2025년 부산대학교

암세포 다양성 분자제어 연구센터(MRC) 성과발표회

2025.11.28.(금)
13:30~

해운대 시그니엘 부산 4F 볼룸 홀

과학기술정보통신부 Ministry of Science and ICT
NRF 한국연구재단
부산광역시 BUSAN METROPOLITAN CITY
CANCER CELL DIVERSITY CDMRC
BrainKorea 21
부산대학교 GRAND 융합의과학 교육연구단

센터장 인사말

안녕하세요? 다사다난했던 2025년 을사년 한 해도 저물어 갑니다.
한 해동안 센터 목표를 향해 쉼 없이 달리면서 얻었던 연구 결과를 공유하고 격려하는 자리를 마련하였습니다. 각 실험실에서 각고의 노력을 다하는 학생과 연구원들이 함께 축하하는 자리가 되길 기대합니다.

올해에는 공동연구를 보다 강화하기 위해 매월 정기적인 공동연구미팅을 진행해왔으며, 새로운 치료기술 개발을 위해 나노입자제조시스템을 센터 내에 구축해오고 있습니다. 올해 내로 구축하려고 했지만, 복잡한 행정절차로 인해 늦어졌습니다. 하지만, 내년 2월 이내에는 구축이 마무리될 것으로 예상합니다. 이 나노입자세조시스템 잘 진행된다면, 분자유형별 암세포/암줄기세포/분자니쉬를 타겟한, 새로운 치료기술이 개발될 수 있을 것으로 기대합니다.

센터연구사업이 단독연구가 아닌 공동연구이기 때문에, 그룹 간 상호 협력이 중요하며, 성과발표회가 이를 위한 소중한 자리이길 기원합니다.

감사합니다.

2025. 11. 28

부산대학교 암세포다양성분자제어연구센터
오세옥 배상

2025년 부산대학교
암세포다양성분자제어연구센터(MRC) 성과발표회

Program

2025년 11월 28일 (금)		
13:30 ~ 13:40	개회사	**오세옥** 교수 (센터장)
Session 1.	**초청 강연**	좌장 : **오세옥** (센터장)
13:40 ~ 14:40	Advances in 3D Bioprinting: Towards Functional Tissue Engineering through Precise Morphological Control	**강현욱** 교수 (UNIST 바이오메디컬공학과)
Session 2.	**연구결과 발표**	좌장 : **권상모**(융합의과학과)
14:40 ~ 15:00	Pan-cancer Analysis of the Coatomer Complex Reveals Its Importance during Cancer Progression	**센서스미타** (융합의과학과)
15:00 ~ 15:20	Aptamer-Based Optical Biosensor Utilizing Metal-Enhanced Fluorescence for Liver Cancer Biomarker Detection	**김나영** (정보융합공학과)
15:20 ~ 15:40	Optimization of a CD166-Targeting Aptamer using an Integrated In Silico - In Vitro Strategy	**이서율** (융합의과학과)
15:40 ~ 16:00	Microenvironment-guided Evolution of ssDNA-SWCNT Probes for Selective Recognition of Aggressive Prostate Cancer Phenotypes	**정상화** (의생명융합공학부)
16:00 ~ 16:20	A Robust Marine Collagen Peptide–Agarose 3D Culture System for In Vitro Modeling of Hepatocellular Carcinoma and Anti-Cancer Therapeutic Development	**라즈봉시라타** (융합의과학과)
16:20 ~ 16:40	Development of Tumor Assembloid latform Via 3D Bioprinting of Spheroids to Investigate Time-Dependent Drug Responses	**최민서** (정보융합공학과)
16:40 ~ 18:00	포스터 발표	
18:00 ~ 18:10	시상식 및 폐회사	**오세옥** 교수 (센터장)
18:10 ~	저녁 만찬	

Session1 **초청강연**

Advances in 3D Bioprinting: Towards Functional Tissue Engineering through Precise Morphological Control

강현욱 교수
UNIST 바이오메디컬공학과

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Academic Career

2009 Pohang University of Science and Technology, Korea, PhD in Mechanical Engineering
2004 Pohang University of Science and Technology, Korea, MS in Mechanical Engineering
2002 Kyungpook National University, Korea, BS in Mechanical Engineering

Professional Experience

2025-Pres.	Professor	Department of Biomedical Engineering, UNIST
2020-2025	Associate Professor	Department of Biomedical Engineering, UNIST
2015-2020	Assistant Professor	Department of Biomedical Engineering, UNIST
2013-2015	Instructor	School of Medicine, Wake Forest University, USA
2009-2013	Postdoctoral Fellow	School of Medicine, Wake Forest University, USA

