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2023

INTERNATIONAL FORUM ON EARLY CANCER

21-22 NOVEMBER 2023

BERLIN, GERMANY



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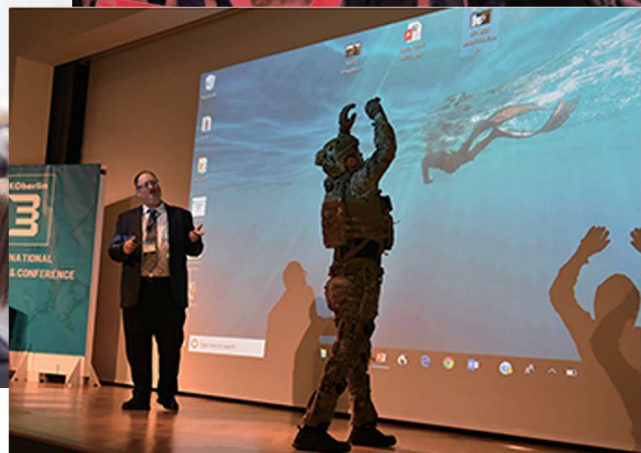
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INDEX

SPEAKER

- DUKSUNG WOMEN'S UNIVERSITY COLLEGE OF PHARMACY / SOUTH KOREA
- EXPERIMENTAL AND CLINICAL RESEARCH CENTER, CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN AND MAX-DEL BRÜCK-CENTER FOR MOLECULAR MEDICINE / GERMANY
- FED RES CTR FUNDAMENTAL & TRANSLAT MED / GERMANY
- FUNDACIÓN RIOJA SALUD / SPAIN
- HUMMINGBIRD DIAGNOSTICS GMBH / GERMANY
- MARIA SKŁODOWSKA-CURIE NATIONAL RESEARCH INSTITUTE OF ONCOLOGY / POLAND
- MASARYK UNIVERSITY / CZECH REPUBLIC
- OTTO-VON-GUERICKE UNIVERSITY MAGDEBURG / GERMANY
- STRATHCLYDE UNIVERSITY / UNITED KINGDOM
- TEXAS A7M UNIVERSITY AT QATAR / QATAR
- UNIVERSITY OF HERTFORDSHIRE / UNITED KINGDOM
- UNIVERSITY OF HERTFORDSHIRE / UNITED KINGDOM
- UNIVERSITY OF WESTMINSTER / UNITED KINGDOM

EXHIBITOR

- HISS DIAGNOSTICS GMBH / GERMANY
- MODULIGHT INC / FINLAND
- QIAGEN GMBH, PREANALYTIX / GERMANY
- QUANTERIX / UNITED STATES
- SINGLERON BIOTECHNOLOGIES GMBH / GERMANY

 Last updated: November 13, 2023

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E-C-Forum Berlin 21-22.11.2023
Conference Schedule

 The conference language is English



Day1: Tuesday, November 21, 2023	TIME	TOPIC	PRESENTER	COUNTRY
	10:00	<i>Opening Remarks</i>		
	10:10	A gene expression signature for identifying higher risk patients with early stage colon cancer	MASARYK UNIVERSITY	CZECH REPUBLIC
	10:30	Data assimilation for GBM human brain tumours modeling	TEXAS A7M UNIVERSITY AT QATAR	QATAR
	10:55	<i>Coffee Break</i>		
	11:25	Prospects of testing diurnal profiles of expressions of TSH-R and circadian clock genes in thyrocytes for identification of preoperative biomarkers for thyroid carcinoma	FED RES CTR FUNDAMENTAL & TRANSLAT MED	GERMANY
	11:50	3R technology platform for development of epigenetic-based blood diagnostics for cancer stem cells	OTTO-VON-GUERICKE UNIVERSITY MAGDEBURG	GERMANY
	12:15	<i>Lunch Time</i>		
	13:30	HAX1 is an independent risk factor for luminal breast cancer metastasis	MARIA SKLODOWSKA-CURIE NATIONAL RESEARCH INSTITUTE OF ONCOLOGY	POLAND
	13:55	Restrict cancer metastasis - save patient life: translating MACC1 gene discovery into clinical application	EXPERIMENTAL AND CLINICAL RESEARCH CENTER, CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN AND MAX-DELBRÜCK-CENTER FOR MOLECULAR MEDICINE	GERMANY
	14:20	The diagnostic potential of microRNAs in pancreatic ductal adenocarcinoma (PDAC)	UNIVERSITY OF WESTMINSTER	UNITED KINGDOM
	14:45	<i>Coffee Break</i>		
	15:15	Comparative analysis of validation standards for early cancer detection biomarkers: a cross-national study	DUKSUNG WOMEN'S UNIVERSITY COLLEGE OF PHARMACY	SOUTH KOREA
	15:35	Early lung cancer detection using small RNAs	HUMMINGBIRD DIAGNOSTICS GMBH	GERMANY
	16:00	Networking		
17:30	<i>End</i>			

