One approach to induce and active TlLs is using vaccines. One of the most well-developed PDAC vaccines is GVAX, which is an allogenic wholecell vaccine derived from two irradiated human PDAC cell lines engineered to release GM-CSF at the vaccination site. Initial phase I trials of GVAX or GVAX in combination with low-dose cyclophosphamide to deplete Treg in patients with advanced PDAC patients showed minimal treatment-related toxicity and evidence of CD8+ T cell activation, as well as induction of intratumoral tertiary lymphoid aggregates.

Vaccinogen's lead product, OncoVAX®, is an active specific immunotherapeutic agent (ASI) that stimulates a patient's immune response to autologous tumor cells. Thus, OncoVAX is a targeted, patient-specific therapy. To prepare OncoVAX, the patient's own tumor is excised, enzymatically dissociated to separate the tumor cells from normal tissue, sterilized and irradiated with gamma radiation (200,000 rads) to prevent the tumor cells from dividing and tumorigenicity, but still remain metabolically active. According to the OncoVAX protocol, the first two injections consist of irradiated tumor cells mixed with freshly frozen mycobacteria of the TICE strain Bacillus Calmette Guérin (BCG). The third and fourth immunizations consist of irradiated tumor cells alone.

In Ukraine, the Kavetsky Institute of Oncology Problems conducted a clinical validation of an antitumor vaccine. It was proved that immunization of patients with malignant gastric tumors with antitumor autovaccine made from autologous tumor tissue of the patient and products of vital activity of Vasillus mesentericus AB-56 led to statistically significant increase in life expectancy in comparison with patients who underwent surgical treatment or surgical treatment in combination with chemotherapy.

Conclusions. Immunotherapy is an instrument, which is usually used with cancer surgery, chemotherapy. There are some mostly used vaccines: Vaccinogen's lead product, OncoVAX®; NeoVax; product of mutated genes FNDC3B; Antigene NY-ESO-1.

DIVERSE APPLICATIONS OF NANOMEDICINE

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Introduction. The design and use of materials in the nanoscale size range for addressing medical and health-related issues continues to receive increasing interest. Research in nanomedicine spans a multitude of areas, including drug delivery, vaccine development, antibacterial, diagnosis and imaging tools, wearable devices, implants, high-throughput screening platforms, etc. using biological, nonbiological, biomimetic, or hybrid materials. Many of these developments are starting to be translated into viable clinical products. Here, we provide an overview of recent developments in nanomedicine and highlight the current challenges and upcoming opportunities for the field and translation to the clinic.

Properties of nanoscale objects are transitional between molecular and bulk regimes. Nanoscale properties exist for all materials, regardless of whether they are found in nature or are synthetic.

Nanomedicine is an interdisciplinary field, where nanoscience, nanoengineering and nanotechnology interact with the life sciences. It is expected that nanomedicine will lead to the development of better devices, drugs, and other applications for early diagnoses or treatment of a wide range of diseases with high specificity, efficacy, and personalization, with the objective being to enhance patients' quality of life.

Aim. Analyze the literature on the use of nanotechnology in medicine and pharmacy.

Materials and methods. Scientific publications on experimental research in nanotechnology.

Research results. A key focus in nanomedicine involves the use of nanomaterials as contrast agents for anatomical and functional imaging. Using nanomaterials as contrast agents enables visualization of structures inside the human body and helps clinicians to delineate healthy from diseased tissues and to recommend proper treatment. Nanoparticles can be engineered with different contrast properties. The most common modalities are computed tomography (CT); magnetic resonance imaging (MRI); imaging of radioactivity, such as positron emission tomography (PET) or single photon emission computed tomography (SPECT); fluorescence imaging; and photoacoustic imaging. For all these techniques, material development is crucial because the NPs are contrast agents that enable visualization of biological tissues. For this application, NPs can be engineered to localize in specific tissues and potentially produce high contrast.

Magnetic resonance imaging is widely used for in vivo applications, due to its safety, spatial resolution, soft tissue contrast, clinical relevance, and ability to record anatomical and functional information about soft tissues and organs. Notably, MRI-responsive contrast agents provide physiological information that complements routine anatomical images. Since the technology is based on the interaction of nuclei with surrounding molecules in a magnetic field, MRI has no need for ionizing radiation and possesses unlimited depth of penetration and unparalleled soft tissue contrast.

