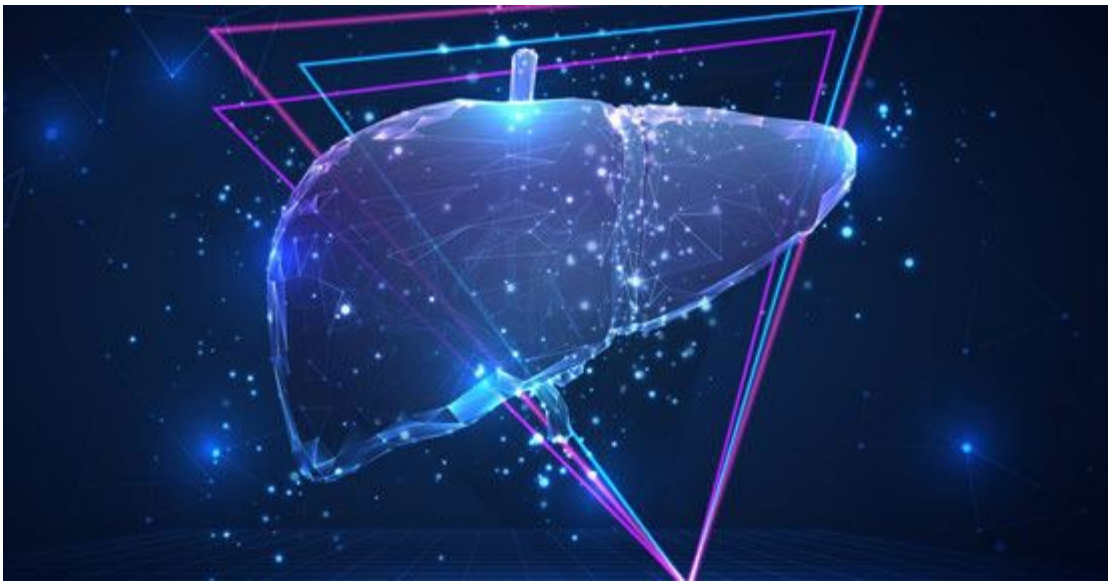
Implen Journal Club | November Issue

Welcome to our November issue of the #Implen #JournalClub in 2021.



In this month's issue of Implen's NanoPhotometer® Journal Club: Tumor Micro-environment Edition, we are highlighting a new technology to help advance personalized medicine for one of the most lethal tumors worldwide - hepatocellular carcinoma (HCC). Feihu Xie et al. recently published in

Biomaterials a novel modeling system using three-dimensional (3D) bioprinting technology which was used to establish individualized patient-derived 3D bio-printed hepatocellular carcinoma (3DP-HCC) models. These models were shown to be reliable in long-term culture in which tumorigenic and histological features were preserved, including stable expression of the biomarker, stable maintenance of the genetic alterations and expression profiles with the ability to predict patient-specific drugs for personalized treatment. Their ultimate goal is to develop a 3D printed tumor model composed of tumor cells, stromal components, and various immune cells to reconstruct a model of the natural tumor environments, which will significantly extend the spectrum of drug screenings for patient-specific treatment, as well as drug screenings for the pharmaceutical industry to aid with new drug discoveries. The NanoPhotometer® was used in this work for the detection of DNA purity.

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Next, we are covering the topic of human lung adenocarcinoma, the most common type of lung cancer. Hai-Tao Luo et al. presented in Nature partner journals a detailed integrative transcriptome and proteome atlas of cancer-released exosomes in human lung adenocarcinoma revealing the diverse functions of exosomal-enriched RNAs and proteins, many of which are associated with tumorigenesis. Lung adenocarcinoma can be viewed as a heterogeneous community, in which cells communicate with each other and are hierarchically organized into distinct functional populations in which exosomes, endosome derived nanovesicles secreted by nearly all cell types into the extracellular space, act as important mediators by transporting specific molecules among different cell populations. It was shown using a 3D culture system that several RNAs and proteins that are associated with poor survival in lung cancer patients are packaged into exosomes. In addition, circulating exosomes may carry cancer recurrence- or therapy resistance associated markers, which may act as therapeutic targets or serve as promising liquid biopsy biomarkers for cancer diagnosis and prognosis. The NanoPhotometer® was used to check RNA purity and integrity.

