prognosis evaluation and the best possible treatment for future patients. Because of the revolution in molecular medicine, learning should be considered as a continuous process, we must provide new physicians with lifelong capabilities to understand new developments and assimilate emerging technologies in

From: The School of Medicine and Health Sciences Department, Catholic University of Maule, Talca, Chile.

Correspondence: Dr A Rojas, School of Medicine, Catholic University of Maule, Ave San Miguel # 3605, Talca, Chile. e-mail: arojasr@ucm.cl

diagnosis and therapeutic approaches in the changing landscape of 21<sup>st</sup> century medicine (14, 15).

At present, many journal publications describe results obtained by means of genomics, proteomics and bioinformatics approaches, not only in a basic research context, but also in the clinical scenario. This point is not only restricted to processes that deal with acquiring knowledge, it goes beyond that because new technical terms, concepts, definitions and techniques are increasingly appearing in these papers, which may represent a conceptual and semantic barrier to those professionals who are not familiar with such concepts and therefore are disabled in the continuing education process.

It is noteworthy that physicians and healthcare professionals in general, should not be converted in molecular biologists or “genomics specialists”, but they must understand the “new language” that would enhance their communicational skills. To face up this new challenge, we must focus our attention not only on healthcare professionals and particularly physicians, but also the general population, the current and future patients.

In this context, teaching molecular medicine to new physicians must be focussed, in addition to “technical” skills, on the development of communication skills that would impact on the education process about genetic testing in general and on educating test recipients about behavioural modifications that could be recommended as a result of a genetic test (16).

This is particularly important because genetic predisposition is not always consistent with phenotypic expression. Although an individual may possess a gene implicated in the development of a disorder, gene activation may not occur until triggered by a particular environmental interaction. The environmental interaction may be a single exposure to a triggering event or one that requires repeated exposures over time before clinical manifestation of disease. Therefore, comprehensive education would serve to inform susceptible people regarding precautionary measures or behavioural modifications to prevent or delay the onset of disease. To do that, physicians must be able to communicate the complexities of molecular medicine in a simple, direct and understandable language to the general population.

The increased use of genetic tests in clinical settings raises the issue of educating the general population and healthcare professionals regarding the tests, their purposes and their implications. Currently, the average person is not properly educated about genetic testing because of its novelty (17, 18). Depending on the outcome of such tests, especially with regard to tests for potentially high-risk genes, education on the scope of risk and follow-up must be provided to ensure proper understanding of the results and the implications to personal health. The result of a genetic test may also represent a profound psychological burden on the individual’s family (19).

On the basis of the potential predictive value of genetic tests, proper follow-up must be established for diseases whose early detection could result in improved treatments and outcomes.

The lack of “genomics/genetics” education currently provided for patients is clearly demonstrated in several studies. In one study, only 18.6% of the subjects received counselling about a genetic test for a hereditary genetic disorder (20). This reiterates the necessity for expanded education programmes, where the principal actors must be healthcare professionals with the adequate knowledge but also with appropriated communicational skills to explain this fact to the general population at large (21).

Furthermore, the population is fearful of the potential misuse of genomic data, particularly in the use of genetic information that could lead to discrimination in the granting of employment and insurance. This has been markedly promoted by distorting presentations in communications media about the meaning and extension of molecular medicine. New physicians must be prepared to properly manage all ethical, legal and social implications of molecular medicine under the basis of the particular legal scenario in every country (22).

All these issues need to be taken into consideration during the dynamic reviewing of medical curricula either for undergraduate medical students or training programmes for residents, as well as in continuing professional development programmes for practising physicians.

In summary, there is a tremendous challenge that all medical educators must embrace in preparing new physicians who will work in the post genomic era of medicine and where individual genome sequences, or at least sections of them, will be part of the medical files they must review. How molecular medicine will be translated into better healthcare will depend on how healthcare professionals and physicians in particular, use and handle this information.

## REFERENCES

1. Sykiotis GP, Kalliolias GD, Papavassiliou G. Pharmacogenetic principles in the hippocratic writings. *J Clin Pharmacol* 2005; **45**: 1218–20.
2. Guttmacher AE, Collins FS. Genomic medicine – a primer. *N Engl J Med* 2002; **347**: 1512–20.
3. Shastry BS. Genetic diversity and new therapeutic concepts. *J Hum Genet* 2005; **50**: 321–8.
4. Single nucleotide polymorphism database. Available at: [http://www.ncbi.nlm.nih.gov/SNP/snp\\_summary.cgi](http://www.ncbi.nlm.nih.gov/SNP/snp_summary.cgi).
5. The International HapMap Consortium. The International HapMap Project. *Nature* 2003; **426**: 789–96.
6. Hohe MR. Haplotypes and the systematic analysis of genetic variation in genes and genomes. *Pharmacogenomics* 2003; **4**: 547–70.
7. Traherne JA, Horton R, Roberts AN, Miretti MM, Hurles ME, Stewart CA et al. Genetic analysis of completely sequenced disease-associated MHC haplotypes identifies shuffling of segments in recent human history. *PLoS Genet* 2006; **2**: 81–91.
8. Papavassiliou AG. Biochemistry versus molecular medicine: what should we be teaching our medical students? *Mol Med Today* 1999; **5**: 100–1.
9. Sykiotis GP, Papavassiliou AG. Molecular medicine: a lifetime of learning, teaching and caring. *Trends Mol Med* 2005; **11**: 484–5.

10. Vermus H. Getting ready for gene-based medicine. *N Engl J Med* 2002; **347**: 1526–7.
11. Childs B, Wiener C, Valle D. A science of the individual: Implications for a medical school curriculum. *Ann Rev Genomics Hum Genet* 2005; **6**: 613–30.
12. Valle D. American Society of Human Genetics Presidential Address 2003: Genetics individuality and medicine in 21<sup>st</sup> century. *Am J Hum Genet* 2004; **74**: 374–81.
13. Collins F, McKusick V. Implications of the Human Genome Project for medical science. *JAMA* 2001; **285**: 540–4.
14. Bodzin J, Kardia SL, Goldenberg A, Raup SF, Bach JV, Citrin T. Genomics and Public Health: Development of Web-based Training Tools for Increasing Genomic Awareness. *Prev Chronic Dis* 2005; **2**: A25.
15. McInerney J. Education in a genomic world. *J Med Philos* 2002; **27**: 369–90.
16. Califf RM. Defining the balance of risk and benefit in the era of genomics and proteomics. *Health Affairs* 2004; **23**: 77–87.
17. Austin MA, Peyser P, Khoury M. The interface of genetics and public health: research and educational challenges. *Annu Rev Public Health* 2000; **21**: 81–99.
18. Caulfield TA, Gold ER. Genetic testing, ethical concerns and the role of patent law. *Clin Genet* 2000; **57**: 370–5.
19. Burke W, Atkins D, Gwinn M, Guttmacher A, Haddow J, Lau J et al. Genetic test evaluation: information needs of clinicians, policy makers and the public. *Am J Epidemiol* 2002; **156**: 311–8.
20. Giardello F, Brensinger JD, Petersen GM, et al. The use and interpretation of commercial apc gene testing for familial adenomatous polyposis. *N Engl J Med* 1997; **336**: 823–7.
21. Subramanian G, Adams MD, Venter JC, Broder S. Implications of the human genome for understanding human biology and medicine. *JAMA* 2001; **286**: 2296–307.
22. NIH-DOE Working Group on Ethical, Legal and Social Implications of Human Genome Research. Final Report of the Task Force on Genetic Testing. Promoting Safe and Effective Testing in the United States; 1997. Available at: <http://www.genome.gov/10001733>.