Day2: Wednesday, November 22, 2023	TIME	TOPIC	PRESENTER	COUNTRY
	9:30	<i>Opening Remarks</i>		
	9:40	Novel Siglec-15-Sialoglycan axis inhibitor leads to colorectal cancer cell death targeting oncogenic multiple pathways	UNIVERSITY OF HERTFORDSHIRE	UNITED KINGDOM
	10:00	Fluorescent plasmonic nanoprobe for detecting cancer biomarker RNA in liquid biopsies	STRATHCLYDE UNIVERSITY	UNITED KINGDOM
	10:20	<i>Coffee Break</i>		
	10:50	New carbonyl compound leads to glioblastoma cell death through inhibition of miR-21 and CORO1C	UNIVERSITY OF HERTFORDSHIRE	UNITED KINGDOM
	11:10	A highly sensitive nanotechnology-based test for the early detection of pancreatic cancer and other epithelial tumors	FUNDACIÓN RIOJA SALUD	SPAIN
	11:30	<i>Lunch Time</i>		
	13:00	Co-located Guest TECH DAY: Explore tumor heterogeneity and biomarkers with single-cell multi-omics	SINGLERON BIOTECHNOLOGIES GMBH	GERMANY
	14:30	Co-located Guest TECH DAY: Ultra-sensitive SiMoA (Single Molecule Arrays) Technology for Extracellular Vesicles Detection and EV-derived Biomarker Profiling	QUANTERIX	UNITED STATES
	16:00	<i>End</i>		

/Be aware that the start and end times for each session are tentative. /This schedule is subject to change without prior notice. Check back for updates on www.e-c-forum.de. (Lasted updated: 13.11.2023)

Workshop

13:30 - 15:00 pm, Wednesday, 22nd November

Exploring tumor heterogeneity and biomarkers with single-cell multi-omics



- From a sample to publication-ready data: an easy and fast workflow
- Advantages and applications of Singleron's SCOPE-chip technology
- Hands-on demonstration of microfluidic chip loading with live imaging



Aparna Sekar
Single Cell Specialist
Singleron Biotechnologies



Dr. Miguel Miñambres
Application Scientist
Singleron Biotechnologies

Meet the experts!

Host: **Lindsey Marsh, Ph.D.**
Quanterix Senior Field Application Scientist



TECH DAY

Wednesday 22nd November

Single Molecule Ultrasensitive Assays for Extracellular vesicle (EV) and EV-derived biomarker detection

14:00 - 14:40 - “Simoa® Technology for ultrasensitive biomarker detection”

- Simoa bead technology and product overview
- Key example oncology assays and their clinical application

14:40 - 15:00 - EV assay development live poll

15:00-15:30 - “Simoa® Homebrew applied to custom assay development for EV research”

- Homebrew implementation/custom development on Simoa beads
- Discover how to elevate your EV research with Simoa technology

