**How to reveal the uniqueness of repetitive DNA ?**

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L1 retrotransposons form the only autonomous and active transposable element family in humans. Several redundant cellular pathways limit L1 expression and mobility in normal tissues. In spite of these defense mechanisms, L1s are reactivated in 50% of all tumors, resulting in extensive genome remodeling. Yet, the cellular mechanisms leading to L1 reactivation in cancer are poorly understood. Here, we combine genome-wide maps of L1 elements in 12 cell lines obtained by our laboratory with publicly available ChIP-seq and RNA-seq data from the same cells, to identify individual active copies and determine if L1 reactivation is mediated by local or global mechanisms and evaluate the contribution of each active copy to the global L1 activity. Altogether, our data impact our understanding of the cellular mechanisms leading to genome plasticity in human tumors.

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