# Super elongation complex

The super elongation complex (SEC) is required for robust and productive transcription through release of RNA polymerase II (Pol II) with its P-TEFb module and promoting transcriptional processivity with its ELL2 subunit. Malfunction of SEC contributes to multiple human diseases including cancer. Here, we identify peptidomimetic lead compounds, KL-1 and its structural homolog KL-2, which disrupt the interaction between the SEC scaffolding protein AFF4 and P-TEFb, resulting in impaired release of Pol II from promoter-proximal pause sites and a reduced average rate of processive transcription elongation. SEC is required for induction of heat-shock genes and treating cells with KL-1 and KL-2 attenuates the heat-shock response from Drosophila to human. SEC inhibition downregulates MYC and MYC-dependent transcriptional programs in mammalian cells and delays tumor progression in a mouse xenograft model of MYC-driven cancer, indicating that small-molecule disruptors of SEC could be used for targeted therapy of MYC-induced cancer [1].

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Liang K, Smith ER, Aoi Y, Stoltz KL, Katagi H, Woodfin AR, Rendleman EJ, Marshall SA, Murray DC, Wang L, Ozark PA, Mishra RK, Hashizume R, Schiltz GE, Shilatifard A. Targeting Processive Transcription Elongation via SEC Disruption for MYC-Induced Cancer Therapy. Cell. 2018 Oct 18;175(3):766-779.e17. doi: 10.1016/j.cell.2018.09.027. PubMed PMID: 30340042.