Selected Publications

1. Han J†, Jeong HJ†, Choi J, Kim H, Kwon T, Myung K, Jung DB, Myung SJ*, Kang HW**, Park TE**, Bioprinted patient-derived organoid arrays capturing intrinsic and extrinsic tumor features for advanced personalized medicine applications. *Advanced Science*. 2025;12/20:2407871.
2. Jeong W†, Hand J†, Choi J, Kang HW**. Embedded bioprinting of breast cancer-adipose composite tissue mode for patient-specific paracrine interaction analysis. *Advanced Healthcare Materials*. 2024;14/3:2401887.
3. Jeong S, Heo JH, Myung N, Shin JY, Kim MK, **Kang HW****, High-efficiency, prevascularization-free macroencapsulation system for subcutaneous transplantation of pancreatic islets for enhanced diabetes treatment. *Advanced Materials*. 2024;2408329, https://doi.org/10.1002/adma.202408329
4. Jeong W, Son J, Choi J, Hang J, Jeong S, Kim MK, Ha W, **Kang HW****. Clinically Relevant and Precisely Printable Live Adipose Tissue–Based Bio-Ink for Volumetric Soft Tissue Reconstruction. *Advanced Healthcare Materials*. 2024.
5. Son J, Mohamed HJ, Ha W, Naren A, Choi CA, Kwon Y, Park S, Joung HC, **Kang HW****. Bioprinting of pre-vascularized constructs for enhanced in vivo neo-vascularization. *Biofabrication*. 2023;15(3):034101.
6. Han J, Jeon S, Kim MK, Jeong W, Yoo JJ*, **Kang HW****. In vitro breast cancer model with patient-specific morphological features for personalized medicine. *Biofabricatio*n. 2022;14(3):034102.
7. Myung N, Jin S, Cho H, **Kang HW****. User-designed device with programmable release profile for localized treatment. *Journal of Controlled Release*. 2022;352:685-699.
8. Son J, Hong SJ, Lim JW, Jeong W, Jeong JH, **Kang HW****. Engineering Tissue-Specific, Multiscale Microvasculature with a Capillary Network for Prevascularized Tissue. *Small methods*. 2021:2100632, Online published, https://doi.org/10.1002/smtd.202100632.
9. Jeon S, Heo J-H, Kim MK, Jeong W, **Kang HW****. High-Precision 3D Bio-Dot Printing to Improve Paracrine Interaction between Multiple Types of Cell Spheroids. *Advanced Functional Materials*. 2020;30:2005324, https://doi.org/10.1002/adfm.202005324.
10. Kim MK, Jeong W, Lee SM, Kim JB, Jin S, **Kang HW****. Decellularized extracellular matrix-based bio-ink with enhanced 3D printability and mechanical properties. *Biofabrication*. 2020;12(2):025003.
11. Noh S, Kim K, Kim JI, Shin JH, **Kang HW****. Direct-write printing for producing biomimetic patterns with self-aligned neurites. *Additive Manufacturing*. 2020;32:101072.
12. Shin JH, Heo JH, Jeon S, Park JH, Kim S, **Kang HW****. Bio-inspired hollow PDMS sponge for enhanced oil-water separation. *Journal of Hazardous Materials*. 2019;365:494-501.
13. Shin J, **Kang HW****. The Development of Gelatin-Based Bio-Ink for Use in 3D Hybrid Bioprinting. *International Journal of Precision Engineering and Manufacturing*. 2018;19(5):767-771.
14. **Kang HW**, Lee SJ, Ko IK, Kengla C, Yoo JJ, Atala A*. A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. *Nature Biotechnology*. 2016;34:312–319.

Advances in 3D Bioprinting: Towards Functional Tissue Engineering through Precise Morphological Control

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The advancement of tissue engineering is unlocking new possibilities for the restoration and treatment of human defects. However, conventional approaches face limitations in replicating complex human tissues and organs. In this context, 3D bioprinting technology offers promising solutions to overcome these challenges. This technology enables the creation of flexible and customized three-dimensional structures using living cells, biomaterials, and biomolecules. It allows for the development of engineered tissues with greater complexity and functionality, surpassing the capabilities of traditional tissue engineering techniques. Various advanced bioprinting technologies have been developed, paving the way for even more intricate engineered tissues.

My colleagues and I have developed bioprinting technologies that can control the morphological features of cellular constructs to create highly functional engineered tissues. We have created a high-precision 3D spheroid printing technology that enhances both cell-to-cell and cell-ECM interactions. Additionally, we have developed a technology capable of precise patterning of microvasculature composed of capillaries. These technologies have shown high efficacy in the artificial regeneration of tissues such as the liver, pancreas, vascular, and adipose tissue. Furthermore, they have demonstrated excellent performance in the development of cancer models and cell therapy. In this presentation, I will present the advanced bioprinting technologies developed in our laboratory and their applications in tissue engineering, including the artificial regeneration of various tissues and organs, as well as their potential in cancer models and cell therapy.

Keywords: 3D bioprinting, engineered tissue, disease model

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Session 2-1 **연구결과 발표**

Pan-cancer Analysis of the Coatomer Complex Reveals Its Importance during Cancer Progression

센서스미타
융합의과학과

Pan-cancer Analysis of the Coatomer Complex Reveals Its Importance during Cancer Progression

Susmita Sen[1]*, Van-Thanh Duong[1], Young-In Hwang[1], Ui Jin Lee[1], Hyojin Kim[1], Han-Sol Park[1], Jeong han Kim[1], Myoung-Eun Han[1*], Sae-Ock Oh[1*]

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The coatomer protein complex I (COPI), classically known for vesicular trafficking between the Golgi and endoplasmic reticulum (ER), is increasingly implicated in cancer biology. We performed a comprehensive pan-cancer analysis of 20 coatomer genes (COPI/COPII subunits) across 33 cancer types. Amplifications were the most frequent alterations, with COPA most commonly amplified, while SEC31B was consistently downregulated. In uterine corpus endometrial carcinoma (UCEC), mutations in COPA and SEC31A were prognostically significant ($p = 0.048$, 0.032). Survival analyses revealed cancer-type specific roles: most subunits were tumor suppressive in kidney renal clear cell carcinoma (KIRC) but oncogenic in low-grade glioma (LGG) and hepatocellular carcinoma (LIHC).

Functional validation in LIHC identified "COPG1" as a novel oncogenic driver. "COPG1" was overexpressed in tumors, and high expression correlated with poor survival. "COPG1" knockdown impaired proliferation, migration, and invasion, suppressed PI3K–AKT–mTOR signaling, and activated the unfolded protein response, accompanied by Golgi fragmentation, impaired Er-resident protein retrieval, and mitochondrial ROS accumulation. Notably, "*COPG1"* silencing significantly increased the sensitivity of HCC cells to sorafenib and doxorubicin.

These findings establish "COPG1" as a multifaceted regulator of organelle homeostasis and oncogenic signaling, positioning it as a potential therapeutic target in HCC and other cancers characterized by coatomer complex dysregulation.

Keywords: Coatomer complex subunits, pan-cancer, COPG1, prognosis, amplification, mutation, overexpression, dependency score, Golgi-ER stress, chemoresistance

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Session 2-1 **연구결과 발표**

Aptamer-Based Optical Biosensor Utilizing Metal-Enhanced Fluorescence for Liver Cancer Biomarker Detection

김나영
정보융합공학과

Aptamer-Based Optical Biosensor Utilizing Metal-Enhanced Fluorescence for Liver Cancer Biomarker Detection

Nayoung Kim[1], Euni Cho[1], Mingyu Bae[1] and Jin-Ho Lee[1,2*]

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Liver cancer is a serious disease with a high mortality rate worldwide, and it is particularly challenging to identify at an early stage. Therefore, sensitive diagnostic technologies capable of rapidly and accurately detecting liver cancer biomarkers are essential for improving patient prognosis.

