

New-generation microRNAs targeting Wnt/ β -Catenin and EMT pathways in colorectal cancer: A systematic mapping of translational potential

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ABSTRACT

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Colorectal cancer (CRC) remains a major global health challenge with poor prognosis, largely driven by dysregulation of the Wnt/ β -catenin signaling and epithelial-mesenchymal transition (EMT) pathways. This systematic review analyzed studies published between 2020 and 2025 focusing on newly identified microRNAs (miRNAs) involved in the modulation of these oncogenic cascades and their translational potential for early diagnosis, metastasis prediction, and therapeutic targeting. Out of 474 screened articles, 45 met the inclusion criteria. Key findings revealed that miR-129, miR-490-3p, miR-224, miR-452, and miR-494 consistently suppressed tumor progression by downregulating critical components of the Wnt pathway (TCF7L2, FZD7, β -catenin) and EMT effectors (ZEB1, Snail, Twist). Preclinical models demonstrated that restoration of miR-129 significantly reduced invasion and liver metastasis, while miR-494 exhibited dual roles depending on tumor context. Despite their promise as diagnostic, prognostic, and therapeutic biomarkers, most of these miRNAs have yet to be validated in patient biofluids or incorporated into clinical biomarker panels. Future research should prioritize the development of multi-miRNA panels and prospective cohort validation to bridge the gap between bench and bedside, ultimately enhancing precision therapy in CRC.

ABSTRAK

Kanker kolorektal (CRC) merupakan salah satu masalah kesehatan global dengan prognosis yang buruk, terutama akibat disregulasi jalur pensinyalan Wnt/ β -catenin dan *epithelial mesenchymal transition* (EMT). Kajian sistematis ini menelaah literatur tahun 2020–2025 mengenai mikroRNA (miRNA) baru yang berperan dalam modulasi kedua jalur tersebut serta potensi translasionalnya dalam diagnosis dini, prediksi metastasis, dan terapi. Dari 474 artikel yang disaring, 45 memenuhi kriteria inklusi. Temuan utama menunjukkan bahwa miR-129, miR-490-3p, miR-224, miR-452, dan miR-494 secara konsisten menekan progresi tumor dengan menurunkan ekspresi gen kunci pada jalur Wnt (TCF7L2, FZD7, β -catenin) dan EMT (ZEB1, Snail, Twist). Studi praklinis memperlihatkan restorasi miR-129 mampu menghambat invasi dan metastasis hati, sementara miR-494 menunjukkan peran ganda tergantung konteks tumor. Meskipun memiliki potensi sebagai biomarker dan target terapi, sebagian besar miRNA ini belum banyak divalidasi pada biofluida pasien maupun diintegrasikan dalam panel klinis. Oleh karena itu, penelitian lanjutan dengan pengembangan panel multi-miRNA dan validasi prospektif sangat dibutuhkan untuk mempercepat translasi dari laboratorium ke praktik klinis dalam meningkatkan presisi terapi CRC.

Keywords:

colorectal cancer;
microRNA;
Wnt signaling;
 β -catenin;
epithelial-mesenchymal
transition;
metastasis;
translational oncology C

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