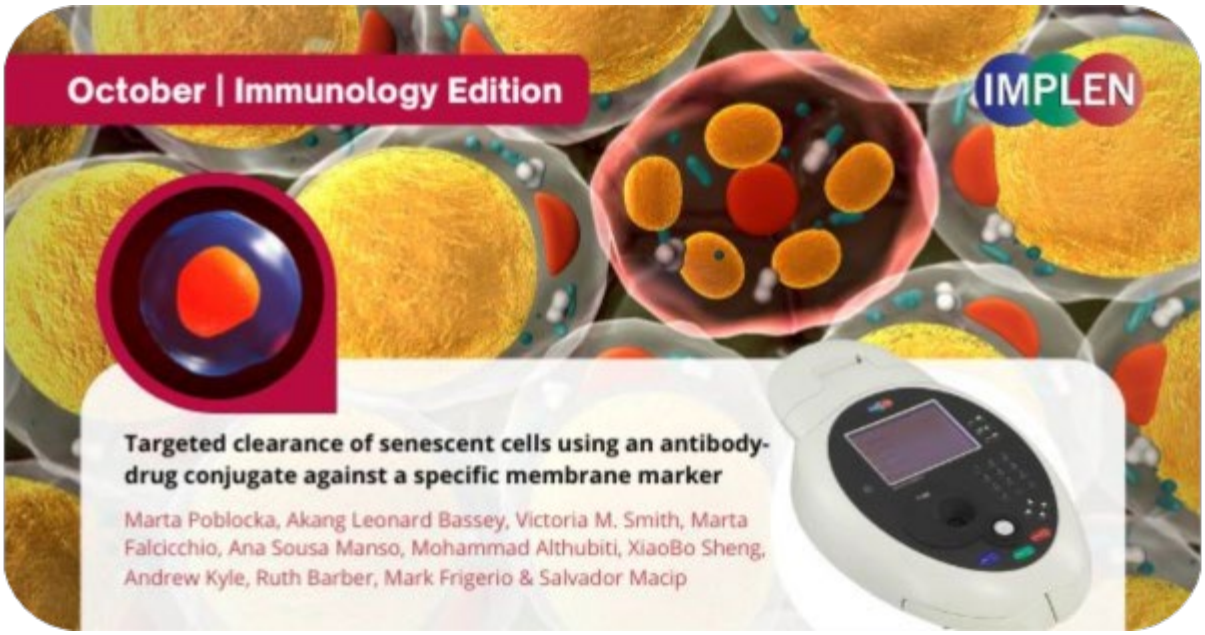
Implen Journal Club | October Issue

Welcome to our October issue of the #Implen #JournalClub in 2022.
Immunology Edition



The first issue of the Implen NanoPhotometer Journal Club - Immunology edition is covering a novel approach to treating a wide range of diseases that have been shown to be influenced by the accumulation of senescent (an irreversible proliferation arrest) cells including fibrosis, diabetes, cancer, Alzheimer's and other age-related pathologies. Consistent with this, clearance of senescent cells can prolong healthspan and lifespan in in vivo models. This provided a rationale for developing a new class of drugs, called senolytics, designed to selectively eliminate senescent cells in human tissues.

The senolytics tested so far lack specificity and have significant off-target effects, suggesting that a targeted approach could be more clinically relevant. Poblocka et. al. recently published in Nature Scientific Reports that a senolytic antibody-drug conjugate (ADC) against B2M, a recently identified membrane marker of senescence, as a target for the specific delivery of toxic drugs into senescent cells, was able to selectively kill senescent cells with no toxicity to proliferating cells, demonstrating the feasibility of antibody-based targeted senolytics and suggests a new avenue for development tools that could be readily used for a wide range of therapeutic applications, which could have clinical applications in pathological aging and associated diseases.

The NanoPhotometer® P300 was used in this study to measure the concentration and purity of extracted RNA.