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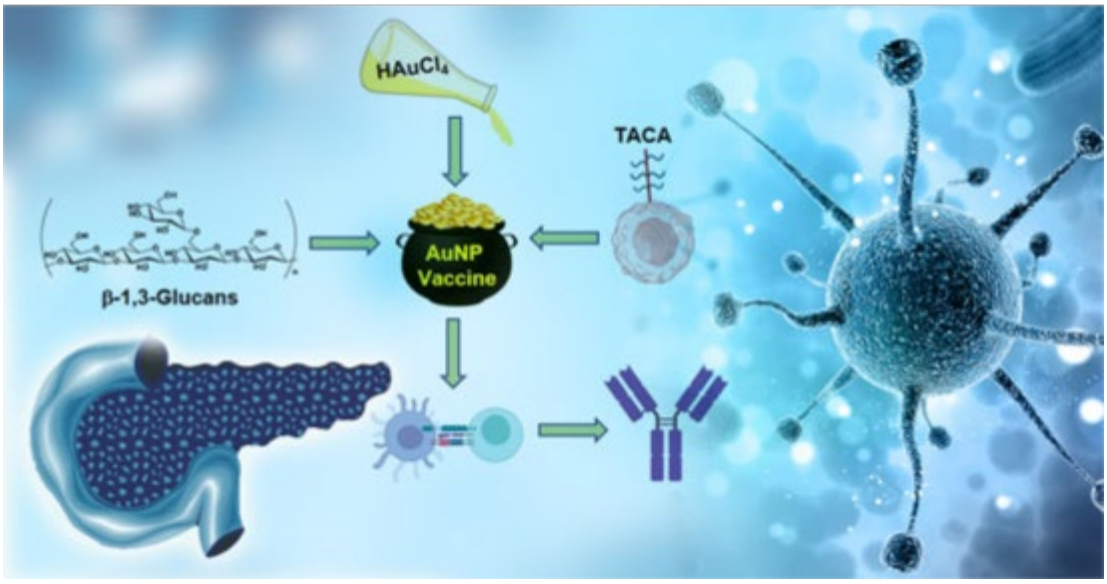

Research into the use of different nanomaterials for a host of medical applications has exploded in recent years, and recently the use of these nanomaterials has been proposed as vaccine platforms to deliver antigens, adjuvants, and T-cell epitopes, either alone or in some combinations to generate functional immune responses against disease. This issue of Implen's NanoPhotometer® Journal club: Tumor Micro-environment Edition is highlighting the work of Kevin Trabbic et al. who developed a robust and simple novel vaccine platform utilizing a complex mixture of a novel tumor-specific glycopeptide antigen for a glycoprotein overexpressed in pancreatic tumors and molecular adjuvant all coated on gold nanoparticles (B13G-AuNPs). The work published in ACS Bio & Med Chem showed these particles elicit strong in vivo immune responses through the production of both high-titer antibodies and priming of antigen-recognizing T-cells. Further examination showed that a favorable antitumor balance of expressed cytokines was generated, with limited expression of immunosuppressive Il-10. This system is modular in that any range of antigens can be conjugated to the AUNPs. The use of a nontoxic, gold nanoparticle platform, combined with pathogen-associated molecular patterns, is an approach that potentially can solve many of the issues associated with vaccine constructs designed to date and could allow for the delivery of many different glycopeptide-type antigens with the potential for true immunotherapy against specific cancers. The particles (B13G-AuNPs) were analyzed by UV/vis with the NanoPhotometer® NP80.