In this study, we developed a highly sensitive biosensing platform based on metal-enhanced fluorescence (MEF) utilizing plasmonic gold (Au) nanostructures to detect liver cancer biomarkers. Laser Interference Lithography (LIL) combined with gold deposition enabled the fabrication of uniform and optimized Au nanostructures. Specific DNA aptamers were immobilized on the precisely fabricated Au nanopatterned array, each designed to selectively recognize target biomarkers. The fluorophores were carefully selected to exhibit strong spectral overlap and resonance with the localized surface plasmon resonance (LSPR) of the Au nanostructures, thereby maximizing fluorescence enhancement.

The detection mechanism relies on conformational changes of the aptamer upon target binding, which modulate the fluorescence intensity depending on the distance between the fluorophore and the surface of the Au nanostructure. By systematically optimizing the nanostructure geometry and aptamer configuration, the MEF effect was significantly enhanced, allowing for highly sensitive detection even at low biomarker concentrations.

This MEF-based aptasensor platform demonstrates strong potential as a versatile and sensitive tool for early diagnosis of liver cancer and could contribute to the advancement of precise and personalized diagnostic strategies.

Keywords: Biosensors; Cancer Diagnosis; Metal-Enhanced Fluorescence; Liver Cancer: Au Nanoarray; Biomarkers; Aptamer

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Session 2-1 **연구결과 발표**

Optimization of a CD166-Targeting Aptamer using an Integrated In Silico - In Vitro Strategy

이서율
융합의과학과

Optimization of a CD166-Targeting Aptamer using an Integrated In Silico - In Vitro Strategy

Seo Yul Lee

Aptamers are next-generation targeting ligands known for their high specificity and stability. This study focuses on an aptamer that targets CD166, a protein involved in cancer stem cell properties and metastasis. The goal is to overcome traditional high-cost, time-consuming in vitro optimization methods by applying an integrated in silico simulation and in vitro experimental strategy. First, we established a foundation for Molecular Dynamics (MD) simulation by developing the world's first new parameters for the modified base (BndU) included in the aptamer. We predicted the 2D/3D structure of the Full-Length aptamer (using mfold and rosetta FARFAR2) and performed MD simulations (Amber) to analyze its structural dynamics. Based on these results, multiple truncated aptamer candidates were designed. MD simulations were then performed for each candidate to secure various in silico metrics, such as structural difference from Full-Length (RMSD-comparison), stability (RMSD-slope), and flexibility (RMSF-corr, RMSF-avg). Concurrently, the actual cancer cell binding affinity (Fluorescence) of each candidate was measured via in vitro Flow cytometry experiments. Analysis of the correlation between the two data sets revealed a very high negative correlation (Pearson's $r = -0.748$, $p = 0.0082$) between the 'structural difference from Full-Length (RMSD)' metric and 'cell binding affinity'. This suggests that in silico analysis alone can significantly predict relative binding affinity. Based on this correlation, T53-40 (a 40 nt sequence) was selected as the final candidate, showing the best structural similarity and high binding affinity. SPR analysis confirmed that the selected T53-40 maintained a high binding affinity (KD 49.4 nM), almost identical to the 76 nt Full-Length aptamer (KD 49.5 nM). Furthermore, epitope mapping (Direct-ELISA) verified that T53-40 binds to the same CD166 C2-3 domain as the Full-Length aptamer. In conclusion, this study successfully optimized a CD166 aptamer through an integrated in silico-in vitro strategy, and the optimization platform established in this process can be effectively utilized for the future development of other aptamers.

2025년 부산대학교
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Session 2-1 **연구결과 발표**

Microenvironment-guided Evolution of ssDNA-SWCNT Probes for Selective Recognition of Aggressive Prostate Cancer Phenotypes

정상화 교수
의생명융합공학부

Microenvironment-guided Evolution of ssDNA-SWCNT Probes for Selective Recognition of Aggressive Prostate Cancer Phenotypes

Sanghwa Jeong

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Despite advances in prostate cancer detection, distinguishing indolent from aggressive phenotypes remains challenging. We report a microenvironment-guided strategy for evolving phenotype-specific molecular probes using single-stranded DNA-functionalized single-walled carbon nanotubes (ssDNA-SWCNTs). Our approach employs 3D tumor models that recapitulate complex cancer microenvironments, enabling identification of ssDNA sequences with differential binding properties. We developed two distinct probes for prostate cancer cells: PC3D2, which preferentially binds hypoxia-adapted stem-like cells associated with treatment resistance, and PC2D2, which shows enhanced binding to mesenchymal-like cells. These probes exhibit characteristic second near-infrared (NIR-II, 1000-1700 nm) fluorescence, enabling non-invasive detection of aggressive phenotypes in heterogeneous tumors using NIR-II optical imaging. We demonstrate their utility for selective drug delivery to prostate cancer spheroids, resulting in enhanced therapeutic efficacy. This platform represents a significant advancement in precision diagnostics and theranostics, potentially transforming prostate cancer management through phenotype-specific targeting. The methodology offers a generalizable approach for developing nanoprobes that recognize clinically relevant cancer phenotypes based on their unique microenvironmental signatures rather than individual biomarkers.

Session 2-1 **연구결과 발표**

A Robust Marine Collagen Peptide–Agarose 3D Culture System for In Vitro Modeling of Hepatocellular Carcinoma and Anti-Cancer Therapeutic Development

라즈봉시라타
융합의과학과

A Robust Marine Collagen Peptide–Agarose 3D Culture System for In Vitro Modeling of Hepatocellular Carcinoma and Anti-Cancer Therapeutic Development

Lata Rajbongshi, Ji-Eun Kim, Su-Rin Lee, Seon-Yeong Hwang, Dongjun Lee, Byoung Soo Kim, Sae-Ock Oh, and Sik Yoon

