Recent trends in biochemistry and biotechnology.

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Accepted on 1 September, 2017

Introduction

ADF Recent scientific era has witnessed a tremendous progression in the field of medical sciences due to development in allied fields of biotechnology and biochemistry. New techniques are constantly being introduced leading to production of remarkable and medicinally valuable molecules, to alter hereditary traits of plants and animals, for diagnosis of various diseases and finally finding novel ways to cure them. The advancement made in the field of biotechnology has resulted in development of new class of potential drugs. It also helps in cloning and expression of various prophylactically important proteins and polypeptides that may be exploited in development of newly designed subunit vaccines. In fact, both biotechnology and biochemistry have great impacts in the fields of health, food, agriculture, and environment.

RNA interference (RNAi) is a natural process that cells use to 'turn off' or silence unwanted or harmful genes. The RNA interference involves chopping of dsRNA by an enzyme complex called Dicer into double stranded small interfering RNA (siRNA) molecules. The produced siRNA binds to an RNA-Induced Silencing Complex (RISC) which guides strand to a specific mRNA site, cleaving it so that the unwanted target protein is not produced. Besides finding its scope as a tool in molecular biology setup, mRNA interference can be exploited as promising way to treat cancer. A key area of research in the use of RNAi for clinical applications is the development of a safe delivery method, which can rely on virosome, liposome or exosome based delivery systems for gene therapy.

Exosomes hold significant potential for developing exciting approaches in drug delivery and cancer immunotherapy. Potent tumoricidal drugs (siRNAs and chemotherapeutic compounds) are being successfully delivered preferentially to cancer cells employing bioengineered exosomes. Besides drug targeting, exosome-based therapeutic cancer vaccines have been widely tried in early-phase clinical trials.

Genome editing and regulation has been made significantly easier implying various technological breakthroughs during the past decade. One recent technology has adapted the CRISPR/Cas 9 bacterial system, which has evolved as a simple, RNA-guided phenomenon for an efficient and specific genome editing and regulation in both bacteria as well as higher eukaryotes. The technology has emerged as a revolutionary tool in biomedical research and open new vistas in treatment of genetic disorders. Taking guidance from RNA, the endonuclease Cas 9 breaks open target sequence of host genome. Imprecise repair mechanism of the generated double strand break generally ensues in insertion or deletion mutations. CRISPR mediated engineering may facilitate introduction of specific point mutations or insertions in the target DNA. Multiple genomic loci can be easily edited at the same time by using Cas9 through introduction of several sgRNAs simultaneously. The strategy can be used to generate large-scale chromosomal rearrangements. The technology has found wide scope in generation of transgenic organisms. The technology also makes it much easier to generate disease models for genetic disorders as well as diseases such as cancer, which facilitates our understanding of the molecular mechanisms of these pathological processes.

The inevitable rise of antibiotic-resistant pathogens and the resulting slow development of new antibiotics have raised the demand for alternative therapeutics. Probiotics are serving as a promising approach, provided their efficacy is enhanced by introducing new genetic circuits to deliver drug biomolecules with site specificity. The ‘designer probiotics’ are basically recombinant probiotics that possess the ability to reduce the gap between the ascending antibiotic resistance and the dearth of new antibiotics. Probiotics are emerging living therapeutics that may mould prototype of disease diagnosis and prevention.

The immune-based therapeutics has become a key asset in treatment of various types of cancer. Success of antibody mediated checkpoint blockades in cell cycle can be used as effective cancer therapy. Cancer cells promote expression of the programmed death-1 (PD-1) receptor, as a strategy to downplay adaptive immune response of the host. Antibody mediated blocking of PD-1 can help in restoring the adaptive immune response against cancer.

The recent era has witnessed expression of therapeutically important recombinant proteins through fine tuning as well as intelligent usage of recombinant technology. In general, over-abundance of protein result in their misfolding that eventually result in development of Inclusion bodies, which are basically bundled mass of denatured protein molecules in the form of particles. There are several ways by which one can regulate higher recovery of bioactive protein from inclusion bodies. Proteins inside inclusion body aggregates have native-like secondary structures. It is assumed that restoration of this native-like secondary structure using mild solubilization conditions will help in improved recovery of bioactive protein in comparison to solubilization using a high concentration of chaotropic agent.

Functional and non-toxic amyloids called bacterial inclusion bodies (IBs) occur in recombinant bacteria. They show analogy with secretory granules of the mammalian endocrine system. Urge to understand that how the cell handles the quality of recombinant polypeptides and the main features of their fascinating molecular organization has triggered the interest in inclusion bodies and prompted their use in diverse technological fields. The engineering and customization of IBs as functional protein particles for materials science and

biomedicine shows how formerly undesired bacterial by products can be retrieved as promising functional materials for a broad spectrum of applications. IBs could be used as a raw material for protein recovery, as immobilized catalysts, as mechanically stable and biocompatible materials and also as protein-releasing agents.

In the field of vaccinology, DNA vaccines have been introduced as a new prophylactic strategy. The genetic material capable of expressing a given set of antigen (pathogen origin) is exploited to activate host immune system. The strategy involves administration of plasmids that usually consist of a strong viral promoter to drive the *in vivo* transcription and translation of the gene (or complementary DNA) of interest. Multicistronic vectors that have potential to express more than one immunogen, or to express an immunogen and an immunostimulatory protein are considered to be more superior to that of a system that can express only one protein.

Zika virus (ZIKV), a member of Flaviviridae family, has emerged as a major health concern. A joint global research effort has provided a better insight to ZIKV pathogenesis. This may result in evolving a better therapeutic or prophylactic intervention to inhibit ZIKV, and have identified targets for drug design. In this regard an electron microscopic study revealing structure of the virus has made significant contribution. Different studies have shown that the inactivated vaccine, viral-vector vaccine, and DNA vaccine are able to induce sufficient antibody responses in different animal models and hence, can confer protection against ZIKV challenge.

The use of nanotechnology in medicine offers a number of exciting avenues. Some techniques are plausible to hypothetical only, while others are at various stages of testing, or actually being used today. The use of nanotechnology has potential to revolutionize the health science relying on the way we detect and treat damage to the human body and disease in the future, and many techniques only imagined a few years ago are making remarkable progress towards becoming realities.

Nanomedicines comprised of several distinct application areas, including drug delivery, drugs and therapies, *in vivo* imaging, *in vitro* diagnostics, biomaterials, and active implants. In these fields, nanomedicine has seen increased research activity during the past decade. Particles with nanodimensions are tailored to locate or identify diseased cells followed by delivery of active payload at desired site only. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease.

Nano-enabled medical products have potential to eclipse other forms of drug formulations. In fact lipid based formulations had been introduced on the market over a decade ago and some have become best-sellers in their therapeutic categories. Nanomedical products generally find application in the ailments that include cancer, CNS diseases, cardiovascular disease, and infection control.

At present, cancer is one of the largest therapeutic areas in which nano medicines have made major contributions. The nano-enabledproducts like Abraxane, Depocyt, Oncospar, Doxil, and Neulasta are in use against cancer worldwide.

Nanocrystalline silver, a nanosized metal based formulation is another product that has been marketed in US and elsewhere. The product exploits powerful antibacterial effect of ionic silver for its powerful antibacterial activity against organisms like MRSA, that may contaminate wound dressing. The nanomedicine market is in early growth. While nano-enhanced drug delivery products are already a commercial reality, more advanced nanotech-based medical devices are still in development, although some are at the clinical testing stage.

Both biotechnology and biochemistry have the potential to generate major economic, health and environmental benefits. With numerous industries, the growth in these sectors has been dynamic.

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