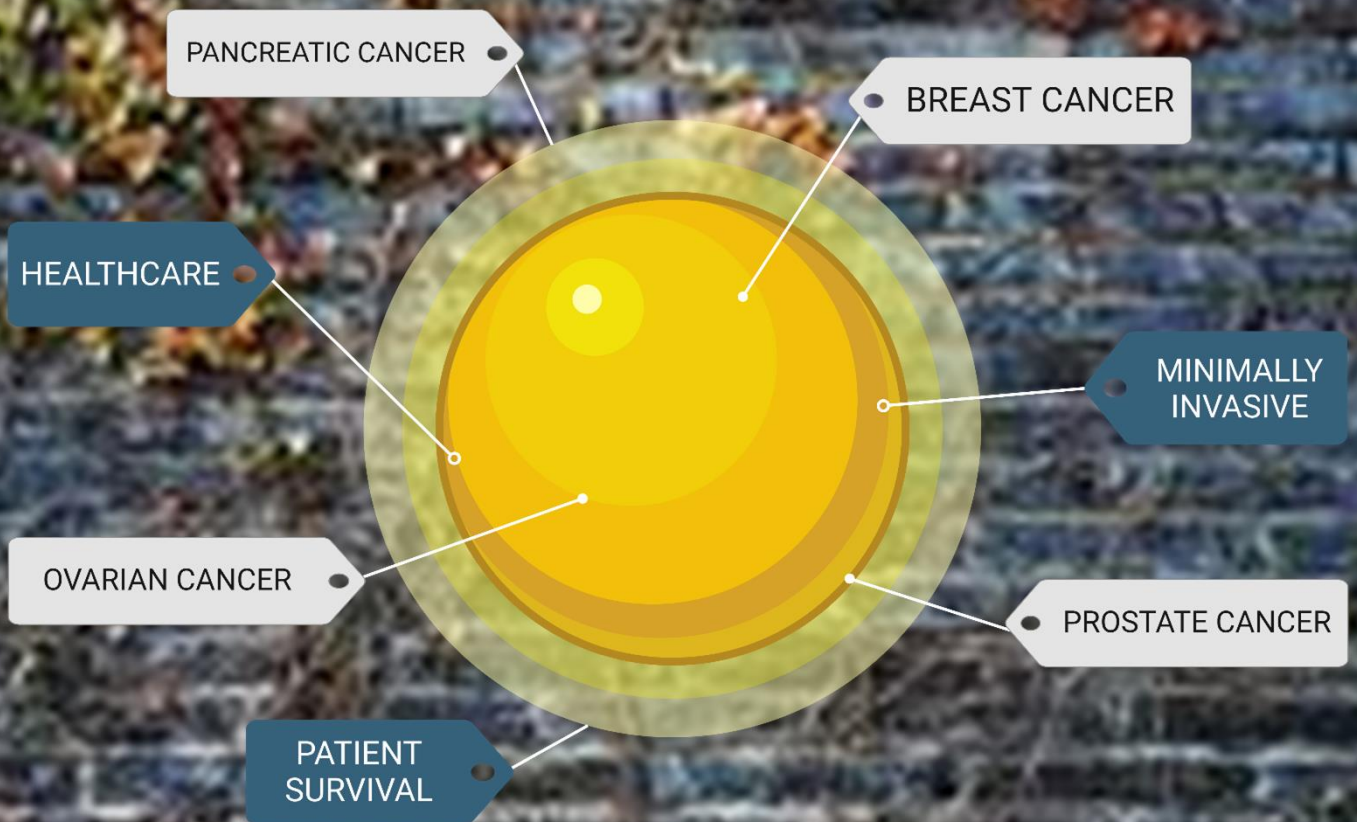
15:30 - 15:45 – Open Q&A

Title : Comparative Analysis of Validation Standards for Early Cancer Detection Biomarkers: A Cross-National Study

Abstract : This cross-national study investigates and contrasts validation standards for early cancer detection biomarkers during regulatory approvals across the United States, Europe, Japan, and South Korea. Analyzing criteria set by regulatory bodies in each country, the research delves into healthcare infrastructure, regulatory benchmarks, and technological evaluations. The study sheds light on disparities in validation standards. Thorough analysis of regulatory guidelines and case studies informs the examination of early cancer detection biomarker validation processes. The study aims to enhance understanding of cross-national differences and promote international cooperation, contributing to the advancement of early cancer detection globally.

