Proceedings of the 6th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/2026.33147

Advances and Prospects of Retinoic Acid in the Treatment of Solid Tumors

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Abstract. Retinoic Acid (RA) is a core active metabolite derived from vitamin A. Its isomer, All-trans-retinoic Acid (ATRA), is one of the most common and classic drugs used in clinical cancer treatment. The core mechanism of action of retinoic acid involves its binding to Retinoic Acid Receptors (RARs) and Retinoic Acid X Receptors (RXRs) to form heterodimers. These heterodimers then bind to Retinoic Acid Response Elements (RAREs) in the promoter regions of target genes, thereby regulating gene expression and primarily influencing cell development, growth, and differentiation. This article systematically reviews the mechanism of action of retinoic acid (especially in leukemia), focusing on its combination strategies in the treatment of solid tumors, including the synergistic treatment of retinoic acid with immune checkpoint inhibitors, targeted drugs, and radiotherapy. It also analyzes the later applications of novel delivery systems and nanosystems. Furthermore, this article summarizes the major developments and discoveries in retinoic acid treatment in the past two years, and explores directions such as artificial intelligence-assisted new drug discovery, in order to provide a reference for the application of retinoic acid in the differentiation-inducing therapy for solid tumors.

Keywords: Retinoic acid, differentiation-inducing therapy, solid tumors, combination therapy

1. Introduction

Retinol (the alcoholic form of vitamin A) is first oxidized to retinaldehyde, and then further oxidized to Retinoic Acid (RA), the compound that plays a regulatory role in biological development. Retinoic acid contains a variety of isomers, mainly including all-trans retinoic acid and 13-cis retinoic acid. Among them, all-trans retinoic acid was the first drug to be used in clinical practice. As early as the 1960s, all-trans retinoic acid had already begun to emerge and was used in skin diseases such as ichthyosis and keratotic skin diseases [1]. In 1985, a team led by Academician Wang Zhenyi in China first discovered that ATRA was more therapeutically effective against APL than 13-cis-retinoic acid, a finding that was successfully translated into clinical practice in 1988, thereby ushering in a new era of APL treatment [2]. Subsequently, in 1999, it was discovered that all-trans-retinoic acid combined with Arsenic Trioxide Injection (ATO) had the potential to cure leukemia [3]. This article reviews the latest applications and future prospects of retinoic acid-based

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DOI: 10.54254/2753-8818/2026.33147

combination therapies with other drugs or treatment modalities, beginning with an overview of the mechanism of action of retinoic acid and its receptors.

2. Mechanism of action of retinoic acids in leukemia

ATRA, the most classic and common isomer, is a drug used in the clinical treatment of Acute Promyelocytic Leukemia (APL). Retinoic Acid (RA) acts as a ligand for Retinoic Acid Receptors (RARs) in the cell nucleus. These RARs bind to Retinoic Acid X Receptors (RXRs) to form heterodimeric complexes. These complexes then bind to Retinoic Acid Response Elements (RAREs) in the promoter regions of target genes to regulate gene transcription [4].

2.1. Acute promyelocytic leukemia

The core pathogenesis of APL involves chromosomal translocations that result in gene fusions. The classic t(15;17) translocation leads to the fusion of the Promyelocytic Leukemia Gene (PML) on chromosome 15 and the Retinoic Acid A Receptor Gene (RARα) on chromosome 17, forming the PML-RARα fusion gene. Through various mechanisms, this fusion protein induces differentiation arrest and malignant transformation of cells, ultimately leading to leukemia [5]. After the discovery in the 1980s that ATRA (or RA) could induce differentiation of the human promyelocytic leukemia cell line HL-60, researchers quickly discovered that ATRA has a specific therapeutic effect on Acute Promyelocytic Leukemia (APL) carrying a typical translocation between chromosomes 15 and 17, and has achieved significant results [6].