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The development of physiologically relevant three-dimensional (3D) culture systems is essential for modeling tumor complexity and improving the translational impact of cancer research. We established a 3D in vitro model of human hepatocellular carcinoma (HCC) using a marine collagen peptide-based (MCP-B) biomimetic hydrogel scaffold optimized for multicellular spheroid growth. Compared with conventional two-dimensional (2D) cultures, the MCP-B hydrogel more accurately recapitulated native tumor biology while offering simplicity, reproducibility, bioactivity, and cost efficiency. HCC cells cultured in MCP-B hydrogel displayed tumor-associated behaviors, including enhanced proliferation, colony formation, migration, invasion, and chemoresistance, and enriched cancer stem cell (CSC) populations. Molecular analyses revealed upregulated expression of genes associated with multidrug resistance; stemness regulation and markers; epithelial–mesenchymal transition (EMT) transcription factors, markers, and effectors; growth factors and their receptors; and cancer progression. The spheroids also retained liver-specific functions, suppressed apoptotic signaling, and exhibited extracellular matrix remodeling signatures. Collectively, these findings demonstrate that the 3D HCC model using MCP-B hydrogel recapitulates key hallmarks of tumor biology and provides a robust, physiologically relevant platform for mechanistic studies of HCC and CSC biology. This model further holds translational value for preclinical drug screening and the development of novel anti-HCC and anti-CSC therapeutics.

Keywords: marine collagen; scaffold; hydrogel; 3D cell culture; spheroid; hepatocellular carcinoma (HCC); liver cancer stem cell; chemoresistance

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Session 2-1 **연구결과 발표**

Development of Tumor Assembloid latform Via 3D Bioprinting of Spheroids to Investigate Time-Dependent Drug Responses

최민서
정보융합공학과

Development of Tumor Assembloid Platform Via 3D Bioprinting of Spheroids to Investigate Time-Dependent Drug Responses

[1] 최민서(부산대학교), [2] 안민준(부산대학교), [1] 이석현(부산대학교), [1,*] 김병수(부산대학교)

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Cancer develops heterogeneous characteristics through dynamic interactions within the tumor microenvironment (TME). Among its components, fibroblasts play a critical role by transforming into cancer-associated fibroblasts (CAFs) via intercellular signaling, thereby significantly influencing co-culture models. However, conventional co-culture models remain limited in their ability to recapitulate the sequential and spatially regulated processes underlying tumor–stroma interactions. To address these limitations, we developed an Assembloid platform that allows spatial control of cancer and fibroblast spheroids. When the two spheroids were positioned at a Pre-contact, active interactions were observed. Nonetheless, the absence of spatial confinement over time resulted in diminished fibroblast activation. To counter this, we incorporated biocompatible alginate lacking RGD peptides, thereby creating an environment that favors cell–cell adhesion over focal adhesion. The alginate-supplemented group exhibited elevated expression of cell adhesion markers relative to focal adhesion markers. Through qualitative analysis, we observed directional and reciprocal migration: fibroblasts migrated toward cancer spheroids, and cancer cells moved toward fibroblast spheroids. This behavior is presumed to be driven by paracrine signaling between the two cell types. Subsequently, the developed Assembloid platform was validated to confirm whether sufficient fusion occurred from both physical and biological perspectives.

Keywords: 3D In-bath bioprinting, CAF, Co-culture, Assembloid platform

Session 2-2

포스터발표

Protein X, a Dynein-1 Motor Complex Component, Drives Tumor Growth and Poor Survival in Hepatocellular Carcinoma

Van-Thanh Duong[1], Young -In Hwang[1], Han-Sol Park[1], Hyojin Kim[1], Jeong Han Kim[1], Sen Susmita[1], Myoung-Eun Han[1], Sae-Ock Oh[1]*

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Protein X, a component of the cytoplasmic dynein-1 motor complex, functions as an intermediate chain that tethers the complex to cargo, thereby facilitating organelle positioning, mitotic spindle assembly, and intracellular trafficking. Aberrant regulation of this protein has been implicated in tumorigenesis. Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and a leading cause of cancer-related deaths worldwide. Here, we investigated the clinical significance and functional role of protein X in HCC. Analysis of The Cancer Genome Atlas (TCGA, n = 369) revealed that Gene X expression was significantly elevated in HCC tissues compared with normal liver tissues, and higher expression was associated with shorter overall survival. To determine its biological role, we performed siRNA-mediated knockdown of Gene X in HCC cells. Loss of Gene X significantly suppressed cell proliferation (EZ-Cytox, colony formation), migration (wound healing, Boyden chamber), and invasion (Matrigel assay), indicating its contribution to HCC progression as an oncogenic driver. Furthermore, RNA-seq analysis showed that silencing Gene X suppressed the intrinsic apoptotic pathway ($p < 0.05$, NES = 1.89) and modulated apoptosis-related genes such as BCL2L1, BAK1, BAX (fold change 1.3 - 2.0), suggesting its role in promoting HCC progression through apoptosis inhibition. Collectively, our results demonstrate that protein X functions as an oncogenic driver in HCC and highlight its potential as both a prognostic biomarker and a novel therapeutic target.

Keywords: Protein X, Hepatocellular carcinoma (HCC), BCL2L1, Biomarker, Apoptosis.

Identification of Proteasome Subunits as a Potential Therapeutic Target for Cancer Therapy using Pan-cancer Analysis and Validation of Protein K as a Target in Hepatocellular Carcinoma

JeongHan Kim [1]*, Han-Sol Park [1], HyojinKim[1], Sen Susmita[1], Van-Thanh Duong[1], Young -In Hwang[1], Myoung-EunHan [1]*, Sae-OckOh [1]*

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Pan-Cancer Functional Analysis of Proteasomal Subunits Reveals Subunit-Specific Therapeutic Vulnerabilities, Validating Protein K in Hepatocellular Carcinoma. The proteasome system is essential for protein homeostasis and frequently altered in cancer. To find subunit-specific therapeutic targets, we systematically analyzed the functional dependency of 49 proteasomal subunits across 54 cancer types using CRISPR and RNAi perturbation data (DepMap). Fifteen subunits (CRISPR) and 31 subunits (RNAi) exhibited selective lethality. Nine subunits, including PSMB5 and PSMB6 (identified as broad-spectrum targets), showed consistent selective dependency across both platforms. Dependency correlation analyses further linked subunit vulnerability to genomic alterations and oncogenic signaling pathways. Crucially, the analysis suggested Protein K as a promising target. We confirmed Protein K overexpression in HCC and demonstrated that Protein K knockdown significantly suppressed HCC cell line proliferation, migration, invasiveness, and tumorigenicity in vitro and in vivo. This comprehensive analysis reveals the functional heterogeneity and therapeutic potential of individual proteasomal subunits. It establishes a foundation for developing subunit specific anti-cancer strategies and validates Protein K as a potent novel target for Hepatocellular Carcinoma therapy.