Keywords: Early cancer detection; Biomarkers; Validation standards; Regulatory approvals; Cross-national study

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Predict responses
Monitor treatment

from a simple blood draw
using small RNAs

Lung Cancer

Accurate detection
of early stage lung cancer
from whole blood

Response prediction NSCLC
anti-PD-1 therapy
from whole blood

mirCator

The new standard for detection &
analysis of small RNAs from blood



WHOLE BLOOD
SAMPLING

EXTRACTION

QUALITY
CONTROL

DETECTION

DATA
ANALYSIS

A gene expression signature for identifying higher risk patients with early stage colon cancer

E. Budinska¹, O. Slaby², B. Bencsikova³, V. Popovici¹

1. Masaryk University, Fac. of Science - RECETOX, 625 00 Brno, Czech Republic

2. Masaryk University, Fac. of Medicine & CEITEC, 625 00 Brno, Czech Republic

3. Masaryk Memorial Cancer Institute, 656 53 Brno, Czech Republic

Introduction

An estimated 80-85% of stage II colorectal cancer (CRC) patients will be cancer-free at five years after surgery, without adjuvant chemotherapy. The benefit of adjuvant chemotherapy is unclear, with an estimated 2% reduction of 5-year relapse likelihood. Among the stage II patients and in the absence of other risk factors, patients harboring stage II pT3N0 tumors are considered low risk and not given adjuvant chemotherapy. However, about 10% of these patients relapse within five years. The question we address here is the discovery of molecular markers that would identify these higher risk patients in a homogeneous population of untreated pT3N0 microsatellite-stable CRC patients, proposing an approach for predicting those that may be candidates for an adjuvant treatment.

Material and Methods

Two cohorts of patients with stage II pT3N0 microsatellite-stable CRC were used (one in-house cohort and a subset of publicly available dataset E-MTAB-863 (ArrayExpress)), with sample size of 39 and 150, respectively. "Early relapse" was defined as relapse within 5 years after tumor resection, while "late relapse" was defined as no relapse for at least 6 years. Differential gene expression followed by gene set enrichment analysis were used for identifying the main differences between the groups at gene and pathway levels. Elastic net regression was used for building predictive models using single sample pathway activation scores as features and performance was estimated using 5-fold cross-validation.

Results and Discussions

The strongest differences at pathway levels between the two groups were found in epithelial-to-mesenchymal transition, TNF-alpha signalling, interferon alpha and gamma response, and hypoxia response. In addition, early relapsing tumors were enriched in myofibroblastic cancer-(ECM-myCAF and wound-myCAF). The predictive model achieved an estimated accuracy of 76.9% (95% CI: 60.3-88.3) and 71.33% (95% CI: 63.3-78.3) on the two datasets. The patients relapsing within 5 years were identified with a precision of 80% (95% CI: 55.7-93.4) and 73.2% (95% CI: 59.5-83.8), respectively.

Conclusion

Several major pathways are differentially activated between patients relapsing within 5 years and those with no relapse for at least 6 years. Interestingly, the presence of specific fibroblasts seem also to be indicative of shorter time to relapse. A classifier built on pathway activation scores was able to predict relapse with good sensitivity in untreated pT3N0 patients, selecting those that may benefit from adjuvant therapy.

3R technology platform for development of epigenetic-based blood diagnostics for cancer stem cells

Ahmed Y. Sanin^{1,4}, Wenjie Shi¹, Thomas Wartmann¹, Erol Sandalcioglu², Can Dincer³, Roland S. Croner^{1,4}, Ulf D Kahlert^{1,4}

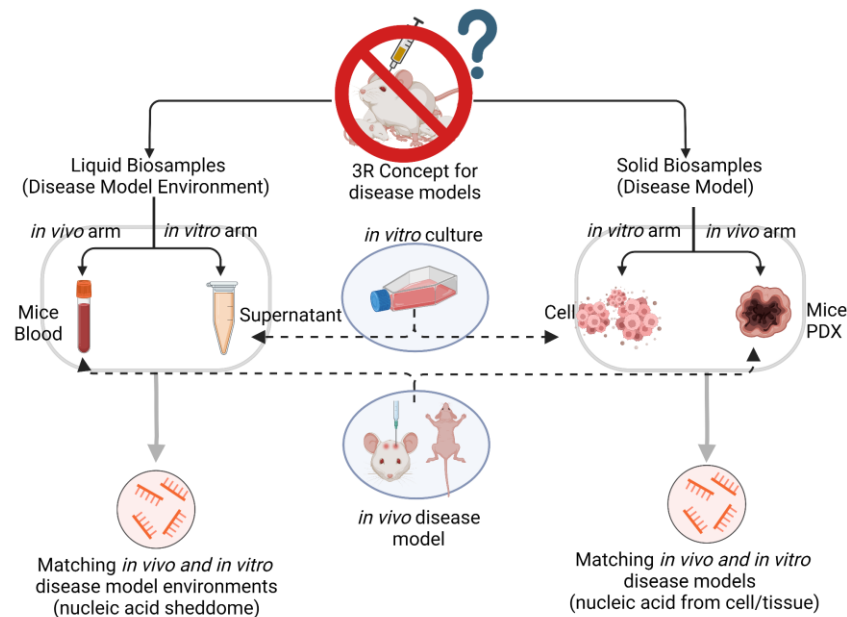
¹ Molecular and Experimental Surgery, Faculty of Medicine and University Hospital Magdeburg, Department of General, Visceral, Vascular and Transplant Surgery, Otto-von-Guericke University, Magdeburg, Germany