2.2. How does retinoic acid treat APL

The treatment regimen for APL is now very clear, changing from the original ATRA combined with chemotherapy to the current chemotherapy-free ATRA combined with arsenic trioxide therapy, with ATRA being the constant treatment [7]. Substantial data indicate that ATRA primarily treats APL through two mechanisms: by activating the transcription of differentiation-related genes, and by degrading the PML-RARα oncoprotein via autophagy [8]. The RARα/RXR heterodimer complex binds to RARE and recruits co-repressive complexes, namely HDAC and co-repressor complexes (SMRT and NCoR1), to inhibit gene transcription. On the one hand, in APL cells, the PML-RARα protein enhances the binding of the co-repressive complex. After the addition of ATRA, ATRA specifically binds to the RARα region to change its conformation, promotes the dissociation of the co-repression complex, and restores the transcription of differentiation genes. First, in APL cells, the PML-RARα fusion protein enhances the recruitment of co-repressor complexes. Upon binding of ATRA to the RARα region, the conformational change induced in the receptor promotes the dissociation of these co-repressor complexes, thereby restoring the transcription of differentiation-related genes.

3. The combined use of retinoic acid with other drugs or technologies in the treatment of solid tumors

3.1. Synergistic effect of retinoic acid and Immune Checkpoint Inhibitors

Immune Checkpoint Inhibitors (ICIs) were developed following the initial discovery of tumor-specific antigens in a mouse model of T-cell lymphoma in 1982 [9] and are now applied in the treatment of malignancies such as melanoma, non-small cell lung cancer, and renal cell carcinoma

DOI: 10.54254/2753-8818/2026.33147

[10]. Retinoic acid, as a classic differentiation inducer, works synergistically with ICIs to excert significant anti-tumor effects. The core mechanism underlying this synergy is that RA can target and regulate Myeloid-derived Suppressor Cells (MDSCs) to assist ICIs in enhancing their efficacy. MDSCs are a class of heterogeneous myeloid cells that inhibit the immune function of T cells by secreting some soluble factors (such as ARG-1, IDO, etc.) and expressing high concentrations of PD-L1 [11]. "Experimental studies have demonstrated that ATRA can rapidly activate the ERK1/2 signaling pathway, upregulate Glutathione Synthase (GSS) in MDSCs, and cause Glutathione (GSH) to accumulate in them, thereby promoting the differentiation of MDSCs into mature bone marrow cells [12].

Based on the established mechanisms, the combined use of ICI and ATRA has shown significant effects in the treatment of solid tumors. For example, a phase I/II clinical trial (NCT03200847) evaluated pembrolizumab combined with ATRA in metastatic melanoma. Among 24 patients with metastatic melanoma who were naïve to anti-PD-1/PD-L1 therapy, the survival rate at the time of analysis was 58%. The subsequent five-year Overall Survival (OS) rate was 54.7% (95% CI: 36.4–82.1). This result fully demonstrates that ATRA can enhance the efficacy of pembrolizumab. However, some experiments have also shown that the therapeutic effects of immunosuppressants vary greatly among patients with different molecular subtypes of endometrial cancer [13].

3.2. Combination strategy of retinoic acid and targeted therapy drugs

The core mechanism underlying the combination of retinoic acid with targeted drugs involves multi-target synergy and the overcoming of drug resistance. Generally, while ATRA and its receptors directly inhibit tumors by initiating the transcription of differentiation-related genes, they can also modulate multiple signaling pathways, thereby assisting targeted drug therapy through various means.

In the field of non-small cell lung adenocarcinoma, Yao et al. first demonstrated that ATRA could prevent the enrichment of cancer stem cells induced by gefitinib by reducing the high expression of ALDH1A1/CD44 in Cancer Stem Cell-like Cells (CSCs) and reverse gefitinib resistance [14]. In colorectal cancer, Yoshida et al. reported that retinoic acid agents strongly and synergistically enhance the antitumor effect of combined BRAF/MEK/EGFR inhibition against BRAF\V600E-mutant tumors by inducing apoptosis through their receptors (RARα or RXRα) [15].

