

Supplementary Table SI. Summary of Key Patterns

Study	Cancer Type	Key Findings
Phosphorylation at Tyrosine 105 (Tyr105)		
(Hitosugi et al., 2009a)	NSCLC	Demonstrated that Tyr105 phosphorylation by FGFR1 inhibits PKM2 tetramerization, promoting aerobic glycolysis.
Yang et al., 2012	Glioblastoma	Showed Tyr105 phosphorylation enables nuclear translocation of PKM2, enhancing β -catenin signaling and tumorigenesis.
(Mohammad et al., 2016)	Colorectal Cancer	Reported high Tyr105-PKM2 levels correlate with enhanced glycolysis and poor survival outcomes.
(Zhao et al., 2011)	HCC	Inhibition of FGFR1 reduced Tyr105 phosphorylation and suppressed tumor growth in xenograft models.
Phosphorylation at Serine 37 (Ser37)		
(Yang et al., 2012)	Brain tumor	Identified ERK2-mediated Ser37 phosphorylation promotes nuclear localization of PKM2 and coactivation of c-Myc targets.
(B. Zhou et al., 2024)	Colorectal Cancer	Demonstrated MEK inhibition decreases Ser37 phosphorylation, impairing metabolic gene expression and cell proliferation.
(Lee et al., 2021)	NSCLC	Reported Ser37-PKM2 enhances EMT and migration through ZEB1 regulation.
Phosphorylation at Threonine 454 (Thr454)		
(C. Wang et al., 2021)	Cervical Cancer	Showed Thr454 phosphorylation by CDK1 enhances cell cycle progression and tumor growth.
(Liu et al., 2023)	Pancreatic Cancer	Indicated that blocking Thr454 phosphorylation reduced stem-like traits and impaired spheroid formation.
Emerging Sites: Ser202, Ser204, Others		
(Q. Li et al., 2025)	Triple-Negative Breast Cancer	Used phosphoproteomics to discover novel Ser202/204 sites involved in DNA repair pathway modulation.
(Liang et al., 2017)	Glioblastoma	Suggested Ser204 phosphorylation promotes mitochondrial localization of PKM2 and regulates ROS response.
(Y. Wang et al., 2017)		The study showed Tyr105 and Ser37 co-phosphorylation synergistically drive metabolic plasticity and resistance to EGFR inhibition.
(Zerdes et al., 2019)		Found multisite phosphorylation patterns linked to PD-L1 expression and immune evasion in lung and breast cancer models.

Supplementary Table SII. Characteristics table for the 58 included studies in the systematic review

Outcome	Certainty of Evidence	Reasons for Downgrading
Metabolic effects of PKM2 phosphorylation	Moderate	Risk of bias (preclinical evidence)
Association with tumor progression and prognosis	Low	Indirectness, imprecision
Predictive value for therapy response	Very Low	Inconsistency, risk of bias, publication bias
Clinical utility in precision oncology	Very Low	Indirectness, lack of validation