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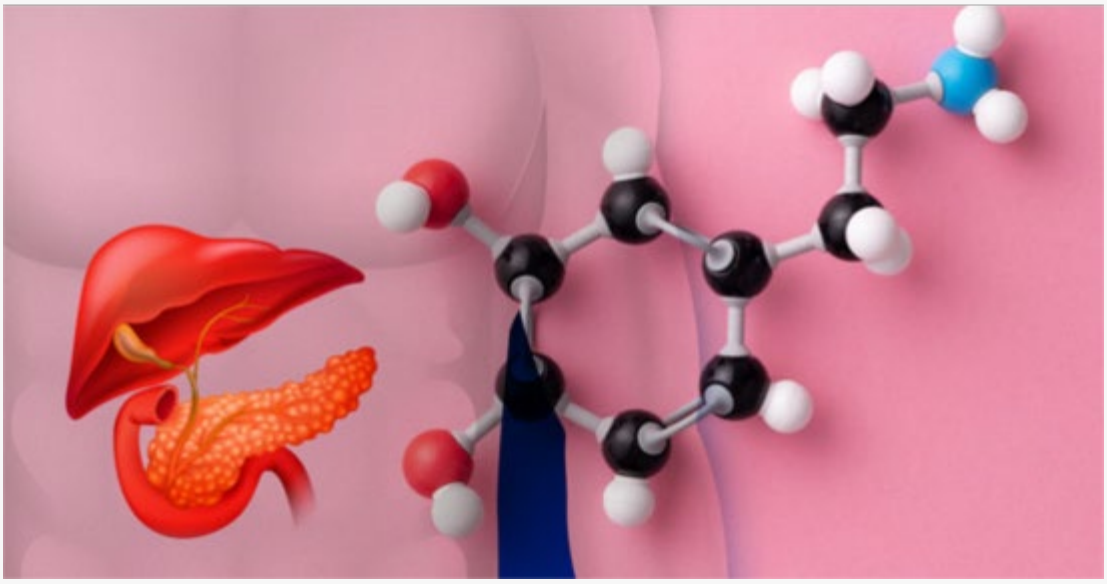

Next, the Implen NanoPhotometer® Journal Club is continuing with covering the topic of pancreatic cancer- which is predicted to be the second most common cause of cancer-related death in the US by 2030. Qiafei Liu et al. recently published in Cancer Immunology, Immunotherapy results that Dopamine improves chemotherapeutic efficacy for pancreatic cancer by regulating macrophage-derived inflammations. Pancreatic cancer is well-known as an inflammatory cancer, and the intra-tumoral inflammations promote the chemotherapeutic resistance, which presents potential therapeutic targets. Increasing evidence has shown that tumor-associated macrophages (TAMs) can promote the malignant behaviors of pancreatic cancer and contribute to chemotherapeutic drug resistance- thus, targeting TAMs may improve the effects of chemotherapy for pancreatic cancer. Multi-omics techniques have shown a powerful ability to uncover the interactions and mechanisms of cancer cells and stromal cells- in this study, transcriptomics and proteomics analyses were performed to explore the interactions between pancreatic cancer cells and TAMs. Multi-omics results revealed that there was a tumor-promoting vicious cycle involving pancreatic cancer cells and TAMs. Dopamine (DA), reported to suppress inflammation, substantially improved the chemotherapeutic efficacy for pancreatic cancer models by suppression of the tumor-promoting inflammation of TAMs. The NanoPhotometer® was used in this study to verify RNA purity and integrity.

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In the last issue of Implen's NanoPhotometer® Journal Club: Tumor Micro-environment Edition, we are discussing Glioblastoma (GBM) - one of the most aggressive and invasive forms of brain cancer, which is highly resistant to anticancer drugs. Soohyun Hong et al. recently published findings that may provide new insights into a better understanding of GBM-immunity interaction and for the development of a novel therapeutic strategy for GBM. GBM constitutes a highly complicated and dynamic in vivo tumor-microenvironment (TME) that modulates and participates in GBM proliferation, invasion, and resistance to drugs. GBM progression is closely associated with microglia activation; therefore, understanding the regulation of the crosstalk between human GBM and microglia may help develop effective therapeutic strategies. It was shown that miR-124 microRNA is enriched in the normal brain, but its levels are downregulated in GBM- so the strategy in this study was to deliver miR-124 to the GBM microenvironment via extracellular vecles (EVs) as an efficient miRNA delivery vehicle as EV drugs have the unique advantage of superior potential of blood brain barrier (BBB) penetration. The therapeutic effects of the EV drug was simulated in complex models in vitro using a 3D microfluidic model to recapitulate the structure, function, and physiological features and to mimic the high complexity and spatial heterogeneity of the GBM TME as a translational tool to bridge the gap between preclinical models and clinical outcomes to test the EV drugs. Analyses of changes in cytokine levels in the TME model showed that the treatment with miR-124 EVs led to tumor suppression and anti-cancer immunity, thereby recruiting natural killer (NK) cells into the tumor. Based on the results, the key advantage of our miR-124 EVs is that their therapeutic effects are exerted by simultaneously targeting both cancer cells and microglia. It was validated that miR-124 delivered via EVs has a suppressive effect on the proliferation and metastatic characteristics of GBM, thereby inducing synergistic anti-cancer therapeutic effects. The NanoPhotometer® P330 was used to measure the RNA yields of the total mRNA extracted.

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