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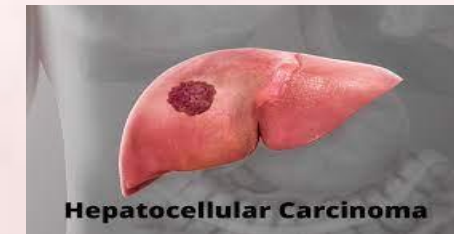
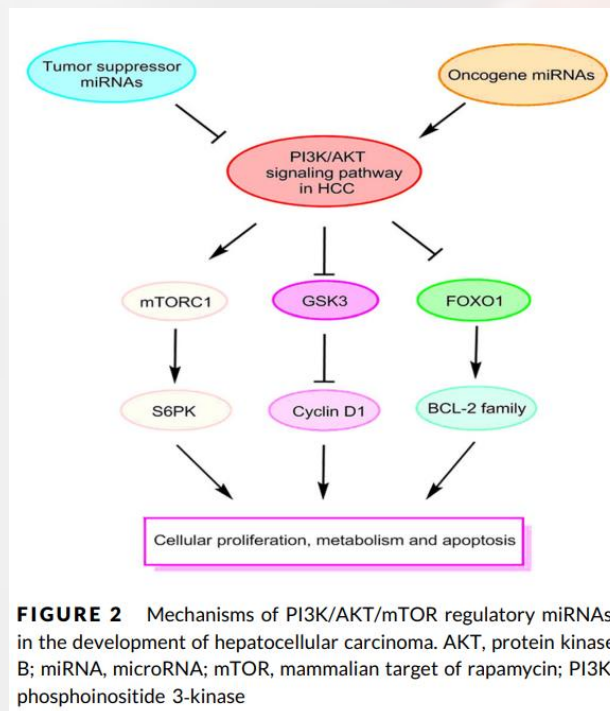
## Interplay of miRNAs and PI3K/AKT/mTOR signaling in Hepatocellular carcinoma

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# Hepatocellular Carcinoma

## • Introduction



Third leading cause of cancer death

over 600,000 deaths annually worldwide

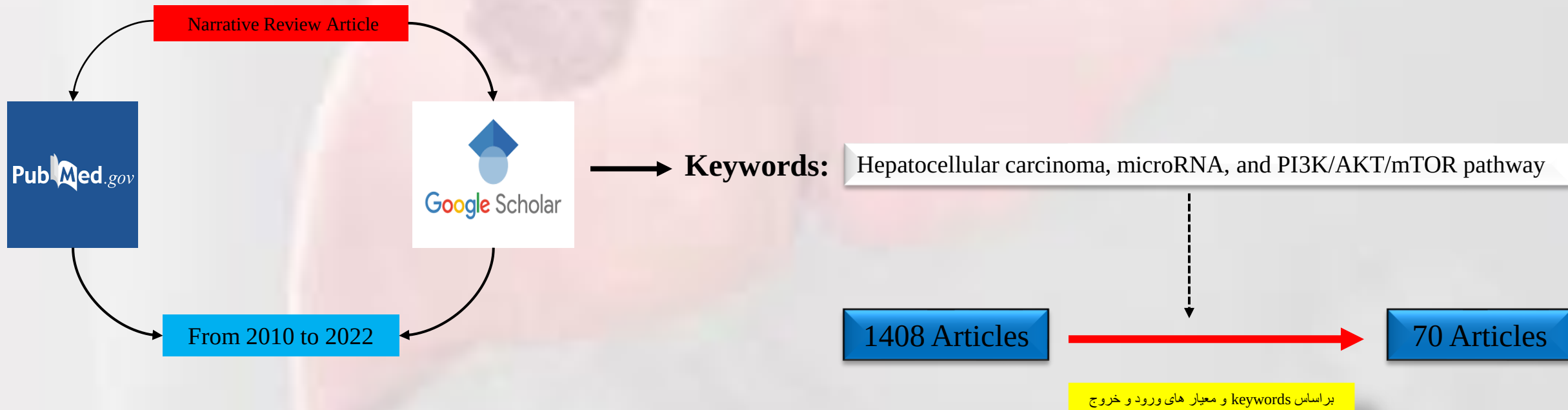


The 5-year survival rate

Remains below 30%

Regulatory roles of miRNAs in PI3K/AKT/mTOR pathway in HCC pathogenesis

## • Material & Method



# Hepatocellular Carcinoma

## • Results

**TABLE 1** Oncogenic miRNAs regulate the pathogenesis of hepatocellular carcinoma through targeting the specific components of the PI3K/AKT/mTOR signaling axis

| MicroRNA  | Target        | Molecular alteration | Function                              | Reference            |
|-----------|---------------|----------------------|---------------------------------------|----------------------|
| miR155-5p | PTEN          | Upregulation         | Cellular proliferation and invasion   | (Fu et al., 2017)    |
| miR-494   | PTEN          | Upregulation         | Cellular proliferation and invasion   | (Liu et al., 2015)   |
| miR-519a  | PTEN          | Upregulation         | Cellular proliferation and invasion   | (Tu et al., 2016)    |
| miR-492   | PTEN          | Upregulation         | Cellular proliferation and invasion   | (Jiang et al., 2014) |
| miR-21    | PTEN, hSulf-1 | Upregulation         | Cellular proliferation and metastasis | (Bao et al., 2013)   |
| miR-93    | PTEN, CDKN1A  | Upregulation         | Cellular proliferation                | (Ohta et al., 2015)  |
| miR-222   | PPP2R2A       | Upregulation         | Cellular proliferation                | (Wong et al., 2010)  |
| miR-3127  | AKT, FOXO1    | Upregulation         | Cellular proliferation                | (Jiang et al., 2015) |

