EDITORIAL

CRISPR and precision medicine

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The deceiving outcome of Jerry Gelsinger's volunteer enrollment in a genetic study threatened to put the brakes on genetic research. Instead, despite the hidden risks, unanticipated and obviously unwanted, knowledge continued to evolve. The tragic death of a naïve volunteer on the altar of genetics ended in four lessons written by the leading personality and at that time, culprit for the obviously surprising collateral loss [1]. These were perceived at the time as a lecture behind the firewall the Penn University managed to build between James M. Wilson (the geneticist in cause) and the prosecutors [2]. Nine years have passed between J. Gelsinger's lethal outcome and Wilson's mea culpa. His death was preceded by seven years of intense research in genetics at the Penn University in the USA.

Today we are confronted with unacceptable mortality in sepsis and septic shock despite large and intense initiatives to oppose it. Antibiotics are either under optimally used, stewardship is reduced sometimes to a matter of perception. These tools are improperly used or inefficient at the end of the day.

Towards the conclusion of his mandate, president Obama launched and supported the initiative of "precision medicine". Precision medicine was defined as an "emerging approach for disease prevention and treatment that takes into account people's individual variations in genes, environment and lifestyle" [3]. The aim of this initiative was to generate the scientific evidence to be used for moving the concept of precision need into clinical practice. This would offer be the best tools to practice individualized medicine and thus become more efficient and make a change to the best in patients' lives. The longer term goals comprised the recruitment of over 1 million American volunteers, the research cohort, who would share genetic data, biologic samples and diet/lifestyle, information, all emerging from their electronic health records [3]. Put this way, it would seem to offer the humanity one exceptional chance to contribute to groundbreaking evidence to support further initiatives and disease management. Naturally, new and ancillary ethic engrams were promoted at this point: engaged participants, responsible data sharing and privacy protection.

Meanwhile, researchers published papers on antibacterial autophagy. Bacteria penetrating the cells are sensed and tagged (the microscopic paint ball war) with molecules called ubiquitin which mark the bacteria for destruction. This process is jeopardized by genetic mutations in the human cells. Invading bacteria are marked by E3 ligases, proteins that decorate the invaders with ubiquitin early in autophagy. According to the Broad Institute, one of the most prestigious North American Institute of Research in bioengineering, there are 617 known ligases [4].

Moreover, it appears that cellular miscommunication plays a crucial role in inflammation. There are cytokines that do not act like switchers to be turned on and off, but rather tuned. Therefor they are considered to behave like biased agonists for triggering some G protein-coupled receptors – GPCRs involved in tunable cytokine activity. It was stated that "variations in a single cytokine can lead to biased downstream signaling and can thereby cause human disease" [5].

The Broad Institute launched recently major research initiatives to study among others, why cancers become drug resistant.

This first 2017 issue of the Acta Medica Marisiensis publishes a welcome review on CRISPR (Clustered Regularly Interspaced Short Pahindromic Repeats) [6]. Genome editing exists since 2012, but in 2013, the TALE Nucleases (Transcription Activator-Like Effector Nucleases) were shadowed by the engineered CRISPR-Cas9 system first harnessed for mammalian genome editing by Fang Zhang of the Board Institute and MIT. The description of the CRISPR-Cas9 system used the words: "efficiency, effectiveness and precision" [4].

The reactions did not wait for long. The United Kingdom expressed its point of view through the Nuffield Council on Bioethics, an organism founded jointly by the Medical Research Council, the Nuffield Foundation and the Welcome Trust. Thus, they published their analysis and conclusions on a generous document on genome editing [7].

A quick search last evening on cccDNA (covalently closed circular DNA) clearance revealed largely over 92000 results for cccDNA. Obviously, the magnitude of the issue and the potential for groundbreaking results of using bioengineering at this stage is impressive to understate the facts.

This editorial was triggered by the seduction of precision medicine mirrored by the review written by Crauciuc et al and hopefully is deprived of any conflict of interest.

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