Molecular Oncology

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EACR 2024 Congress Abstracts

Contents

Proffered Papers

10-minute talks awarded for the highest scored abstracts, embedded in the scientific symposia sessions. These presentations are not accompanied by a poster.

Posters in the Spotlight

Tuesday 11 June, 18:15 - 18:40, Poster and Exhibition Hall
Wednesday 12 June, 18:15 - 18:40, Poster and Exhibition Hall

Dedicated sessions taking place in the spotlight area within the Poster and Exhibition Hall. Poster presenters with high scoring abstracts will give short presentations of up to 5 minutes each. Their posters will also be available to view during the Poster Discussion Sessions.

Late-breaking Abstracts

Late-breaking abstracts are those for which full data were not available at the time of the regular abstract deadline.

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The transition from identifying predictive spatial biomarkers, known as spatial signatures, for immunotherapy responses to their clinical implementation requires a cohesive strategy that connects ultrahigh-plex discovery experiments with high-throughput translational investigations. This research focuses on integrating Akoya Biosciences' spatial multiplexed imaging technologies with advanced data analysis methods to achieve comprehensive spatial phenotyping from discovery to clinical applications.

Material and Methods

Human formalin-fixed, paraffin-embedded (FFPE) cancer tissues underwent profiling using ultrahigh-plex PhenoCode™ Discovery panels to assess cell lineage, immune activation, and checkpoint markers through the PhenoCycler®-Fusion spatial biology platform. Then, PhenoCode™ Signature panels were used to target specific biomarkers related to immune profile, immune contexture, tumor-infiltrating lymphocytes (TIL), macrophage polarization, and T cell status using the PhenoImager® HT platform. Whole slide image analysis was utilized for precise image analysis tasks, such as region of interest (ROI) segmentation, cell detection, classification, exploration of spatial interactions, and identification of distinct spatial signatures.

Results and Discussions

Our investigation unveiled unique spatial relationships across different tumor categories, providing quantification of immune cell distributions and their interconnections. The ultrahigh-plex data demonstrated strong correlation with high-throughput signature panel analyses, thereby paving the way for a streamlined approach to pinpointing and crafting predictive spatial signatures for immunotherapy efficacy.

Conclusion

Leveraging ultrahigh-plex discovery panels, high-throughput signature panels, and advanced deep-learning image analysis offers a holistic comprehension of cellular interactions within the tumor microenvironment. This integrated methodology, leveraging Akoya's end-to-end workflows, expedites the discovery of predictive spatial biomarker signatures across various human tissue samples.

EACR2024-0816

Assessing anti-tumor efficacy of tumor-dendritic cell reprogramming using immuno-competent 3D tumor microtissue models

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Introduction

Despite the extensive use of mouse models in pre-clinical cancer research, their translatability is often limited by inter-species differences. Recent studies have reported that overexpression of the transcription factors PU.1, IRF8, and BATF3 (PIB) in cancer cells induces reprogramming into functional antigen-presenting type 1 conventional dendritic cells (cDC1s). This suggests a novel strategy for cancer immunotherapy based on the recreation of cDC1s´ functional properties in tumor cells by in-vivo reprogramming, forcing presentation of endogenous tumor neoantigens and inducing personalized anti-tumor immunity. Here, we evaluate efficacy of cDC1 reprogramming using innovative in-vitro 3D human immunocompetent tumor microtissue (TMT) models.

Material and Methods

TMTs were generated by co-aggregation of T98G or A375 human tumor cell lines with cancer-associated fibroblasts in proprietary AKURA™ 384 well plates. We transduced TMTs with PIB-mCherry-encoding lentiviral particles at different multiplicities of infection (MOIs) and profiled cDC1 reprogramming efficiency by immunofluorescence staining and high-content confocal imaging. We observed that cDC1 reprogramming progresses in 3D TMTs and is associated with expression of the dendritic cell markers CD45 and HLA-DR. Additionally, we observed that higher MOI is associated with higher transduction and reprogramming efficiency and decreased TMT size. To further investigate *ex vivo* antitumor efficacy, we co-cultured TMTs with HLA-matched PBMCs and profiled cytokine secretion and TMT size as readouts for T cell activation and cytotoxicity.

Results and Discussions

We observed increased secretion levels of IFNγ, TNFα, and Granzyme B, accompanied by reduced TMT size, in the co-cultures containing PIB-mCherry-transduced TMTs compared to those with mCherry-transduced TMTs. Importantly, both readouts were correlated with the percentage of reprogrammed tumor-cDC1s within the 3D TMT in a dose-dependent manner, suggesting that in situ cDC1 reprogramming promotes T cell activation and cytotoxicity.

