

The Next Gold Rush: Potential Therapeutic Applications of miRNA–AuNPs in Testicular Cancer

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Background

- Testicular germ cell tumors (TGCTs) represent the most common solid tumor in males between the ages of 13-39 and exhibit remarkable phenotypic heterogeneity¹
- Despite excellent cure rates with cisplatin-based chemotherapy, patients face significant long-term toxicities including cardiovascular disease, infertility, and secondary malignancies²
- microRNAs (miRNAs) play key roles in TGCT pathogenesis and have emerged as both promising biomarkers and potential therapeutic targets^{3,4}
- Gold nanoparticles (AuNPs) are highly tunable nanocarriers capable of protecting and delivering miRNA mimics or miRNA inhibitors (antimiRs) into tumor cells⁵⁻⁹
- The therapeutic integration of TGCT miRNA biology with AuNP-mediated nucleic acid delivery has not yet been investigated.

Purpose

- To explore how AuNP-mediated delivery of miRNA mimics and antimiRs could be leveraged to therapeutically target TGCT molecular pathways.

Methods

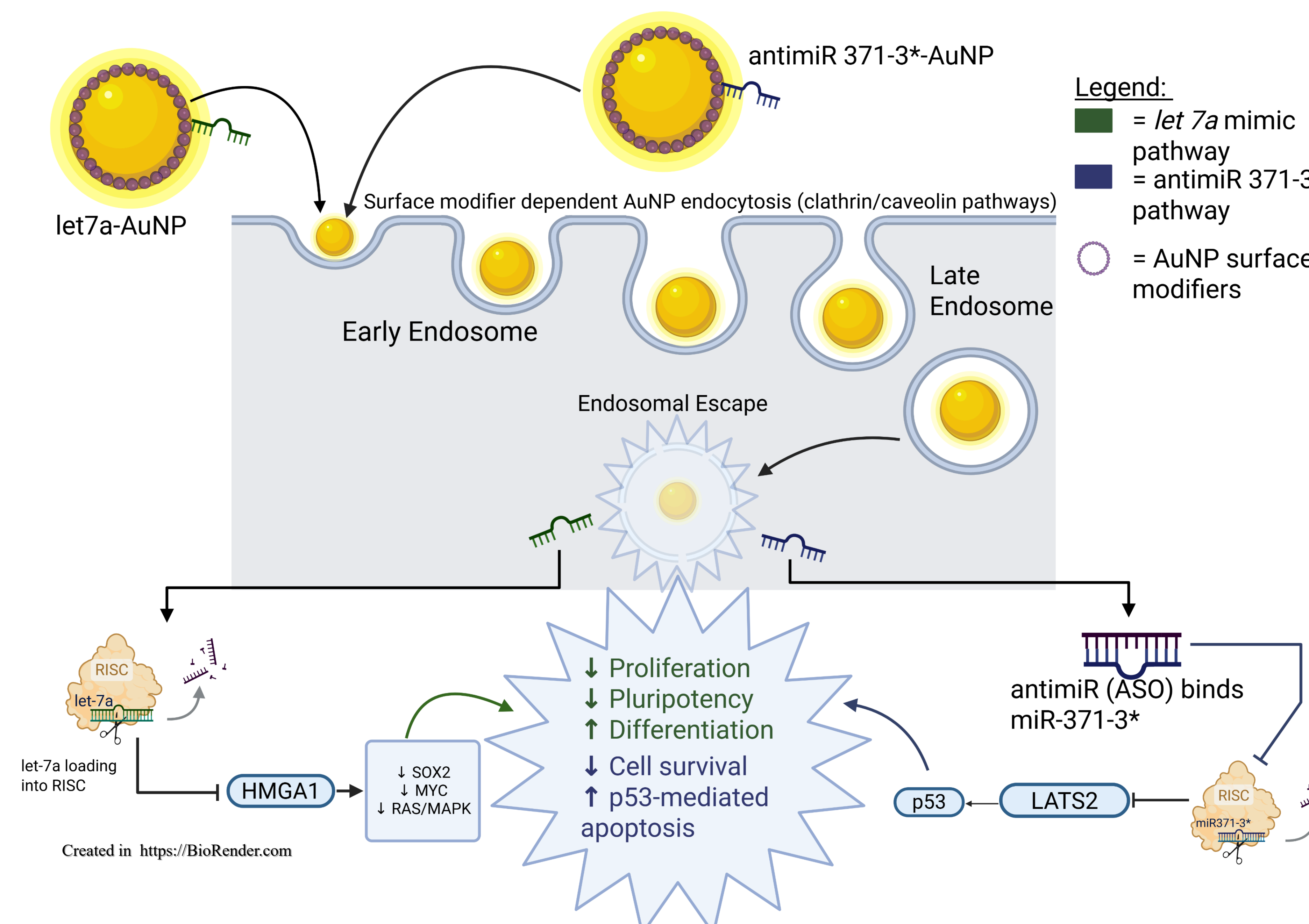
- Study Design: Narrative Review
- The search strategy incorporated the terms “testicular germ cell tumors” (“TGCTs”), “microRNAs” (“miRNAs”), “TGCT pathogenesis,” “germ cell neoplasia in situ” (“GCNIS”), “conjugated gold nanoparticles” (“AuNPs”), and “anti-microRNAs” (“antimiRs”)
- Searches were conducted in PubMed, Scopus, and Google Scholar between May 2025 and November 2025
- Because no studies examining miRNA–AuNP therapeutic applications in TGCTs currently exist, PRISMA-ScR methodology was not applicable

Table 1:

Explored applications of miR and antimiR conjugated AuNPs in cancer treatment				
AuNP	Cancer Type	Cell Line	Mod.	Ref.
AuNP miR 206	ER ⁺ /PR ⁺ BC	MCF-7; xenografted mice	NH ₂ -PEG-SH	5
AuNP antimiR 135b	TNBC	4T1	<i>Fusarium oxysporum</i>	6
AuNP antimiR 29b	MCL	HeLa	αRNAI-AMO	7
AuNP miR 375	HCC	HepG2, Hep3B; xenografted mice	-	8
AuNP miR 326	HCC	Huh-7 cells; xenografted mice	-	9

Abbreviations: AuNP, gold nanoparticle; miR, microRNA; antimiR, microRNA inhibitor; TNBC, triple-negative breast cancer; ER⁺/PR⁺, estrogen receptor-positive/progesterone receptor positive; HCC, hepatocellular carcinoma; MCL, myeloid cell leukemia.

Figure 1: Conceptual Illustration of Predicted let-7a and miR371-3 Pathway Effects Following AuNP Delivery in TGCTs



- AuNP-conjugated let-7a mimics and antimiR constructs are depicted entering TGCT cells via endocytosis, escaping endosomal compartments, and modulating key pathways including HMGA1-driven pluripotency signaling and the LATS2–p53 tumor suppressor axis

Implications & Limitations

- Preclinical studies across multiple malignancies demonstrate that AuNPs can deliver functional miRNA and antimiR cargo, producing measurable modulation of tumor-associated pathways
- Restoring tumor suppressive let7a activity and inhibiting oncogenic miR371-3 signaling represents a biologically plausible strategy for altering TGCT survival
- Current challenges in translation include limited TGCT faithful cell lines and the undetermined biodistribution and safety profile of miRNA–AuNPs
- Future studies should investigate the efficacy of miRNA–AuNPs in established GCT-lineage specific models: TCam2 (seminoma) and NTERA-2 (embryonal carcinoma).

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Disclosures

- *NGCs spouse works as a Senior Medical Officer for Janssen Pharmaceuticals*