Keywords: HCC, hepatocellular carcinoma, proteasome, UPR, unfolded protein reaction, Pan-cancer

A COP9 Signalosome Subunit, as a Therapeutic Target in hepatocellular carcinoma (HCC), regulates the tumorigenicity of HCC cells via ER Stress–UPR Pathway.

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The COP9 signalosome (CSN) complex regulates protein degradation and cellular homeostasis through ubiquitination and neddylation. Abnormal CSN activity contributes to tumorigenesis by interfering with normal angiogenesis, DNA repair, and the cell cycle. Hepatocellular carcinoma (HCC) is a major cause of cancer mortality, necessitating the development of novel biomarkers and therapeutic targets. In this study, we targeted gene H, a CSN subunit, to elucidate its role and associated pathways in HCC. Significant overexpression of gene H was observed in liver cancer patient tissues from the TCGA (n = 372), and high gene H expression levels were associated with poor patient survival. Functionally, decreased gene H expression inhibited HCC cell proliferation, migration, invasion, and colony formation. Furthermore, gene H deficiency induced upregulation of UPR markers and target genes. The UPR is a cellular adaptive pathway activated by endoplasmic reticulum (ER) stress. It restores protein homeostasis, but dysregulated expression can also induce apoptosis. This suggests that gene H may partially regulate hepatocellular carcinoma (HCC) progression by modulating ER stress and UPR signaling. Based on these findings, we conclude that gene H may be a tumorigenic factor in HCC, suggesting that it may serve as a prognostic biomarker as well as a potential therapeutic target. Current research aims to elucidate further the molecular mechanisms linking gene H, UPR activation, and HCC progression.

Keywords: COP9 signalosome (CSN) subunit, Hepatocellular carcinoma (HCC), ER Stress–UPR Pathway.

Gene S Promotes Hepatocellular Carcinoma Progression via Ribotoxic Stress and Atypical UPR Pathways

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Background: Hepatocellular carcinoma (HCC) remains a leading cause of cancer-related mortality, with limited therapeutic options and poor prognosis. Recent evidence suggests that ribosomal proteins exert extra-ribosomal functions contributing to tumorigenesis.

Objective: We aimed to investigate the role of the small ribosomal subunit protein Gene S in HCC, focusing on its expression, prognostic significance, and involvement in ribotoxic stress and unfolded protein response (UPR) pathways.

Methods and Results: TCGA analysis revealed significant overexpression of Gene S in HCC compared to normal liver tissues ($p<0.001$), and high Gene S expression was associated with poor overall survival in Kaplan–Meier analysis. Functional assays demonstrated that siRNA-mediated knockdown of Gene S markedly reduced proliferation, migration, invasion, and tumorigenicity in HCC cell lines. Mechanistic studies further showed that Gene S depletion induced phosphorylation of ZAK and subsequent activation of the p38/JNK–CHOP axis, consistent with ribotoxic stress signaling. In contrast, while GCN2 phosphorylation was increased, ATF4 expression was decreased, indicating a non-canonical UPR pattern distinct from the conventional ISR pathway.

Conclusion: Gene S is overexpressed in HCC and correlates with poor prognosis. It promotes tumor progression through ribotoxic stress and atypical UPR signaling, suggesting its potential as a novel prognostic biomarker and therapeutic target in HCC.

Keywords: HCC, ribotoxic stress, prognostic biomarker

Splicing Factor Gene X Promotes Hepatocellular Carcinoma Progression via the Unfolded Protein Response

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Analysis of The Cancer Genome Atlas (TCGA) data revealed that **Gene X** is significantly overexpressed in hepatocellular carcinoma (HCC) tissues and correlates with poorer patient survival. To elucidate its functional role, we performed siRNA-mediated knockdown experiments in HCC cell lines. Gene X silencing markedly reduced cell proliferation, migration, and invasion, suggesting that Gene X functions as an oncogenic driver in HCC progression. Transcriptomic analysis further demonstrated activation of the **Unfolded Protein Response (UPR)** pathway following Gene X knockdown, indicating a link between splicing dysregulation and proteostasis imbalance. Collectively, our findings identify Gene X as a potential diagnostic biomarker and promising therapeutic target for HCC.

Keywords: Splicing factor, Hepatocellular carcinoma (HCC), Unfolded protein response (UPR)

PPARα antagonist is a potential therapeutic target to overcome sorafenib resistance in hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related death worldwide. Sorafenib is the first-line systemic therapy for advanced HCC; however, long-term treatment often leads to the development of drug resistance, contributing to tumor recurrence and poor prognosis. The Peroxisome Proliferator-Activated Receptor α (PPARα) plays a critical role in cell proliferation, metabolic regulation, and drug resistance in various cancers. Therefore, this study aimed to evaluate the anti-cancer efficacy of a PPARα antagonist (Compound A) and its synergistic potential with sorafenib in HCC. The SNU475 cell line, a sorafenib-resistant HCC model, was treated with Compound A alone or in combination with sorafenib. PPARα expression and enzymatic activity were significantly upregulated in SNU475 cells compared with sorafenib-sensitive cells, and treatment with Compound A effectively suppressed PPARα activity. Compound A alone reduced cell viability and metabolic activity, while co-treatment with sorafenib exhibited synergistic cytotoxic effects and enhanced apoptotic signaling. Furthermore, colony formation was markedly reduced by the combination treatment. Collectively, PPARα inhibition effectively blocks the metabolic adaptation underlying sorafenib resistance and enhances the anti-tumor efficacy of sorafenib. These findings suggest that the combination of sorafenib and Compound A may represent a promising therapeutic strategy for overcoming drug resistance in hepatocellular carcinoma.