Nanoparticles can also be used for detection of molecules, cells, and tissues outside the human body. In this diagnostic application, the function of the NP is to identify unique biological molecules in biological fluids that are associated with the health of the patient. The NPs act as transducers and are coated with ligands to enable the biorecognition of unique biological molecules in the fluid in the in vitro sensing applications. For example, AuNPs have been modified with ligands that specifically bind to a complementary protein. The presence of these proteins induces the cross-linking of the NPs. This controlled agglomeration can be observed colometrically by the change of color of the NP solution. These concepts have been later refined, for example in rapid colorimetric DNA sensing. This AuNP-based diagnostic technology has advanced to testing of patient samples and is now used in the clinic. Nanotechnology presents an opportunity to improve the overall diagnostic process by lowering the limit of detection, thus enabling high throughput and multiplexed detections of biological targets with high sensitivity.

Nanoenabled tools can be designed for diagnostics and therapies based on the mechanical properties of cells. At the subcellular and cellular levels, many biophysical properties have recently emerged as indicators of cell physiology and pathology, as complementary or regulatory alternatives for disease development. Cell migration, for example, can be traced by removing the trail of adherent cells left on a substrate coated with AuNPs or with QDs. The morphology of the trails correlates with the metastatic potential of the cells. The force that adherent cells exert on a substrate can also be measured. For example, cell-traction-force microscopy based on the deformation of the polymer substrates on which cells are grown is able to spatiotemporally map cell traction force as precise as a nanonewton. It can also be used to uncover previously hidden details of drug–cell interactions and mechanical contributions during cell migration. For example, previously retarded cell migration upon NP uptake was attributed to cytoskeleton disruption. However, the uptake of the NPs actually transforms cells from the motile phenotype into an adhesive phenotype, as revealed by the increased cell traction force and altered patterns of cell traction force. More importantly, ultrasensitive cell traction force microscopy could be competitive to traditional cell biology methods such as the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assays, WB, and flow cytometry, since early changes can be readily observed under cell-traction-force microscopy.

The cancer drug delivery process to a solid tumor consists of five critical steps, termed the CAPIR cascade: circulation in blood, accumulation and penetration into the tumor, cellular internalization, and intracellular drug release. Thus, the overall therapeutic efficiency of a

nanomedicine is determined by its efficiency in each step A nanomedicine efficiently accomplishing the whole CAPIR cascade should have a high therapeutic index.

A vast number of classes of nanoparticulate delivery vehicles have been reported. As demonstrated by Huynh et al., drug-loaded delivery vehicles are attractive because they can be passively or actively targeted to cancer tissues to improve anticancer drug selectivity and thereby reduce severe side effects. Liposomes are perhaps one of the most advanced delivery vehicles concerning clinical translation, with several formulations approved by the U.S. Food and Drug Administration (FDA). Liposome-based systems encapsulating drugs are already used in some cancer therapies. However, liposomes have some significant drawbacks: they have a low capacity to encapsulate lipophilic drugs, they are manufactured through processes involving organic solvents, they are often leaky and are unstable in biological fluids and aqueous solutions.

Conclusions. New NPs tuned for nanomedicine applications are emerging, especially in the fields of drug delivery, antibiotic resistance, imaging, diagnostics, and cancer therapies. Recent studies have shown that the use of multiple nanomaterials (i.e., NDs and proteins) or a single nanoplatform functionalized with several therapeutic agents can successfully image and treat tumors with improved efficacy. NPs-based drug delivery has been included in the rational, biomimetic, and systematic design of optimal therapeutic combinations.

Nanomedicine in cellular, preclinical, and clinical studies has led to many important advances, both fundamental and translational. Many of these advances, however, have been in the field of cancer diagnosis and treatment. This disproportionate focus is expected to be addressed in upcoming years with research focuses expanding to other medical challenges such as antibiotic resistance and artificial organs. Nanomedicine is poised to be of benefit in these areas by virtue of the versatility of the nanomaterial platform design, be it through multimodal therapeutic approaches or through highly specialized multifaceted design for relevant biological applications.

Although nanomedicine has raised exciting expectations for many medical problems, scientific challenges have arisen as well, mainly due to the lack of knowledge about the behavior of nanomaterials inside living organisms. However, due to the basic research focused on these issues, we are now closer to solving them and to reaching “real” medical solutions based on nanomedicine.

EFFECT OF OMEGA-3 FATTY ACIDS ON TELOMERES

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Introduction. Telomeres are complexes consisting of tandem repeat DNA combined with associated proteins that play a key role in protecting the ends of chromosomes and maintaining genome stability. They are considered a biological clock, as they shorten in parallel with aging. Furthermore, short telomeres are associated with several age-related diseases. However, the variability in telomere shortening independent of chronological age suggests that it is a modifiable factor. In fact, it is regulated inter alia by genetic damage, cell division, aging, oxidative stress, and inflammation. A key question remains: how can we prevent accelerated telomere attrition and subsequent premature replicative senescence?

Aim. To study the possible effect of omega-3 fatty acids on telomere shortening.