In Hepatocellular Carcinoma (HCC), sorafenib is a popular drug for prolonging patient survival. In 2015, Guang et al. found that ATRA could enhance its efficacy and improve prognosis by reducing AKT activity [16]. In the same year, Ishijima N in Japan confirmed that ATRA could enhance the toxicity of sorafenib to hepatocellular carcinoma by activating AMP-activated protein kinase and regulating the energy metabolism of hepatocellular carcinoma cells [17]. Subsequently, another research team found that ATRA could directly inhibit hepatocellular carcinoma by downregulating PAK1 or enhance the efficacy of sorafenib [18].

In breast cancer, studies have found that in HER2-positive breast cancer, the combination of ATRA and trastuzumab can induce apoptosis and inhibit cell proliferation via related signaling pathways, thereby enhancing the efficacy of trastuzumab [19,20]. Subsequent studies have shown that MYC mediates retinoic acid resistance in HER2 breast cancer cells. Therefore, in HER2 breast cancer patients with low MYC expression, the use of RA combined with trastuzumab may overcome the resistance problem [21].

Furthermore, in melanoma cells, PLX4032 resistance caused by abnormal PIN1 expression can be alleviated by ATRA-regulated related signaling pathways [22]. In recent years, it has also been found that ATRA can downregulate potential targets for resistance to PARP inhibitors in various

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Epithelial Ovarian Cancers (EOCs) [23]. Even in rare tumors that are less understood, such as Adenoid Cystic Carcinoma (ACC), the combination of ATRA and PI3K inhibitors has been found to be beneficial [24].

3.3. The sensitizing effect and mechanism of retinoic acid in radiotherapy

The radiosensitizing mechanism of retinoic acid mainly includes: Direct sensitization: Early studies have shown that ATRA can directly induce the expression of RAR-β receptors and enhance the apoptosis pathway of tumor cells, resulting in a direct sensitizing effect, but it has obvious cell specificity [25]. Subsequent research on cervical cancer HeLa cells confirmed that 4-HPR (a retinoic acid derivative) can increase radiosensitivity when combined with chemotherapeutic agents [26].

Immunomodulation: According to an article published in Science Immunology, the current mainstream ATRA sensitization mechanism is that ATRA can induce an increase in Inflammatory Macrophages (Inf-MACs) that produce Tumor Necrosis Factor-α (TNF-α) and Inducible Nitric Oxide Synthase (iNOS), enhance the tumor infiltration of $CD4^+$ and $CD8^+$ effector T cells, strengthen the local anti-tumor effect, and also increase the remote effect of radiotherapy. Inhibition of DNA Repair and Tumor Stem Cell Markers: ATRA can interfere with the expression of DNA repair proteins following radiation-induced damage, increasing the tumor cell apoptosis rate by approximately 45%. Concurrently, it can downregulate stemness markers (e.g., CD133, ALDH1) in cancer stem cells, thereby rendering them more vulnerable to therapy.

4. Novel drug delivery systems and nanotechnology applications

In order to overcome the shortcomings of ATRA itself (such as poor water solubility, short half-life, etc.), drug resistance problems and the problem of tumor microenvironment suppressing immunity, researchers have begun to consider how to more efficiently and conveniently target and deliver drugs to exert their effects. Among these, nanodelivery systems are the most representative.

The key objectives of liposomal delivery systems are to encapsulate ATRA, thereby improving its solubility, reducing its metabolic clearance, and protecting it from degradation [27]. In the study by Parthasarathy et al., liposomes did not have many additional functions, but played a role in helping drugs enter the tumor microenvironment and exist effectively. In a recent study (2025) by He et al., liposome delivery systems are no longer limited to a single delivery function. Researchers modified liposomes to develop Liposomal All-trans Retinoic Acid Nanoparticles (LATRA), which have both delivery function and the ability to target and inhibit tumor cells and remodel the tumor immune microenvironment [28].