BRD4 Degrader Enhances Synthetic Lethality in Drug-Resistant Ovarian Cancer

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Ovarian cancer is often asymptomatic in its early stages and is frequently diagnosed at advanced stages (FIGO stage III or IV), contributing to its high mortality rate among gynecologic malignancies. The standard therapeutic approach involves surgical resection of the tumor followed by chemotherapy. However, most patients eventually develop chemoresistance, leading to recurrence and metastasis. The underlying mechanism of this resistance involves enhanced DNA damage repair capacity. the antitumor efficacy of proteolytic targeting chimera (PROTAC) that targets BRD4, which plays a critical role in DNA damage repair, was evaluated in both parental and drug-resistant ovarian cancer models. Comparative analyses of two PROTAC compounds were performed using drug-resistance ovarian cancer cell lines, including A2780-R and PEO1-R cells. Compound B exhibited superior BRD4 degradation and lower IC50 values compared to compound A, particularly in A2780-R, a doxorubicin-resistant ovarian cancer cell line. Combination treatment with compound B and DNA-damaging agents synergistically reduced cell viability, while enhancing DNA damage and apoptosis. Importantly, BRD4 degradation sensitized PEO1-R, a homologous recombination-proficient cell line, to olaparib, suggesting a synthetic lethality mechanism independent of BRCA1/2 status. These results support compound B as a promising drug candidate for overcoming drug resistance and enhancing the efficacy of DNA-damaging agents in ovarian cancer.

Transdermal Delivery of Polysccharide-Conjugated W-Peptide Ameliorates Bleomycin-Induced Skin Fibrosis

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Systemic sclerosis is an autoimmune disease that causes extensive fibrosis and inflammation of the skin and internal organs. Subcutaneous administration of W-peptide, a formyl peptide receptor agonist, alleviated fibrosis and inflammation in skin. However, the skin barrier requires repeated and invasive administration of Wm into skin tissue. Polysaccharide (PS), a natural mucopolysaccharide, is used as a drug carrier for transdermal protein delivery. To elucidate the effects of PS on the transdermal delivery of W-pep, we conjugated PS and W-pep, and investigated the effects of topical treatment with PS-conjugated W-pep (PS-W) on a bleomycin-induced skin fibrosis mouse model. Topical treatment with PS-W-pep significantly reduced dermal thickness and collagen deposition in the bleomycin-induced skin fibrosis model. However, topical treatment with neither W-pep nor PS significantly affected fibrosis or inflammation. PS-W treatment reduced the numbers of α-SMA-positive myofibroblasts and CD68-positive macrophages in the fibrotic skin. PS-W treatment inhibited lipopolysaccharide-induced chemotactic migration of macrophages and the expression of TNF-α, and IFN-γ in macrophages *in vitro*. However, PS-W treatment had no significant effect on bleomycin-induced skin fibrosis and inflammation in the *Fpr2*-knockout mice. Taken together, these results suggest that topical treatment with PS-W alleviates bleomycin-induced fibrosis and inflammation via an FPR2-dependent mechanism.

UFMylation of Protein A: A Potential Novel Regulator in Colorectal Cancer

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Colorectal cancer (CRC) remains one of the leading causes of cancer-related mortality worldwide, underscoring the importance of finding new regulatory mechanisms and therapeutic targets. Post-translational modifications (PTMs) play a crucial role in cancer progression; however, the function of UFMylation in CRC is poorly understood. In this study, we have discovered that Protein A is a new target of UFM1-mediated UFMylation and have confirmed its conjugation through biochemical analyses. This modification suggests a potential role in cellular homeostasis, protein stability, and oncogenic signaling regulation. Although the precise impact of UFMylation on CRC progression remains to be fully elucidated, its involvement in key cellular pathways highlights its significance. Further studies on the UFM1-Protein A axis may uncover novel mechanisms underlying CRC tumorigenesis and provide potential therapeutic strategies targeting UFMylation-related pathways.

Role of Gene A in Regulating Proliferation and Metastatic Potential of Hepatocellular Carcinoma

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This study investigated the role of Gene A in regulating the proliferative and metastatic properties of hepatocellular carcinoma (HCC) cells. Analysis of TCGA and GEO datasets revealed that Gene A expression was elevated in patients with HCC compared with normal individuals. Based on this finding, Gene A knockdown was performed in HepG2 cells, which exhibited the highest basal level of Gene A among tested HCC cell lines. Silencing of Gene A significantly reduced cell viability and proliferation, as confirmed by EdU assays, and resulted in dysregulated cell-cycle control characterized by decreased Cyclin D1 and increased CDK2 and Cyclin B1 expression. PI staining based cell-cycle analysis further showed a reduction in the G1 population accompanied by a relative accumulation of cells in the S/G2 phases, indicating impaired G1/S checkpoint regulation. In addition, scratch-induced migration, Transwell migration, and invasion assays demonstrated that Gene A knockdown markedly suppressed cellular motility and invasiveness. Anchorage-independent colony formation and 3D spheroid/organoid growth were significantly reduced, reflecting decreased tumorigenic potential. Moreover, reduced expression of β-catenin, Snail, and Slug suggested the inhibition of EMT. Collectively, these results demonstrate that Gene A depletion attenuates the proliferative, migratory, and tumorigenic capacities of HCC cells, highlighting Gene A as a key molecular regulator and potential therapeutic target in HCC.

Targeting Gene A in Hepatocellular Carcinoma: Antitumor Efficacy and Mechanistic Analysis of Combined *Drug A* Treatment

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Hepatocellular carcinoma (HCC) accounts for nearly 80% of primary liver cancers and remains one of the leading causes of cancer-related mortality worldwide. Despite the clinical availability of sorafenib, the overall survival rate of advanced HCC patients remains unsatisfactory, mainly due to drug resistance and the absence of reliable biomarkers predicting therapeutic response. Gene A, a member of the protein disulfide isomerase family, has been reported overexpressed in multiple malignancies, including HCC, and is associated with tumor proliferation, invasion, metastasis, and poor prognosis. However, the therapeutic potential of Gene A inhibition in HCC has not been fully explored.

In this study, we investigated the oncogenic role of Gene A and evaluated the antitumor efficacy of a novel drug-repositioning strategy using *Drug A*, a calcium channel blocker known to target Gene A. Gene A was found to be highly expressed in HCC cell lines and tumor tissues compared with normal controls. *Drug A* treatment significantly suppressed HCC cell proliferation. Our finding highlights Gene A as a tumor-specific oncogenic chaperone and a promising therapeutic target in HCC. Building on the premise that *Drug A* targets Gene A, this study provides new insights into improving therapeutic outcomes for HCC.

