Pin1-mediated modulation of p53 diffusion properties and impact on phase separation

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Résumé

The TP53 gene coding for the tumorsuppressor p53 protein is mutated in 50% of human cancers. Missense mutations in the DNA binding domain impair p53 binding to DNA response elements (loss-of-function). In addition, certain mutations, which are conserved in several types of cancers (hotspot mutations), induce the acquisition of oncogenic functions through new protein-protein interactions (gain-of-function). Both wt and mutant p53 (p53 mut) proteins undergo liquid-liquid phase separation (LLPS) in the nucleus. Notably, p53 mut proteins show an accelerated solid-like phase transition (SLPT) compared to wt p53.The peptidyl-prolyl cis-trans isomerase Pin1 binds to multiple P-Ser/Thr-Pro motifs located within the disordered regions of p53. Pin1 is overexpressed in cancer cells where it appears to enhance the oncogenic gain-of-function activities of p53 mutproteins. The aim of this study is to evaluate the effect of Pin1 activity on p53 diffusion and phase transition properties.

Mots-Clés: p53, liquid liquid phase separation, diffusion

*Intervenant