The main purpose of self-assembling nanoparticles is to polymerize two synergistic drugs or drugs with other polymeric materials to form a novel amphiphilic molecule that can spontaneously assemble into nanoparticles. In a 2019 study, researchers synthesized a conjugate of ATRA and the histone deacetylase inhibitor vorinostat, termed Retinoic Hydroxamic Acid (RHA), which proved to be a highly effective and low-toxicity agent for treating melanoma [29]. In 2022, a prodrug delivery system was developed for the treatment of breast cancer. Researchers polymerized ATRA with Poly-β-amino Ester (PBAE) to make it pH sensitive, overcoming the limitations of ATRA in the treatment of breast cancer [30]. It is not difficult to understand that self-assembled nanoparticles and drug co-presentation systems are inseparable. The self-assembly technology facilitates the entry of multiple drug molecules into the tumor microenvironment. Two years later, people turned their attention to the combined treatment of radiotherapy and ATRA. Researchers drove Zoledronic Acid (Zol) and Gadolinium Ions (Gd3+) to self-assemble into Z-NPs (zoledronic acid-gadolinium coordination

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polymers) through coordination of metal bonds. A-NPs (albumin-encapsulated retinoic acid nanoparticles) were then firmly encapsulated in the grid of Z-NPs through physical encapsulation and chemical coordination. ATRA and Zol are both drugs, which play the roles of anti-tumor effect and improving antigen presentation efficiency, respectively [31]. By 2025, research strategies had evolved further. A system was designed to co-deliver ATRA and siCYP26A1 (to counteract ATRA's short half-life) using liposomes modified with Folic Acid (FA) on their surface. This design leverages the fact that ATRA upregulates Folate Receptor B (FRβ), creating a positive feedback loop that resulted in an order-of-magnitude increase in intratumoral ATRA concentration [32].

5. Conclusion

In 2025, Esposito et al.'s team developed a method that integrates computer simulation and high-throughput screening for screening Aldehyde dehydrogenase 1a3 (ALDH1A3) [33], and a new retinoic acid analog ZSH-512 was also developed based on digital pathological image analysis of artificial intelligence [34]. In the same year, retinoic acid analogs such as ZSH-2208 and Sulfarotene were also launched [35, 36]. What is particularly innovative is the development of a new fluorescent synthetic retinol, which can perform anti-tumor effects without linking fluorescent groups for imaging [37].

These advancements underscore the broad therapeutic potential of retinoic acid and its derivatives in oncology. Looking forward, the maturation of Artificial Intelligence (AI) promises to further revolutionize this field. For instance, performance benchmarks (e.g., on the FrontierMath dataset) indicate that leading AI models like GPT-5.4 Pro can solve a significant portion of intermediate to highly complex problems. This capability suggests that AI will play an increasingly important role in assisting the precise and efficient application of therapies, including retinoic acid-based regimens, in complex medical domains such as cancer treatment.

References

[1] STUETTGEN G. [On the local therapy of keratosis with vitamin A acid]. Dermatologica. 1962; 124: 65-80. German. PMID: 13917997.

[2] Wang ZY, Chen Z. Acute promyelocytic leukemia: from highly fatal to highly curable. Blood. 2008 Mar 1; 111(5): 2505-15. doi: 10.1182/blood-2007-07-102798. PMID: 18299451.

[3] Chen L, Chen SJ. The road to cure acute promyelocytic leukemia and China's contributions [J]. Chinese Journal of Hematology, 2025, 46(5): 377-384. DOI: 10.3760/cma.j.cn121090-20250307-00119.

[4] Ghyselinck NB, Duester G. Retinoic acid signaling pathways. Development. 2019 Jul 4; 146(13): dev167502. doi: 10.1242/dev.167502. PMID: 31273085; PMCID: PMC6633611.

[5] Testa U, Pelosi E. Function of PML-RARA in Acute Promyelocytic Leukemia. Adv Exp Med Biol. 2024; 1459: 321-339. doi: 10.1007/978-3-031-62731-6_14. PMID: 39017850.