Early Liver Cancer Diagnosis via a Machine Learning-Enabled Fluorescent Nanosensor Array

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Liver cancer is one of the leading causes of cancer-related deaths worldwide, largely due to its late diagnosis and rapid progression. Early-stage detection dramatically improves prognosis, with survival rates exceeding 70% when diagnosed early but dropping below 20% at advanced stages. However, conventional diagnostic approaches relying on single biomarkers such as alpha-fetoprotein (AFP) suffer from low sensitivity and specificity, cannot represent the complex biological changes that happen in the early stages of liver cancer.

This study presents a digital biomarker platform that integrates a fluorescence-based multi-nanosensor array with machine learning for early liver cancer detection. Single-walled carbon nanotubes (SWCNTs) were functionalized with various amino acids via covalent conjugation and single-stranded DNA (ssDNA) sequences via non-covalent adsorption, forming 25 distinct corona phases on the SWCNT surface. These nanosensors were used to analyze 200 serum samples, generating high-dimensional fluorescence data reflecting molecular interactions specific to liver cancer progression.

The nanosensor array operates analogously to an electronic tongue, where each nanosensor responds uniquely to a wide range of biomolecules in patient serum. Variations in fluorescence intensity before and after exposure create a multidimensional fingerprint representing the biochemical state associated with early-stage liver cancer. These fluorescence patterns were analyzed using machine learning algorithms for classification and feature extraction.

This platform provides a rapid, cost-effective, and scalable approach for the early and accurate diagnosis of liver cancer, offering potential for integration into clinical screening systems and personalized oncology diagnostics.

Polydopamine Coating Enhances Adhesion, Migration, Proliferation, Chemoresistance, Stemness, and Epithelial–Mesenchymal Transition in Human Hepatocellular Carcinoma and Human Prostate Cancer Cells via FAK/JNK Signaling

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Surface modification using polydopamine (PDA) has emerged as a versatile technique with broad applications in various fields such as materials science, regenerative medicine, and theranostics. While PDA coatings have shown promising results in enhancing cell adhesion, proliferation, and migration in diverse cell types, their impact on cancer cell behavior remains poorly understood. In this study, we investigated the effects of PDA-coated surfaces on hepatocellular carcinoma (HCC) and prostate cancer (PC) cells and elucidated the underlying mechanisms. Our findings reveal that PDA coating significantly increases cell adhesion, proliferation, and migration of HCC and PC cells, leading to the induction of epithelial-mesenchymal transition (EMT) and chemoresistance. Moreover, we identified the involvement of integrin-mediated activation of the FAK/JNK signaling pathway. These results provide valuable insights into the role of PDA in cancer progression and suggest new avenues for its application in HCC and PC cancer research and therapy.

Marine Collagen as a Culture Media Additive Enhances Spheroid Circularity and Malignant Phenotypes in Three-Dimensional Hepatocellular Carcinoma Models

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Three-dimensional (3D) spheroid culture systems have become valuable tools for modeling tumor biology and assessing drug efficacy. However, variability in spheroid morphology often limits the reproducibility and comparability of results across cell types. Achieving consistent, circular spheroids is critical for maintaining physiologically relevant gradients of oxygen, nutrients, and drugs within the 3D architecture. In this study, we investigated the effect of incorporating marine collagen (MC) as a media additive on the formation, morphology, and biological characteristics of hepatocellular carcinoma (HCC) spheroids. The addition of MC significantly improved spheroid circularity and compactness, yielding more uniform and physiologically relevant structures. Notably, HCC cells cultured in MC-supplemented media exhibited enhanced malignant behaviors, including increased proliferation, migration, invasion, and chemoresistance. Molecular analyses revealed upregulation of genes associated with multidrug resistance, stemness, epithelial–mesenchymal transition (EMT), and tumor progression. The spheroids also retained liver-specific functions and displayed extracellular matrix remodeling signatures. Collectively, our findings demonstrate that MC supplementation promotes the structural and functional maturation of HCC spheroids, recapitulating key hallmarks of tumor biology. This optimized 3D culture system provides a robust, reproducible, and physiologically relevant platform for mechanistic studies of HCC progression, CSC regulation, and preclinical drug screening.

mTOR and heat shock protein 90 are involved in inflammation induced by 27-hydroxycholesterol

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Atherosclerosis is a disease in which extracellular cholesterol and inflammatory cells are deposited and accumulated in arterial blood vessel walls. 27-hydroxycelosterol(27HC) is the most abundant cholesterol metabolite in atherosclerosis. 27HC is a bioactive immune oxysterol that induces inflammatory responses, such as activation of immune cells and secretion of chemokine, but its molecular mechanisms are not well known. In this study, we investigated the roles of mechanistic target of rapamycin (mTOR) and heat shock protein 90 (Hsp90) in 27HC-induced inflammation using rapamycin and ganetespib, respectively. When THP-1 monocytic cells were treated with rapamycin, the expression of CCL2, which was increase by 27HC, was reduced. It also suppressed the effect of 27HC, which upregulates the expression and phosphorylation of S6 and 4EBP1. Treatment with ganetespib not only reduced the production of CCL2 but also inhibited the expression and phosphorylation of S6, 4EBP1 and AKT increased by 27HC. Together, these results indicate that 27HC induces inflammation by activating the HSP90/AKT/mTOR signaling pathway and demonstrate that rapamycin and ganetespib can be useful for the treatment of inflammatory diseases involving 27HC.

