**Fig. S1 IGF2BP3 is up-regulated in colorectal cancer. a** Expression of IGF2BP3 in Oncomine Database in Colorectal Cancer and Other Tumor Database. **b** Expression of IGF2BP3 in embryonic, normal, adenoma, and cancer tissue from GSE71187 dataset. **c** Expression of IGF2BP3 in cBioProtal database. **d** Western blot analysis of IGF2BP3 in 12 cases of fresh CRC tissues. **e** Expression of IGF2BP3 in mouse embryonic intestine tissue in different days of embryonic development from GSE38831 dataset. N, normal. T, tumor, ns, no significance; \*\* p < 0.01; \*\*\* p < 0.001;

**Fig. S2 IGF2BP3 regulates the stability of EGFR mRNA. a** Schematic depicting the establishment of IGF2BP3 stably knockout monoclonal cell lines. **b** Target gene sequence identification (Up) and protein identification (Down) of IGF2BP3 stably knockout monoclonal cell lines. **c** The overexpression and knockdown efficiency of IGF2BP3 was confirmed by Western blot. **d** Western blot analysis of the expression of EGFR signaling pathway in IGF2BP3 overexpression and knockdown cell lines. **e** The alteration frequency of EGFR in colorectal cancer by cBioprotal. **f** Relative expression of EGFR mRNA in GSE41258.\*\* p < 0.01;

**Fig. S3 IGF2BP3 stabilizes EGFR mRNA in an m6A-dependent manner. a** The proportion of readers, writers, and erasers of m6A regulators. **b** Previous study (left) and HOMER motif analysis (right) both revealed the top consensus m6A motif ‘GGAC’. **c** The top three most likely m6A binding sites of IGF2BP3 protein and the 3'UTRs of EGFR mRNA predicted by bioinformatics.

**Fig. S4 IGF2BP3 induces tumor cell proliferation and tumorigenesis depending on the expression of EGFR in CRC.** a-d The ability of proliferation of CRC cells were evaluated by the colony formation assay (**a**-**b**), soft agar assay (**c**-**d**) in the indicated cells with different treatments.

**Fig. S5 IGF2BP3 affects the sensitivity of colorectal cancer cells to cetuximab. a** Expression of IGF2BP3 in response (r) and non-response (non-r) to cetuximab from GSE56386 dataset. **b** Western blot analysis of the expression of EGFR and its downstream effector molecules in indicated groups. **c-d** Colony formation assay validated the effect of different cetuximab treatments on the proliferation rate in indicated groups.