[6] Nowak D, Stewart D, Koeffler HP. Differentiation therapy of leukemia: 3 decades of development. Blood. 2009 Apr 16; 113(16): 3655-65. doi: 10.1182/blood-2009-01-198911. Epub 2009 Feb 12. PMID: 19221035; PMCID: PMC2943835.

[7] Tøstesen M, Østergård LSG, Kjeldsen E, Stentoft J, Nørgaard JM. [Acute promyelocytic leukaemia]. Ugeskr Laeger. 2018 Jan 15; 180(3): V06170490. Danish. PMID: 29336301.

[8] Liang C, Qiao G, Liu Y, Tian L, Hui N, Li J, Ma Y, Li H, Zhao Q, Cao W, Liu H, Ren X. Overview of all-trans-retinoic acid (ATRA) and its analogues: Structures, activities, and mechanisms in acute promyelocytic leukaemia. Eur J Med Chem. 2021 Aug 5; 220: 113451. doi: 10.1016/j.ejmech.2021.113451. Epub 2021 Apr 15. PMID: 33895500.

[9] Allison JP, McIntyre BW, Bloch D. Tumor-specific antigen of murine T-lymphoma defined with monoclonal antibody. J Immunol. 1982 Nov; 129(5): 2293-300. PMID: 6181166.

[10] Haanen JB, Robert C. Immune Checkpoint Inhibitors. Prog Tumor Res. 2015; 42: 55-66. doi: 10.1159/000437178. Epub 2015 Sep 4. PMID: 26382943.

