RNA M1A METHYLTRANSFERASE TRMT61A FACILITATES COLORECTAL CANCER BY INDUCING M1A-ONECUT2-MAPK/ERK AND IS A THERAPEUTIC TARGET

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RNA methyltransferase TRMT61A is overexpressed in colorectal cancer, promotes tumor growth and metastasis through the ONECUT2-MAPK/ERK pathway, and represents a potential prognostic marker and therapeutic target.

KEY POINTS

- TRMT61A was overexpressed in 81.3% and 84.0% of primary colorectal cancers in two independent cohorts and high expression predicted poor patient survival (n=179, P<.05)
- TRMT61A knockout inhibited colorectal cancer xenograft growth and lung and liver metastasis in vivo, while overexpression increased proliferation, migration, and invasion in vitro
- TRMT61A catalyzes m1A modification of ONECUT2 mRNA to stabilize it, leading to ONECUT2-mediated activation of the MAPK/ERK pathway that facilitates colorectal cancer development
- A small molecule inhibitor PGG directly binds TRMT61A and suppressed colorectal cancer xenograft growth and intestinal tumorigenesis in Apc^Min/+ mice with decreased RNA m1A levels
- Nanoparticle-delivered TRMT61A-siRNA demonstrated strong inhibitory effects against colorectal cancer growth in vivo

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