BOSE INSTITUTE COLLOQUIUM

MARCH 4, 2024 (MONDAY) at 4 PM

Main Auditorium, Unified Academic Campus
Bose Institute

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Title and Abstract :

Telomeres and Tumor Immunity - Signal From the Ends

The role of telomeres in sustained tumor growth is well understood. However, mechanisms of how telomeres might impact the tumor microenvironment (TME) are not clear. Upon examining tumor associated macrophages (TAMs) in 94 breast cancer cases we found infiltration of tumor-associated M2-like macrophages (TAMs) to be telomere sensitive: Tumors with relatively short telomeres had higher abundance of TAM and vice versa. This observation was consistent in clinical tissue, patient-derived organoids, tumor xenografts and cancer cells with long/short telomeres. Together these reveal a heretofore unknown function of telomeres in immunosuppression within the TME. Implicating telomeres as a key factor in the often-reported variation in patient response to immunotherapy.

Mechanistically, we found non-telomeric binding of TRF2, a telomere-repeat-binding-factor, at the interleukin receptor *IL1R1* promoter. This directly activated *IL1R1* through recruitment of the histone-acetyl-transferase p300 and consequent H3K27 acetylation. TRF2 binding at the *IL1R1* promoter was sensitive to telomere length.