² Department of Neurosurgery, University Hospital Magdeburg, Otto-von-Guericke University, Magdeburg, Germany

³ Disposable Microsystems, Department of Microsystems Engineering (IMTEK), University of Freiburg, Freiburg i.Br. Germany

⁴ Research Campus STIMULATE, Otto-von-Guericke University, Magdeburg, Germany

Liquid biopsy-based nucleic acid diagnostics (LD) revolutionizes clinical diagnostics. However, oncological LD development primarily relies on clinical samples, offering limited correlative data. Functional precision oncology, through disease modeling (DM), bridges the clinic-experiment divide, enabling mechanistic insights. It addresses discriminating tumor therapy resistances and inflammation effects, beyond clinical perfusion imaging's scope.



Guided by science policy and socio-ethical considerations (3R principles) and focusing on low 5-year survival rate tumors, we employ NGS, as we assess RNA content in cancer stem cells (CSC) and their disease model environments (DME). Utilizing diverse computational tools and machine learning, we identify valuable CSC-RNA sheddome candidates on our DM (spheroids vs. xenografts in immune-deficient mice) and derived DMEs (cell supernatant vs. blood plasma, post-exposure to clinical cancer treatments). Their potential lies in coherent epigenomic signals shared between *in vitro* and animal models. This advances therapy optimization insight, questioning the necessity of further animal perfusion studies in early-stage LD development.

Fluorescent plasmonic nanoprobes for detecting cancer biomarker RNA in liquid biopsies

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³Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0RE, Scotland, UK

RNA imaging and detection have become increasingly important for identifying disease biomarkers and developing new diagnostic tools. In this study, we present a new approach for RNA imaging and detection using bespoke fluorescent nanoprobes. These nanoprobes are composed of plasmonic nanoparticles functionalised with fluorophore-labelled thiolated single-stranded hairpin DNA designed to target cancer biomarker RNA.^{1,2} The fluorescence intensity and lifetime of the nanoprobes was found dependent on the hybridisation of nanoprobes with target RNA, as assessed by steady-state and time-resolved fluorescence spectroscopy.^{3,4} Utilizing lifetime imaging microscopy, fast fluorescence lifetime analysis methods were employed to generate spatial maps of target RNA within cells, enabling the differentiation of cancer cells exhibiting elevated levels of target RNA from control cells. Nanoprobe's ability to detect target RNA in cell-derived exosomes was also evaluated, and they were shown to differentiate cancer exosomes from health control. Furthermore, we demonstrated the nanoprobes' effectiveness in detecting intracellular RNA at single cell level in both cell models and clinical samples using flow cytometry. Our results underscore a substantial potential of these bespoke fluorescent nanoprobes for rapid detecting cancer biomarker RNAs in liquid biopsies.

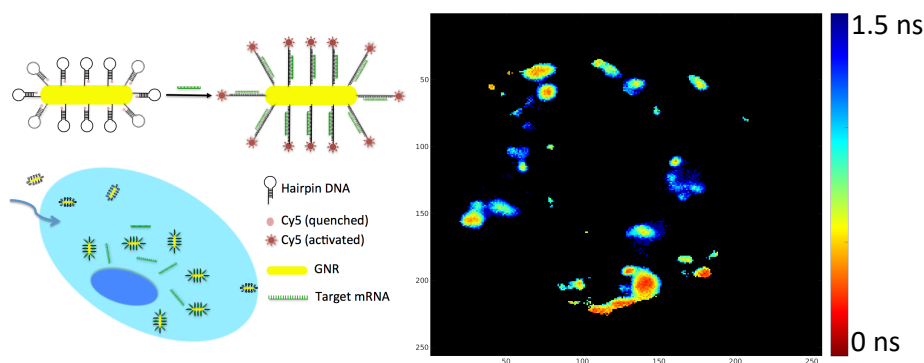


Figure A A fluorescent plasmonic nanoprobe functions through energy transfer and fluorescence lifetime analysis of nanoprobes in cell.

