第 15 回　生化学セミナー

日時：2017 年 9 月 27 日（水曜日）17:00 - 18:30

場所：東邦大学医学部 1 号館 8 階 東邦会館　第 1, 2 会議室

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Can we target telomerase in cancer?

While telomerase is recognized as a key target in cancer, telomerase inhibitors despite being good drugs are unsuccessful due to their side effects on stem cells. Unlike in stem cells, levels of telomerase catalytic subunit TERT are limiting in reconstituting telomerase activity in normal somatic cells. However, in 90-95 % of human cancers, TERT is transcriptionally reactivated and telomerase activity is reconstituted which is necessary for cancer progression. If TERT transcriptional reactivation in cancer cells can be blocked, telomerase reconstitution in cancers can be prevented. How *TERT* promoter is reactivated in cancers has been a fundamental unanswered question in cancer biology. The recent discovery of 2 prevalent somatic mutations - C250T and C228T in the *TERT* promoter in various cancers including 85% of melanomas and glioblastomas has provided insight into the plausible mechanism of telomerase reactivation in cancers. We have identified mechanisms by which mutant *TERT* promoters are reactivated. I will describe these mechanisms of *TERT* promoter firing and propose how we can selectively target *TERT* reactivation and hence telomerase activity in mutant cancer cells.

References

Akıncılar SC et al. Long-Range Chromatin Interactions Drive Mutant TERT Promoter Activation. ***Cancer Discovery.*** 2016 Nov;6(11):1276-1291.

Khattar E et al. Telomerase reverse transcriptase promotes cancer cell proliferation by augmenting tRNA expression. ***J Clin Invest*** 2016 Oct 3;126(10):4045-4060. doi: 10.1172/JCI86042.

Li Y et al. Non-canonical NF-κB signalling and ETS1/2 cooperatively drive C250T mutant TERT promoter activation. ***Nat Cell Biol*** 2015 Oct;17(10):1327-38. doi: 10.1038/ncb3240.

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