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Molecular Therapy
Editorial

Tuning the Engines of Nanomedicine

In 2004, the United States National Cancer Institute (NCI) Alliance for Nanotechnology in Cancer inaugurated an integrated initiative dedicated to using nanotechnology to radically change cancer diagnosis, treatment, and prevention. Under three funding phases, which saw a >$300 million investment, many Centers of Cancer Nanotechnology Excellence (CCNEs) were created, but, recently, the NCI decided to halt CCNE funding.[1] This decision has sparked a flurry of debate[2–4] and generated a negative perception of nanomedicine research and development programs as a whole.[2] So, what has gone wrong and what needs to change?

Overselling

Since its inception, nanomedicine has been a victim of unrealistically high expectations, where the predominant research focus has been on the design and engineering of nanoparticles with exquisite specificities and functionalities as applied to tumor drug delivery. These expectations coupled with overenthusiastic market projections and superfluous pressure from grant review panels has increasingly driven a new generation of scientists to explicitly focus on accelerated product development and the societal impact at the expense of outstanding fundamental and mechanistic work in nanomedicine. This growing trend, therefore, has paid insufficient attention to the complex nature of physiological barriers and transport processes across them, disease heterogeneity and dynamics, cellular cannibalism and the role of adjacent healthy tissues, the immune system, as well as the necessary regulatory attributes for reproducible pharmaceutical development.[5] Notwithstanding, the literature continues to oversell accelerated product development-oriented research and the therapeutic potential of such engineering marvels. It is not that genuine innovation and disruptive technologies are not welcome, but the field must also recognize that increasing complexity hinders development and commercialization.[5,6] It is therefore not surprising to see that the majority of translational nanomedicine initiatives, as particularly witnessed with anti-cancer nanomedicines, have shown limited clinical success.[2,5]

Overlooking

The current criticism of anti-cancer nanomedicine research is inadvertently spreading to other areas in nanomedicine research where considerable progress is being made or is underway. Nanomedicine is not all about targeted drug delivery (to tumors), as has been increasingly perceived within the community and the broader public. It also involves improving and facilitating drug synthesis (e.g., by exploiting catalytic activities of nanomaterials) and formulation science (e.g., enhancing drug solublization as in nanocrystals), developing sensitive and precision *in vitro* diagnostics (e.g., ultra-sensitive plasmonic-based disease biomarker screening), wearable, injectable, and ingestible electronics and other monitoring devices. These are a few examples of promising areas in nanomedicine research and development, which are not getting the credit that they deserve. Fundamentally, nanomedicine is also about turning nanotechnological advances (e.g., semiconductor nanowires and nanosensors) into functional tools for studying, modulating, and monitoring dynamic and integrated multicellular events, thus enhancing our understanding of interrelated processes that contribute to disease progression or regression and eventually leading to identification of better drug screening approaches, drug design, and advanced therapeutic avenues per se. Therefore, the community should be optimistic about nanomedicine as an exciting discipline of nanotechnology that has a potential not only to solve pharmaceutical and broader clinical issues, but also fundamental biomedical problems.

Overstep

Science is curiosity-driven and methodological, and most scientific breakthroughs take years of research and are often the result of serendipity, and, in many cases, this involves a process of overcoming opposition. Recombinant DNA technology[7] and CRISPR (clustered regulatory interspaced short palindromic repeats)[8] were borne of curiosity but laid the foundation of modern genetic engineering, genome editing, and advanced cell therapies, and, yet, these technologies increasingly benefit from nanomedicine advances (e.g., ionisable lipid nanosystems for protection, delivery, and release of nucleic acid medicines). Nevertheless, such breakthroughs were punctuated by periods of discontinuities before changing the paradigm. In nanomedicine, we need more of those types of advances of which the utility is not immediately salient. Therefore, we should be supportive of fundamental research in nanomedicine and avoid setting excessive priorities and strategies to direct short-term goals solely toward solving clinical problems.

Override

Policymakers continuously encourage scientists to conduct research that has an impact on society, and funding agencies have introduced metrics in evaluating the impact of its grants to justify the investment.[9] It is policymakers that must listen to scientists, but scientists must stop thinking like marketers who are influenced by political and commercial forces. Let curiosity work and drive fundamental research in nanomedicine even in the absence of immediate obvious benefits to society. After all, one cannot predict from where the next disruptive discovery will arise.[10]

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