Acknowledgments: This work was supported by grants from BBSRC, EPSRC and MRC.

References: [1] Zhang Y. et al., Faraday Discussion. **2015**, 178, 383. [2] Mbalaha Z.S. et al., ACS Omega. **2019**, 4(9) 13740. [3] Wei G. et al., J. Biomed. Opt. **2016**, 21, 097001. [4] Wei G. et al., Optics Letters, **2015**, 40, 5738.

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Novel Siglec-15-Sialoglycan axis inhibitor leads to colorectal cancer cell death targeting oncogenic multiple pathways

Ahmad M.S¹, Braoudaki M¹, Patel H¹, Ahmad I², Shagufta ², Siddiqui S.S¹

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²Department of Biotechnology, School of Arts and Sciences, American University of Ras Al Khaimah, Ras Al Khaimah, United Arab Emirates (UAE).

Small molecule inhibitors targeting Siglec-15 are not explored alongside characterised regulatory mechanisms involving microRNAs in CRC progression. Therefore, a small molecule inhibitor to target Siglec-15 was elucidated *in vitro* and microRNA-mediated inhibitor effects were investigated. We demonstrated that the SHG-8 molecule exerted significant cytotoxicity on cell viability, migration, and colony formation, with an IC₅₀ value of 20µM. Notably, miR-6715b-3p was the most upregulated miRNA via high-throughput sequencing, which was validated via RT-qPCR. Additionally, molecular docking studies revealed SHG-8 interactions with the Siglec-15 binding pocket with the binding affinity of -5.4 kcal/mol, highlighting its role as a small molecule inhibitor. Importantly, Siglec-15 and PD-L1 are expressed on mutually exclusive cancer cell populations, suggesting the potential for combination therapies with PD-L1 antagonists.

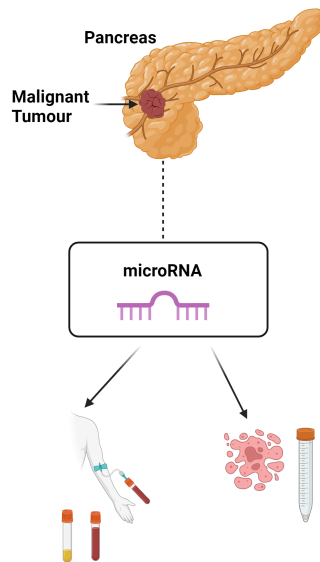
Keywords:

Siglec-15, sialic acid, β-amino ketone, RNA-sequencing, colorectal cancer

The Diagnostic Potential of microRNAs in Pancreatic Ductal Adenocarcinoma (PDAC)

Pinar Uysal-Onganer, PhD
Cancer Mechanisms and Biomarkers Research Group, University of Westminster, London, UK

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive malignant disease of the pancreas, with a global annual death toll of over 400,000 individuals, and an overall five-year survival rate of ~10%. Early detection is particularly difficult due to the lack of disease-specific symptoms and reliable diagnostic biomarkers. Recently, microRNAs (miRNAs) have emerged as important players in tumorigenesis in different cancers including PDAC. miRNAs, short non coding RNAs, regulate gene expression at a post-transcriptional level, affecting protein levels and, as such, form an integral part of many biological processes. We and the others have demonstrated that miRNAs as novel sensitive biomarkers because of their significant correlation with disease development and metastasis of PDAC. We have identified a panel of miRNAs that can be used for early detection for PDAC based on our *in silico*, *in vitro* and *in vivo* studies. These miRNAs play pivotal roles in a multitude of cancer-related mechanisms, encompassing cell growth, differentiation, metastasis, invasion, and apoptosis. Based on our data, we propose that strategies targeting miRNAs should be explored to develop improved therapies for PDAC.