Conclusion

In summary, we used 3D cocultures of human tumor, stromal, and immune cells in automation-compatible AKURA™ 384 well plates to demonstrate that cDC1 reprogramming progresses within TMTs, promoting antitumor immunity. Ultimately, these findings provide proof-of-principle for a novel cancer immunotherapy based on in situ cDC1 reprogramming and demonstrate the versatility of the AKURA™ platform for evaluating efficacy of novel anti-cancer therapies.

EACR2024-0827

Expanding the Landscape of Professional Project Management to Support Cancer Research in Serbia

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Introduction

Research Management Offices (RMOs), separate organizational units within universities, research and healthcare centers, serve as advisory and supporting entities along the entire research process. Their purpose is to ensure and promote high-quality research thus contributing to excellence, sustainability and open science principles. This study aimed to analyze the advantages of the establishment and development of the first RMO at the Institute for Oncology and Radiology of Serbia (IORS) and to propose further R&D strategies for the efficient implementation of EU grants to ensure sustainability of research ecosystems in Serbia.

Material and Methods

Within the framework of the STEPUPIORS Horizon Europe project, the first RMO was established at IORS as a project delievarble. The initial steps were to define the scope of activities and to develop project management competencies through training, workshops and seminars. Human capacities for project management were built through intensive training and expert visits. The grant management offices from partner institutions provided focused training on pre-award and post-award processes with adequate on-site training in project management.

Results and Discussions

Good pre- and post-award grant management practices were established within the first 12 months of the project. The RMO organized 5 training events on omics analyses, project management and education capacities, reaching over 200 Serbian researchers from 7 institutions. A training module was established on the dedicated project website (https://www.stepupiors.eu/training-webinars/) following Open Science principles. The RMO coordinated the development of 2 newsletters and 1 patient brochure on genetic testing in hereditary colorectal cancer. Five manuscripts on colorectal cancer patient management were published with the deposition of 2 datasets. Seven new grant applications were submitted. One female project member enrolled in a Master's program for Management in the Health Care System. IORS guidelines for the management of international grants and depreciation of equipment were prepared.

Conclusion

The establishment of the IORS RMO induced a rise in cancer research excellence and professionalism in the implementation and coordination of their projects. The RMO will strive to support IORS staff in education, research and administration activities, with special reference to the digitalization of cancer research, open science and integrity and equity in the cancer research community in Serbia and the region.

EACR2024-0893
ctDNA profiling of HR+/HER2-low and HR+/HER2-0 metastatic breast cancer patients

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Introduction

Despite the substantial progress in the treatment of hormone receptor-positive (HR+) breast cancer (BC), there is still a significant proportion of patients with lower benefit from endocrine-based treatments. A meaningful proportion of these patients have HER2-low disease. As a subset of HER2-negative BC, they have traditionally been thought not to benefit from anti-HER2 therapies. However, recent studies involving HER2-low advanced BC patients have shown significant clinical benefits from HER2-targeted antibody-drug conjugates (ADCs) just based on the low expression of the HER2 protein. We performed a circulating tumor DNA (ctDNA)-based analysis of tumor fraction and mutational profiles to potentially identify different clinical behavior and therapeutic targets within these two groups.

Material and Methods

113 plasma samples from 103 metastatic breast cancer patients (HR+/HER2-low, n=76; HR+/HER2-0, n=37) were collected either before starting 1st line or 2nd line treatment. Tumor fractions were assessed using an untargeted aneuploidy screening and expressed as z-scores (mFAST-SeqS). The mutational landscape of ctDNA was established using a 77-gene panel (AVENIO ctDNA Expanded). Tumor fractions, the number of somatic variants and variant allele frequencies (VAF) were compared between HER2-low and HER2-0 patients.

Results and Discussions

HER2-low patients had significantly higher z-scores compared to HER2-0 patients (median 2.96 vs. 1.58, rank-sum p-value 0.023). In contrast, neither the highest nor the average VAF differed significantly between the two groups. While both groups presented with a median of 3 detected variants (HER2-low range: 1-20, HER2-0 range: 1-12), a significant difference was observed in the number of clonal variants between HER2-low and HER2-0 patients (median 2 vs. 3, rank-sum p-value 0.035). In contrast to previous reports, *PIK3CA* mutations were more prevalent in HER2-0 patients (58.06%) compared to HER2-low patients (40%), whereas *TP53* mutations were identified with 32.26% in HER2-0 and 26.67% in HER2-low patients.

Conclusion

Our results suggest a significant difference in the tumor fractions in plasma between HER2-0 and HER2-low in our patient cohort. Additionally, HER2-0 patients had a