[11] Weber R, Fleming V, Hu X, Nagibin V, Groth C, Altevogt P, Utikal J, Umansky V. Myeloid-Derived Suppressor Cells Hinder the Anti-Cancer Activity of Immune Checkpoint Inhibitors. Front Immunol. 2018 Jun 11; 9: 1310. doi: 10.3389/fimmu.2018.01310. PMID: 29942309; PMCID: PMC6004385.
[12] Nefedova Y, Fishman M, Sherman S, Wang X, Beg AA, Gabrilovich DI. Mechanism of all-trans retinoic acid effect on tumor-associated myeloid-derived suppressor cells. Cancer Res. 2007 Nov 15; 67(22): 11021-8. doi: 10.1158/0008-5472.CAN-07-2593. Erratum in: Cancer Res. 2008 Jan 15; 68(2): 626. PMID: 18006848.
[13] Picheta N, Piekarz J, Kułak K, Tarkowski R. The Efficacy of Pembrolizumab Immunotherapy in the Treatment of Endometrial Cancer: A Systematic Review. Int J Mol Sci. 2025 Sep 9; 26(18): 8789. doi: 10.3390/ijms26188789. PMID: 41009360; PMCID: PMC12469525.
[14] Yao W, Wang L, Huang H, et al. All-trans retinoic acid reduces cancer stem cell-like cell-mediated resistance to gefitinib in NSCLC adenocarcinoma cells [J]. BMC cancer, 2020, 20(1): 315.
[15] Yoshida Y, Takahashi M, Taniguchi S, Numakura R, Komine K, Ishioka C. Tretinoin synergistically enhances the antitumor effect of combined BRAF, MEK, and EGFR inhibition in BRAFV600E colorectal cancer. Cancer Sci. 2024 Nov; 115(11): 3740-3754. doi: 10.1111/cas.16280. Epub 2024 Aug 22. PMID: 39175203; PMCID: PMC11531965.
[16] Guan D X, Shi J, Zhang Y, et al. Sorafenib enriches epithelial cell adhesion molecule–positive tumor initiating cells and exacerbates a subtype of hepatocellular carcinoma through TSC2-AKT cascade [J]. Hepatology, 2015, 62(6): 1791-1803.
[17] Ishijima N, Kanki K, Shimizu H, et al. Activation of AMP-activated protein kinase by retinoic acid sensitizes hepatocellular carcinoma cells to apoptosis induced by sorafenib [J]. Cancer science, 2015, 106(5): 567-575.
[18] Wang K, Qiu X, Zhang Z, et al. ATRA sensitized the response of hepatocellular carcinoma to Sorafenib by downregulation of p21-activated kinase 1 [J]. Cell Communication and Signaling, 2023, 21(1): 193.
[19] Koay DC, Zerillo C, Narayan M, Harris LN, DiGiovanna MP. Anti-tumor effects of retinoids combined with trastuzumab or tamoxifen in breast cancer cells: induction of apoptosis by retinoid/trastuzumab combinations. Breast Cancer Res. 2010; 12(4): R62. doi: 10.1186/bcr2625. Epub 2010 Aug 9. PMID: 20696059; PMCID: PMC2949655.
[20] Vanderhoeven F, Redondo AL, Martinez AL, Lopes FL, Romero I, Sánchez-Muñoz A, Pérez-Ruiz E, Rueda A, Jiménez B, Aránega A. Synergistic antitumor activity by combining trastuzumab with retinoic acid in HER2 positive human breast cancer cells. Oncotarget. 2018; 9(41): 26527-26527. doi: 10.18632/oncotarget.25515. PMID: 29899860; PMCID: PMC5995143.
[21] Choi WS, Liu RZ, Mak C, Maadi H, Godbout R. Overcoming retinoic acid resistance in HER2-enriched breast cancers: role of MYC. FEBS J. 2024 Aug; 291(15): 3521-3538. doi: 10.1111/febs.17151. Epub 2024 May 6. PMID: 38708519.
[22] Kim G, Bhattarai P Y, Oh C H, et al. All-trans retinoic acid overcomes acquired resistance to PLX4032 via inhibition of PIN1 in melanoma cells [J]. Anticancer Research, 2019, 39(12): 6537-6546.
[23] Mei B, Li J, Wang D, Feng L, Huang J, Zhang G. All-trans Retinoic Acid Sensitizes Epithelial Ovarian Cancer to PARP Inhibition after Exposure to Cisplatin. Mol Cancer Ther. 2025 Mar 4; 24(3): 453-463. doi: 10.1158/1535-7163.MCT-24-0140. PMID: 39676352; PMCID: PMC11876957.
[24] Sun B, Wang Y, Sun J, Yu W, Yin H, Tao R, Wei Y, Xu H, Li G, Mao Y. Establishment of patient-derived xenograft models of adenoid cystic carcinoma to assess pre-clinical efficacy of combination therapy of a PI3K inhibitor and retinoic acid. Am J Cancer Res. 2021; 11(3): 773-789. PMID: 33791145; PMCID: PMC7992093.
[25] Seo JH, Lee KN, Park SH, Choi CW, Kim BS, Shin SW, Kim YH, Kim JS. Retinoic Acid as a Radiosensitizer on the Head and Neck Squamous Cell Carcinoma Cell Lines. Cancer Res Treat. 2001 Aug; 33(4): 335-42. doi: 10.4143/crt.2001.33.4.335. PMID: 26680805.
[26] Zhu Lijuan. Study on the radiosensitization effects of 4-HPR and cisplatin on cervical cancer HeLa cells [D]. Nanjing Medical University, 2007.
[27] Parthasarathy R, Sacks PG, Harris D, Brock H, Mehta K. Interaction of liposome-associated all-trans-retinoic acid with squamous carcinoma cells. Cancer Chemother Pharmacol. 1994; 34(6): 527-34. doi: 10.1007/BF00685666. PMID: 7923565.
[28] He H, Zheng Y, Ji J, Ye C, Sun Y, Peng Y, Zhang Y, Zhong Z. Liposomal all-trans retinoic acid boosts anti-tumor immunity of radiotherapy via mitigating cancer stemness and remedying tumor microenvironment. J Control Release. 2025 Sep 10; 385: 113995. doi: 10.1016/j.jconrel.2025.113995. Epub 2025 Jun 30. PMID: 40602432.
[29] Liao H, Zhao S, Wang H, Liu Y, Zhang Y, Sun G. Self-Assembly Of Retinoid Nanoparticles For Melanoma Therapy. Int J Nanomedicine. 2019 Oct 1; 14: 7963-7973. doi: 10.2147/IJN.S196974. PMID: 31632011; PMCID: PMC6778447.

