Inhibition of Transcription in *c-myc* by G-quadruplex DNA-Binding Protein Engineered from the RGG Domain of TLS/FUS

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The G-quadruplex in the promoter regions has a significant biological function, such as transcriptional regulation.[1] The G-rich sequences in *c-myc* promoter, which is one of the oncogenes, forms a parallel-stranded G-quadruplex in K^+ containing solution.[2] It suggests that G-quadruplex in *c-myc* promoter has a potential as a drug target because it regulates *c-myc* expression. Several G-quadruplex-binding small molecules have been developed for suppressing *c-myc* transcription[3], but low binding selectivity to G-quadruplex and high toxicity of them are disadvantage. We previously reported a novel G-quadruplex DNA binding protein (RGGF) engineered from Arg-Gly-Gly repeat (RGG) domain of translocated in liposarcoma (TLS; also termed fused in sarcoma [FUS]).[4]

Here we show that RGGF recognizes DNA loops in G-quadruplex and preferentially binds to G-quadruplex DNA with long loops. Furthermore, RGGF binds to G-quadruplex DNA of the *c-myc* promoter *in vitro* with a dissociation constant (K_d) of 2.7 ± 0.2 μM. In addition, RGGF overexpression in HeLa cells repress *c-myc* transcription as much as 47.5 ± 5.0% *in vivo* (Figure 1). On the basis of these findings, G-quadruplex binding protein engineered from RGG domain might be useful for investigating the function of the G-quadruplexes transcriptional in the promoter regions.

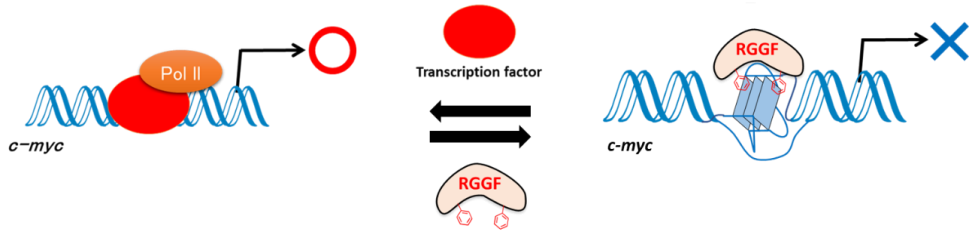

Figure 1. RGGF-binding G4 DNA inhibited *c-myc* transcription

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