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

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Abstract

Background:
Testicular germ cell tumors (TGCTs) are the most common solid tumor among males ages 13–39 years old, despite their relatively low overall incidence. The treatment of TGCTs is widely regarded as one of the greatest successes in modern oncology, with progression-free survival (PFS) rates approaching 100% in early-stage disease. However, challenges persist in patients with metastatic disease, for whom improvements in 5-year PFS rates have been modest over the past 25 years. In addition, patients remain at risk for disease recurrence following surgery, and those treated with standard cisplatin-based chemotherapy face significant long-term toxicities, including secondary malignancies, cardiovascular disease, metabolic syndrome, and infertility. These limitations highlight the need for novel therapeutic strategies with improved safety profiles. Furthermore, the phenotypic heterogeneity of TGCTs limits the sensitivity and specificity of current serum biomarkers, restricting their ability to guide clinical decision-making. This review examines emerging research in microRNA (miRNA) biology and the potential of gold nanoparticle (AuNP)-mediated drug delivery to address these unmet clinical needs.

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

Methods:
This narrative review integrates current knowledge on TGCT miRNA biology with advances in AuNP-mediated delivery systems and proposes a conceptual framework for applying miRNA and antimiR therapeutics to GCT-specific molecular circuitry. 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 to identify primary research articles and review manuscripts published in English within the previous 15 years. Additional articles were identified through backward citation screening. Given that this review did not involve human subjects, identifiable private information, or experimental intervention, it was exempt from institutional review board (IRB) oversight. Because no studies directly examining miRNA–AuNP therapeutic applications in TGCTs currently exist, PRISMA-ScR methodology was not applicable.

Abbreviations:
AuNPs, gold nanoparticles; GCNIS, germ cell neoplasia in situ; miRNAs, microRNAs; TGCTs, testicular germ cell tumors.

Implications and Limitations:
Recent advances in molecular oncology have identified miRNAs as promising biomarkers and potential therapeutic agents. The miR-371–373 cluster is consistently overexpressed across most TGCT subtypes, excluding post-pubertal teratomas, and demonstrates superior diagnostic and prognostic performance compared with conventional serum markers. In contrast, downregulation of the tumor-suppressive let-7 miRNA family in seminomas highlights its potential as a therapeutic target. miRNA-based diagnostics and AuNP-enabled delivery platforms are best viewed as complementary to existing TGCT management rather than replacements for established platinum-based regimens. In the absence of TGCT-specific studies directly evaluating miRNA–AuNP therapeutics, this review proposes a conceptual framework for integrating miRNA modulation with AuNP-based vectors. By targeting key regulators of TGCT biology, including HMGA1-driven pluripotency pathways and the LATS2–p53 tumor suppressor axis, miRNA mimics and antimiRs delivered via optimized AuNP systems may enhance therapeutic precision, reduce treatment-related toxicity, and expand options for patients with high-risk disease. Continued progress at the intersection of GCT biology and nanomedicine will be critical for translating these conceptual strategies into clinically viable therapies.