[30] Li W, Gong H, Fu Y, Sun J, Wang Y. Novel pH-sensitive nanoparticles based on prodrug strategy to delivery all-trans retinoic acid for breast cancer. Colloids Surf B Biointerfaces. 2022; 219: 112838. doi: 10.1016/j.colsurfb.2022.112838.
[31] Ma S, Hu K, Xue J, Li R, Li D, Zhang J, Wu A, Zhang Y, Liu J. Self-assembly nanoparticles potentiate in-situ tumor vaccine of radiotherapy by regulating tumor immunogenicity and tumor-associated macrophages. Chem Eng J. 2024; 497: 154663. doi: 10.1016/j.cej.2024.154663.
[32] Yang H, Pu Y, Hu X, Zhang H, Li S, Zhang W, Chen M, Zhang H, Jin R, Nie Y. ATRA derived lipid nanoparticles for co-delivery of siCYP26A1 to overcome metabolic limitations of differentiation therapy in solid tumors. J Control Release. 2025 Aug 10; 384: 113933. doi: 10.1016/j.jconrel.2025.113933. Epub 2025 Jun 4. PMID: 40480520.
[33] Esposito M, Fang C, Wei Y, Pozzan A, Beato C, Su X, Hutton JE 3rd, Reed T, Hang X, Perini ED, Wang W, Cheng X, Pan Y, Yu J, Kane M, Manoharan M, Proudfoot J, Cristea IM, Kang Y. Development of retinoid nuclear receptor pathway antagonists through targeting aldehyde dehydrogenase 1A3. iScience. 2025 Oct 3; 28(11): 113675. doi: 10.1016/j.isci.2025.113675. PMID: 41210994; PMCID: PMC12595434.
[34] Li S, Zhao W, An Q, Wang L, Zhu M, Ni J, Huang X, Jiang Y, Li M, Hou J, Yu Y, Yu S, Wei L, Jiao H, Liu T, Cao X. Novel cancer stem cell-targeted retinoid ZSH-512 impedes colorectal cancer progress via KDM3A-mediated epigenetic reprogramming. Innovation (Camb). 2025 Jan 30; 6(4): 100831. doi: 10.1016/j.xinn.2025.100831. PMID: 40470327; PMCID: PMC12130993.
[35] Chen R, Huang X, Hou J, Ni J, Zhao W, Li Q, Jiao H, Cao X. ZSH-2208: A novel retinoid with potent anti-tumour effects on ESCC stem cells via RARγ-TNFAIP3 axis. Clin Transl Med. 2025 Jan; 15(1): e70148. doi: 10.1002/ctm2.70148. PMID: 39724264; PMCID: PMC11670471.
[36] Du X, Qi Z, Chen S, Wu J, Xu Y, Hu S, Yu Z, Hou J, Fang Y, Xia J, Cao X. Synthetic Retinoid Sulfarotene Selectively Inhibits Tumor-Repopulating Cells of Intrahepatic Cholangiocarcinoma via Disrupting Cytoskeleton by P-Selectin/PSGL1 N-Glycosylation Blockage. Adv Sci (Weinh). 2025 Jan; 12(3): e2407519. doi: 10.1002/advs.202407519. Epub 2024 Nov 28. PMID: 39605300; PMCID: PMC11744644.
[37] Ibrahim E, Mansour YE, Soror S, Haffez H. New Fluorescent Synthetic Retinoids as Potential RAR Agonists with Anticancer, Molecular Docking and ADME Assessments. J Fluoresc. 2025 Nov; 35(11): 11103-11134. doi: 10.1007/s10895-025-04343-6. Epub 2025 May 23. PMID: 40410548; PMCID: PMC12718261.