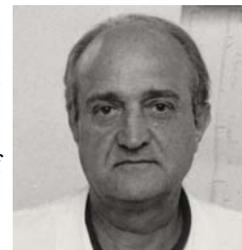


EDITORIAL

Complex Therapeutical Approaches to Complex Diseases

In the last decades the enormous advances in genetics and biology have made clear that cancer is a very complex disease sustained by many genetic and epigenetic alterations. They activate a great deal of pathological molecular pathways governing relevant physiological processes. In 2000, Hanahan and Weinberg identified six hallmarks of cancer diseases: 1) self-sufficiency in growth signals, 2) insensitivity to antigrowth signals, 3) limitless replicative potential, 4) ability to evade apoptosis, 5) support to angiogenesis, 6) invasion of tissue and ability to give metastasis. In addition, the lost differentiation of cancer cells was proposed recently by Biava P.M. e coll. (*Current Medicinal Chemistry* 2014) to the hallmarks of Hanahan and Weinberg.

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Moreover, it was demonstrated for normal cells to become cancerous, transformation also depends on a complex network of surrounding microenvironmental signals from cell-to-cell “cross-talking” or from soluble extracellular factors. For example, it has been demonstrated that inflammatory cells can sustain, instead of fighting tumor growth. Thus, the whole context is decisive in determining cell fate in line with a complex view of cell biology.

The current special issue describes why chronic diseases including, not only cancer, but also the metabolic syndrome, chronic inflammation, chronic degenerative diseases etc. make the diagnosis, prevention and targeted therapeutic treatment particularly difficult. Recognition that chronic inflammation may induce genetic, neuro-endocrine, immune and metabolic changes in a series of diseases is useful for designing new ways for prevention and treatment. A new approach may include reprogramming suppressive immune cells and pro-inflammatory mediators factors, restoring in this way the balance of neuro-endocrine-immune and metabolic network systems disrupted by chronic inflammation. Differentiation factors, reprogramming therapies and immunotherapy are innovative biological means with more systemic approach to cancer and chronic degenerative diseases treatment. In particular, this special issue records some articles which highlight how growth and differentiation factors taken from Zebrafish embryo could be able to address the fate of normal and pathological (stem) cells. In fact, these factors taken during the early developmental stage of Zebrafish embryo may represent a useful tool to enhance stem cell expression of multipotency and activate both telomerase-dependent and -independent antagonists of cell senescence. On the contrary, these factors taken during the late developmental stages decrease cell viability and address cells toward senescence. This strategy did not require cumbersome gene manipulation through viral vector mediated gene transfer, or expensive synthetic chemistry. This data show, for the first time that it is possible to address human mesenchymal stem cells towards different and opposite directions, tuning in specific, physiological way the regulation of different genes. This is possible only when the specific networks of factors are enough complex because single substances are not able to obtain any significant results. These data make us to consider a major shift in scientific paradigm (from reductionism to complexity) for preparing new treatments for chronic degenerative diseases. In fact, these diseases entail unexpected degree of complexity and dysregulation, making the single-molecule-to-specific-target paradigm totally obsolete and inadequate. Rather, only a systemic approach can be envisioned as a successful strategy to deal with such complexity. It is believed that time is ready for a “trans-disciplinary approach” in the treatment of degenerative diseases so that a new culture of collaboration can promote many important innovations and new therapeutic approaches.

Keywords: Stem Cells, Cancer, Cancer Stem Cells, Inflammation, Metabolic disease, Immune System, Neuro-Endocrine System, Immunotherapy, Biological Therapies of Cancer, Biological Therapies of Chronic Degenerative Diseases, Prevention of Neuro-degeneration, Stem Cell Differentiation Factors, Differentiation and Reprogramming Therapies of Cancer Cells, Tuning Normal Stem Cells.

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