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### The dysregulated telomere binding proteins are correlated with aberrant expression of splicing factors and RNA splicing profiles in Myeloproliferative neoplasm (MPN)

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Myeloproliferative neoplasms (MPNs) are a group of clonal neoplastic diseases originating from the myeloid lineage of the bone marrow and include essential thrombocythemia (ET), polycythemia vera (PV) and myelofibrosis (MF). A subset of patients eventually evolve into acute myeloid leukemia. A number of genetic alterations have been identified as MPN drivers, but the exact pathogenesis of MPNs remain incompletely understood. Our recent study showed a widespread dysregulation of telomere binding proteins (TBPs) or shelterins (TRF1, TRF2, TPP1, POT1, TIN2 and RAP1) in MPNs. It is well known that the aberrant expression of shelterins causes telomere dysfunction and genomic instability, however, it is unclear whether such abnormal change has other biological activities that promote the development of MPNs. In the present study, we found that the expression of TPP1, one of key TBPs, was positively correlated with expression of splicing factors SF3A1, ZRSR2 and SRSF2, while POT1 levels were negatively correlated with U2AF1 expression, in myeloid cells derived from patients with MPN. RNA sequencing results demonstrated significant alterations in RNA splicing and editing profiles in MPN patient cells compared to normal myeloid cells from healthy adults. The induction of telomere dysfunction in the MPN-derived cell line similarly leads to dramatic alterations in RNA splicing. Collectively, the dysregulated shelterin expression directly or indirectly induces significant changes in RNA splicing, thereby contributing to the MPN pathogenesis.

#### Biography

Dawei Xu has completed his PhD in 1999 from Karolinska Institutet. He is currently working as an Associate Professor at Department of Medicine, Karolinska Institutet. He has published more than 80 papers in peer-reviewed journals.

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