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The second issue is continuing the discussion on the topic of of senescence - one of the hallmarks of aging is the progressive accumulation of senescent cells in organisms, which has been proposed to be a contributing factor to age-dependent organ dysfunction. Ekpenyong-Akiba et. al recently reported that Bruton's tyrosine kinase (BTK) is an upstream component of the p53 responses to DNA damage. BTK binds to and phosphorylates p53 and MDM2, which results in increased p53 activity. Consistent with this, blocking BTK impairs p53-induced senescence with their most recent study presenting evidence that BTK inhibition can have a positive impact on mammalian healthspan and that interfering with the p53 pathway by removing BTK's regulation could reduce certain features of the aging phenotype and that using already clinically approved and well-tolerated drugs results in an amelioration of the age-related functional decline.

An immediate one could be the repurposing of ibrutinib (and other BTK inhibitors currently in clinical trials) to treat progeroid syndromes, rare genetic disorders that mimic the acceleration of aging. Eventually, they may be shown to be useful to prevent senescent cell accumulation in

certain situations, such as Alzheimer's disease, as well as reducing the frailty associated with normal aging. This provides a blueprint to devise strategies to slow or delay the age-dependent functional decay of tissues and organs.

The concentration of RNA was measured using a NanoPhotometer® P300.

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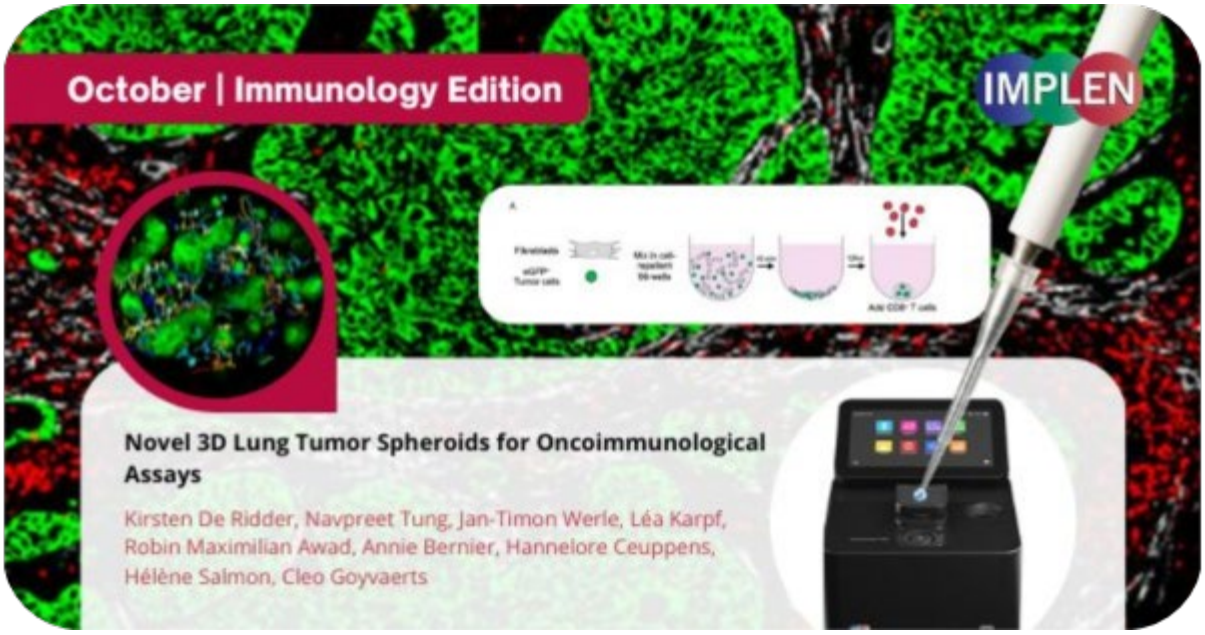

Next issue is highlighting the work of Kristen De Ridder et al. who recently reported on a murine and human lung tumor spheroid platform to evaluate drug interactions that influence the overall response to immunotherapies in a straightforward and accessible model for high-throughput screening compatible with standard liquid handling equipment to serve the exciting yet rapidly evolving field of oncoimmunological gene, cell, and drug discovery. In marked contrast to conventional treatments, immunotherapy does not target tumor cell division directly, but blocks immunosuppressive checkpoints that are heterogeneously expressed throughout the complex lung tumor microenvironment (TME).