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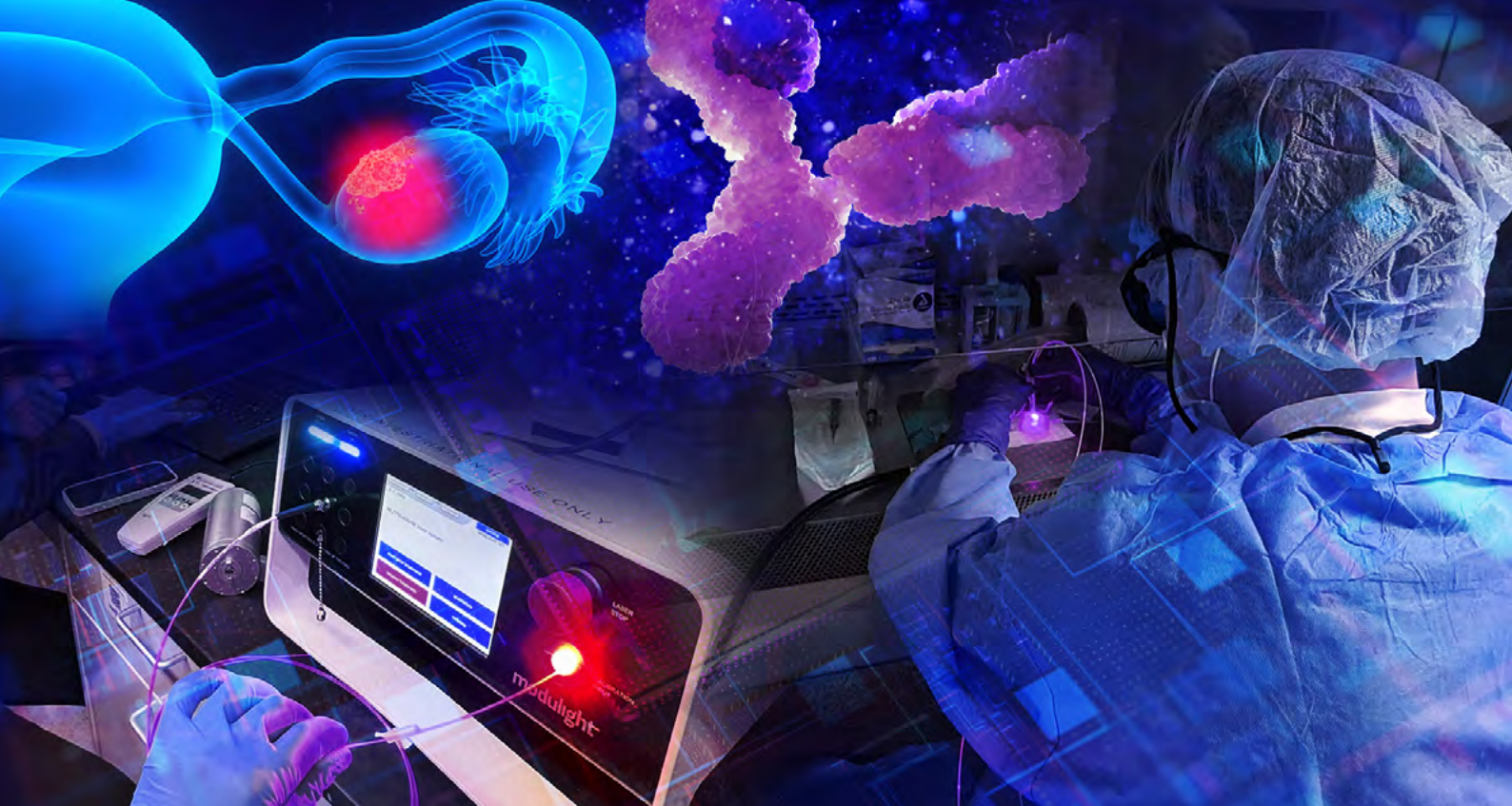
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PAXgene Bone Marrow RNA Kit (RUO) | 764133

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PAXgene Tissue RNA/miRNA Kit (RUO) | 766134

PAXgene Tissue DNA Kit (RUO) | 767134

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