Promotion of Bone Formation in a Rat Osteoporotic Vertebral Body Defect Model via Suppression of Osteoclastogenesis by Ectopic Embryonic Calvaria Derived Mesenchymal Stem Cells

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Osteoporotic vertebral compression fractures (OVCFs) are the most prevalent fractures among patients with osteoporosis, leading to severe pain, deformities, and even death. This study explored the use of ectopic embryonic calvaria derived mesenchymal stem cells (EE-cMSCs), which are known for their superior differentiation and proliferation capabilities, as a potential treatment for bone regeneration in OVCFs. We evaluated the impact of EE-cMSCs on osteoclastogenesis in a RAW264.7 cell environment, which was induced by the receptor activator of nuclear factor kappa-beta ligand (RANKL), using cytochemical staining and quantitative real-time PCR. The osteogenic potential of EE-cMSCs was evaluated under various hydrogel conditions. An osteoporotic vertebral body bone defect model was established by inducing osteoporosis in rats through bilateral ovariectomy and creating defects in their coccygeal vertebral bodies. The effects of EE-cMSCs were examined using micro-computed tomography (μCT) and histology, including immunohistochemical analyses. In vitro, EE-cMSCs inhibited osteoclast differentiation and promoted osteogenesis in a 3D cell culture environment using fibrin hydrogel. Moreover, μCT and histological staining demonstrated increased new bone formation in the group treated with EE-cMSCs and fibrin. Immunostaining showed reduced osteoclast activity and bone resorption, alongside increased angiogenesis. Thus, EE-cMSCs can effectively promote bone regeneration and may represent a promising therapeutic approach for treating OVCFs.

Shear Stress-Mediated Heat Shock Protein Upregulation Orchestrates Monocytic Pro-Inflammatory Activation: Therapeutic Implications for Atherogenesis

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Endothelial denudation in arterial regions correlates with the recruitment and accumulation of mononuclear phagocytes, which demonstrate pronounced responsiveness to biomechanical forces, particularly hemodynamic shear stress. Despite this established relationship, the mechanistic influence of biomechanical stimulation on monocytic cellular responses remains inadequately characterized. To elucidate these mechanisms, we investigated the effects of laminar shear stress on inflammatory mediator expression and surface protein dynamics in human THP-1 monocytic cells.

Our findings demonstrate that exposure to physiological shear stress significantly upregulated the inflammatory chemokine CCL2, concomitant with enhanced transcriptional activation and proteomic alterations in monocytes, alongside elevated production of tumor necrosis factor (TNF)-α and interleukin (IL)-1β. Comprehensive mass spectrometry-based proteomic analysis revealed substantial augmentation of surface-associated heat shock protein 70 (HSP70), HSP90, and HSP105 expression levels, which were subsequently validated through complementary methodologies including immunoblotting, flow cytometric analysis, and immunofluorescence microscopy.

Pharmacological inhibition of HSP70/HSP105 and HSP90 significantly attenuated CCL2 expression, secretion, and monocytic chemotaxis, establishing a mechanistic link between heat shock protein expression and inflammatory cascade activation. Furthermore, immunohistochemical examination of atherosclerotic lesions from apolipoprotein E-deficient mice maintained on atherogenic diets and human femoral artery endarterectomy specimens

revealed enhanced HSP90 immunoreactivity with notable co-localization with CD68-positive macrophages.

These observations collectively indicate that shear stress-mediated polarization of monocytes/macrophages toward a pro-inflammatory phenotype is mechanistically associated with enhanced surface expression of heat shock proteins. Therapeutic modulation of HSP regulation in mononuclear phagocytes may represent a promising novel intervention strategy for mitigating shear stress-induced vascular inflammation.

Construction of a Fibrosis-Encapsulated Tumor model with Enhanced Barrier Function via In-Bath Bioprinting and Stepwise Stiffness Modulation

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Fibrosis is a hallmark of liver cancer, contributing to therapeutic resistance. However, conventional tumor models fail to recapitulate the progressively stiffening fibrotic microenvironment, and bridging this physiological gap is essential for the development of effective anti-fibrotic strategies. To address this, we developed a liver tumor model using hybrid spheroids fabricated via in-bath bioprinting with stepwise stiffness control. Liver-derived decellularized ECM (LdECM) was optimized at 1.5%, showing an elastic modulus (~1 kPa) comparable to native liver tissue and printability. Stepwise stiffening was induced through dual-step ionic crosslinking with low-molecular-weight alginate, allowing independent temporal control over matrix stiffening. A 60-minute saturation time enabled uniform alginate diffusion in 1 mm-thick LdECM gels. We established three stiffness profiles: Soft, Stiff (immediate), and Stepwise (after FA). Stepwise stiffening enhanced actin bundling, focal adhesion, and mechano transduction, inducing stiffness-dependent behaviors similar to those in the tumor microenvironment. These results demonstrate the potential of stepwise stiffness tunability to recapitulate fibrotic tumor microenvironments with functional barriers. This platform may serve as a relevant model for studying fibrosis-driven malignancy and evaluating barrier-targeted therapies.

Keywords: 3D In-bath bioprinting, Fibrosis, Stepwise Stiffness modulation, Hybrid Spheroids

Development of 3D Fibrotic Tumor Platform via Coaxial Bioprinting of 3D Spheroids

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Cancer cells activate neighboring fibroblasts into CAFs and promote ECM remodeling around the tumor, increasing tumor stiffness and drug resistance. Therefore, to overcome drug resistance caused by increased ECM stiffness through interactions between cancer cells and CAFs, it is necessary to develop a platform that precisely recapitulates these conditions. To faithfully replicate fibrotic tumors in vitro, this study developed a fabrication strategy using coaxial in-bath 3D bioprinting to create fibroblast-covered tumor structures. We hypothesized that replicating this physiologically relevant microenvironment would enhance CAF induction and promote fibrotic tumor development. To verify this, core-shell structured spheroids were fabricated using the breast cancer cell line MDA-MB-231. By adjusting core size and shell thickness, we optimized fibrotic tumor-mimetic spheroids that exhibited enhanced structural integrity and compartmentalization. Compared to mixed spheroids, the core-shell structures exhibited higher proliferation, reduced apoptosis, and elevated markers of CAF activation and ECM remodeling. The fibrotic shell significantly hindered doxorubicin penetration, leading to an increase in drug resistance. Furthermore, treatment with the TGF-β receptor inhibitor SB431542 suppressed fibrosis-related gene expression and improved drug sensitivity. These findings suggest the printed core-shell spheroid is a robust in vitro model for evaluating anti-fibrotic strategies and drug responses in fibrotic tumors

Keywords: 3D In-bath bioprinting, Fibrotic tumor, CAF, Coaxial Spheroids

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