Although T-cell-based immunotherapy revolutionized the treatment paradigm for advanced lung cancer patients, this only holds true for a minor subset of patients. Thus, international efforts of ongoing research aim to identify predictive biomarkers and novel drug targets within the TME that can synergize with immunotherapy to improve therapeutic response rates. This 3D lung tumor spheroid platform can serve as a blueprint for other solid cancer types to comply with the need for straightforward murine and human oncoimmunology assays.

The NanoPhotometer® was used in this work to quantify the extracted RNA.

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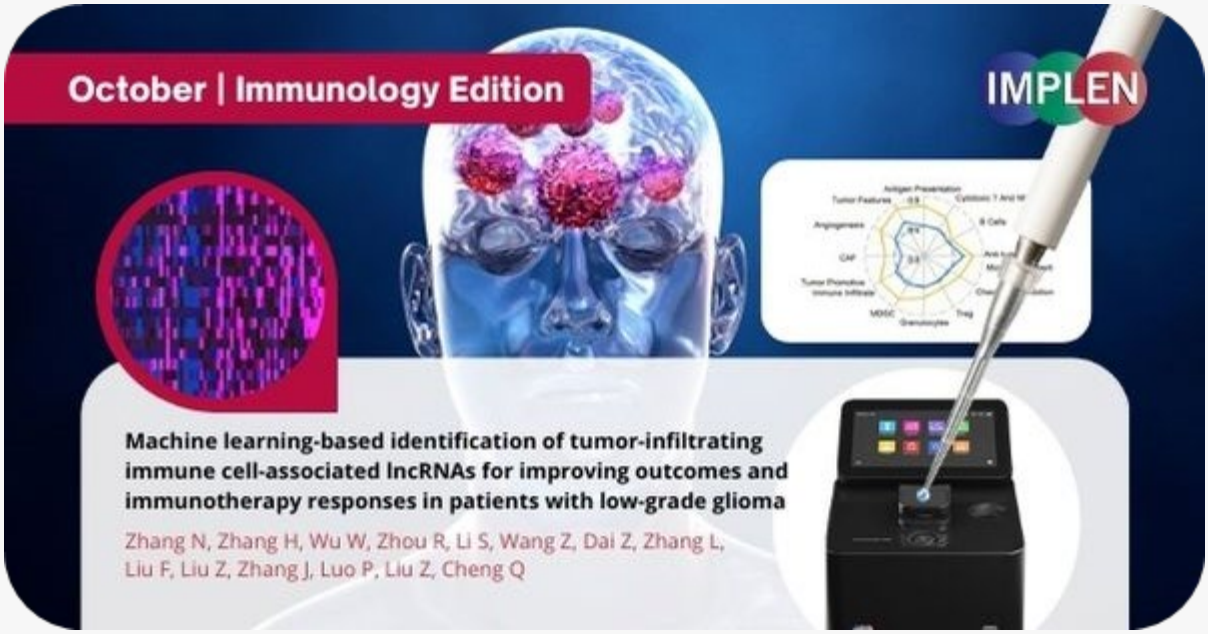

In the last issue of Immunology edition we are covering the work published this year by Zhang et al. in the journal of Theranostics using a novel computational framework and many machine learning based approaches to identify tumor-infiltrating immune cells associated long noncoding RNAs (TIIClncRNAs) to predict and improve outcomes and immunotherapy responses in glioma patients. The TIIClnc signature was strongly correlated to immune characteristics, including microsatellite instability, tumor mutation burden, and interferon γ, and exhibited a more active immunologic process. Furthermore, the TIIClnc signature predicted superior immunotherapy response in multiple datasets across cancer types. Notably, the positive correlation between the TIIClnc signature and CD8, PD-1, and PD-L1 was verified. The TIIClnc signature enabled a more precise selection of the glioma patient population who are potential responders to immunotherapy.

The NanoPhotometer® was used in this study to assess RNA purity and integrity.

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