Editorial

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Laboratory medicine does matter in science (and medicine)… yet many seem to ignore it

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At the end of the year 2014, Van Noorden et al. published an interesting analysis in the journal *Nature* entitled "The top 100 papers", in which the 100 most cited research of all time were described [1]. Most of the readers of *Clinical Chemistry and Laboratory Medicine* would now argue that this has probably little to do with our education, expertise and daily activities, at least until exploring the full list of papers. Despite the fact that the vast majority of these articles deal with topics of biology and medicine, eight papers in the "top 10" describe laboratory methods or applications (Table 1). Most of these articles should be regarded as milestones, providing essential contributions to development and evolution of modern laboratory science. Indeed, the eldest of us can recall using the Lowry and Bradford techniques for measuring protein extracts for both routine and research applications, transferring proteins from polyacrylamide gels to nitrocellulose sheets according to the procedure of Towbin et al., or even analyzing genetic material with techniques based on the original method described by Sanger and Chomczynski. Even the Laemmli buffer, described in the second most cited paper, has represented a vital refinement of sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) for separating proteins according to their relative electrophoretic mobility.

Although it is unlikely that anybody will be ever able to truthfully appraise the contribution of diagnostic testing to the clinical reasoning and the therapeutic management, it is now undeniable that laboratory medicine provides a kind of information that increasingly supports (and occasionally replaces) the clinical judgment. The remarkable progress in genetics, genomics and other "omics" experienced in the last decades have enabled a paradigmatic change in the role of laboratory medicine, leading the way to enhanced personalized health care and disease prevention based on the identification of risk factors and more effective biomarkers [2, 3]. Crossing the boundaries from research to clinical application requires standardization and harmonization of pre-, intra- and post-analytical issues, and laboratory professionals must play an active role in this enterprise [4–6]. In spite of this bright future, the daily scenario is actually dramatic. Squeezed between an unprecedented economic crisis and shortage of vocations around the globe, the ecosystem of laboratory medicine is increasingly seen as a commodity

Table 1: Mostly cited scientific papers of all time (up to the year 2014), according to Van Noorden et al. [1].

1. **Lowry OH, et al. Protein measurement with the folin phenol reagent. J Biol Chem, 1951.**
2. **Laemmli UK. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature, 1970.**
3. **Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal Biochem, 1976.**
4. **Sanger F, et al. DNA sequencing with chain-terminating inhibitors. Proc Natl Acad Sci USA, 1977.**
5. **Chomczynski P. Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. Anal Biochem, 1987.**
6. **Towbin H, et al. Electrophoretic transfer of proteins from polyacrylamide gels to nitrocellulose sheets: procedure and some applications. Proc Natl Acad Sci USA, 1979.**
7. Lee C, et al. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. Phys Rev B, 1988.
8. Becke AD. Density-functional thermochemistry. III. The role of exact exchange. J Chem Phys, 1993.
9. **Folch J, et al. A simple method for the isolation and purification of total lipids from animal tissues. J Biol Chem, 1957.**
10. **Thompson JD, et al. Improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice. Nucleic Acids Res, 1994.**

Articles dealing with laboratory techniques are in bold.

by most stakeholders [7]. Indeed, clinical laboratories are categorized among the healthcare services, and in particular among the 10 health care services that produce tangible health benefices [8]. However, what is seemingly unclear to certain clinicians, hospital administrators, policymakers and even to some colleagues, is that the laboratory is "at service", but not "a servant". The valuable analysis published by Van Noorden and colleagues provides – maybe unconsciously – a clear support to this concept, wherein no major advance in science and medicine has been (and will likely be) possible without the use of laboratory techniques (Table 1). It is also understandable that some wicked politics of closure or irrational consolidation of clinical laboratories would not be effective to generate favorable revenues for a bankrupt health care, especially when economic analyses are the main drivers for reorganization or networking. This is clearly true if one considers that the expenditure for in vitro diagnostic testing represents <2% (at best) of the total budget of the healthcare systems worldwide [9, 10].

Thanks to the analysis of Van Noorden et al., we can strengthen the concept that the contribution of laboratory medicine is virtually unreplaceable in science (and medicine)… yet many (inside and outside the laboratory) seem to ignore it.

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References

1. Van Noorden R, Maher B, Nuzzo R. The top 100 papers. Nature 2014;514:550–3.
2. Pasche B, Absher D. Whole-genome sequencing: a step closer to personalized medicine. J Am Med Assoc 2011;305:1596–7.
3. Khoury MJ, Gwinn M, Yoon PW, Dowling N, Moore CA, Bradley L. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention? Genet Med 2007;9:665–74.
4. Plebani M. Evaluating laboratory diagnostic tests and translational research. Clin Chem Lab Med 2010;48:983–8.
5. Plebani M, Marincola FM. Research translation: a new frontier for clinical laboratories. Clin Chem Lab Med 2006;44:1303–12.
6. Plebani M, Laposata M. Translational research involving new biomarkers of disease: a leading role for pathologists. Am J Clin Pathol 2006;126:169–71.
7. Plebani M. Clinical laboratories: production industry or medical services? Clin Chem Lab Med 2015;53:995–1004.
8. Institute of Medicine Committee on defining and Revising Essential Health Benefits Package for Qualified Health Plans. Report on essential health benefits: balancing coverage and costs, Washington DC, October 2011 Available from: http://iom.edu/~/media/Files/Report%20Files/2011/Essential-Health-Benefits-Balancing-Coverage-and-Cost/Essential%20Health%20Benefits%20RB_FINAL.pdf. Accessed 26 July, 2015.
9. Barletta G, Zaninotto M, Faggian D, Plebani M. Shop for quality or quantity? Volumes and costs in clinical laboratories. Clin Chem Lab Med 2013;51:295–301.
10. Lippi G, Mattiuzzi C. Testing volume is not synonymous of cost, value and efficacy in laboratory diagnostics. Clin Chem Lab Med 2013;51:243–5.

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