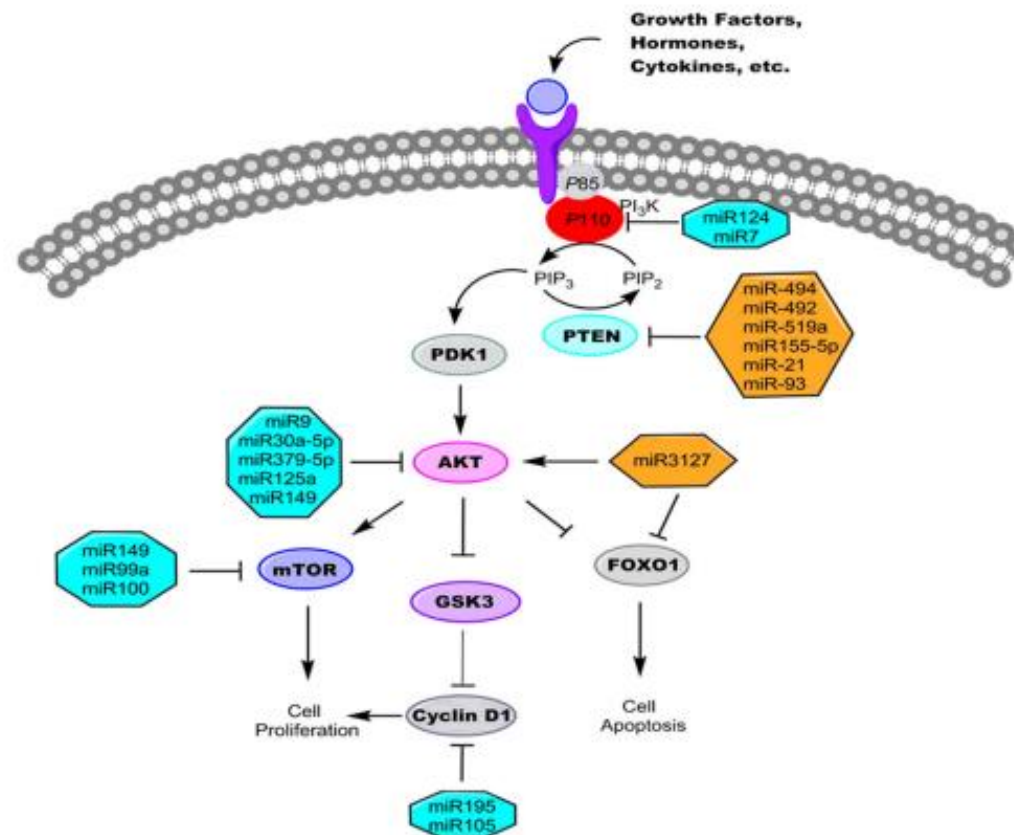
Abbreviations: AKT, protein kinase B; miRNA, microRNA; mTOR, mammalian target of rapamycin; PI3K, phosphoinositide 3-kinase.

**TABLE 2** Tumor suppressor regulatory microRNAs for the PI3K/AKT/mTOR signaling pathway in hepatocellular carcinoma pathology

| MicroRNA   | Target            | Molecular alteration | Function                              | Reference              |
|------------|-------------------|----------------------|---------------------------------------|------------------------|
| miR-195    | Cyclin D1, CDK6   | Downregulation       | Cell cycle arrest                     | (Xu et al., 2009)      |
| miR-124    | PIK3CA            | Downregulation       | Cell cycle arrest                     | (Lang & Ling, 2012)    |
| miR-7      | PIK3CD            | Downregulation       | Cell cycle arrest                     | (Fang et al., 2012)    |
| miR-132    | PIK3R3            | Downregulation       | Inhibits cellular proliferation       | (Liu, Li et al., 2015) |
| miR-9      | IGF2BP1, AKT, ERK | Downregulation       | Inhibits cellular proliferation       | (Zhang et al., 2015)   |
| miR-30a-5p | MTDH, PTEN, AKT   | Downregulation       | Inhibits cellular proliferation       | (W. Li et al., 2016)   |
| miR-105    | Cyclin D1         | Downregulation       | Inhibits cellular proliferation       | (Shen et al., 2014)    |
| miR-26a    | VEGF-A            | Downregulation       | Inhibits tumor angiogenesis           | (Chai et al., 2013)    |
| miR-125a   | PI3K/AKT/mTOR     | Downregulation       | Inhibits promalignant features of HCC | (Tang et al., 2015)    |
| miR-149    | AKT1, mTOR        | Downregulation       | Inhibits cellular proliferation       | (Zhang et al., 2014)   |
| miR-99a    | mTOR              | Downregulation       | Cell cycle arrest                     | (Li et al., 2011)      |
| miR-100    | mTOR, IGF-1R      | Downregulation       | Cancer cell apoptosis                 | (Ge et al., 2014)      |
| miR-379-5p | FAK, AKT          | Downregulation       | Inhibits HCC progressive feature's    | (Chen et al., 2016)    |
| miR-1296   | SRPK1             | Downregulation       | Inhibits cellular metastasis          | (Xu et al., 2017)      |

Abbreviations: AKT, protein kinase B; FAK, focal adhesion kinase; HCC, hepatocellular carcinoma; MTDH, metadherin; mTOR, mammalian target of rapamycin; PI3K, phosphoinositide 3-kinase.

## • Conclusion



**FIGURE 1** Regulatory roles of miRNAs on PI3K/AKT/mTOR signaling pathway in HCC. AKT, protein kinase B; GSK3, glycogen synthase kinase 3; HCC, hepatocellular carcinoma; mTOR, mammalian target of rapamycin; PDK1, phosphoinositide-dependent kinase 1; PI3K, phosphoinositide 3-kinase

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