

ETV4 PROMOTES COLORECTAL CANCER PROGRESSION AND METASTASIS THROUGH LIQUID-LIQUID PHASE SEPARATION

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Poster

Colorectal

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Multi-omics analysis identifies the transcription factor ETV4 as a driver of colorectal cancer progression and metastasis through liquid-liquid phase separation mediated by its intrinsically disordered region IDR1.

KEY POINTS

- ETV4 expression was significantly elevated in colorectal cancer tissues compared to adjacent normal tissues and positively associated with distant metastasis and advanced tumor stage based on TCGA data.
- Purified ETV4 formed droplet-like condensates in vitro and in transfected cells, exhibiting dynamic liquid-like properties confirmed by fluorescence recovery after photobleaching assays.
- The first intrinsically disordered region (IDR1) of ETV4 was both essential and sufficient for phase separation, as deletion of IDR1 abrogated condensate formation while expression of IDR1 alone restored it.
- ETV4 overexpression significantly enhanced migratory and invasive capacities of colon cancer cells in vitro, while knockdown suppressed these phenotypes; mice injected with wild-type ETV4 cells developed significantly more lung metastases than controls, whereas the phase separation-deficient mutant failed to enhance metastasis.
- This study demonstrates that the pro-metastatic function of ETV4 is mechanistically dependent on its liquid-liquid phase separation capability.

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