

The “speed gene” effect of *myostatin* arises in Thoroughbred horses due to a promoter proximal SINE insertion

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In the finely-tuned athletic species of Thoroughbred horses, polymorphisms (Intro 1 SNP g.66493737C>T and SINE insertion 227bp in promoter) in the *myostatin* gene (*MSTN*), a pronounced inhibitor of skeletal muscle growth, have been shown to almost singularly account for gene-based race distance aptitude. Until now, it was not clear which variant affected skeletal muscle phenotypes or whether both impacted racing performance. Complete concordance between the SNP and the SINE insertion was observed in our Thoroughbred cohort. We isolated the SNP variant from the SINE polymorphism *in vitro* and showed the latter is exclusively responsible for adversely affecting transcription initiation and gene expression thereby limiting myostatin protein production. Mapping the *MSTN* transcription start site likewise revealed anomalous transcription initiation in the presence of the SINE insertion. Our data provides mechanistic evidence that the SINE insertion uniquely accounts for the *MSTN* “speed gene” effect on race distance aptitude in the Thoroughbred horse.