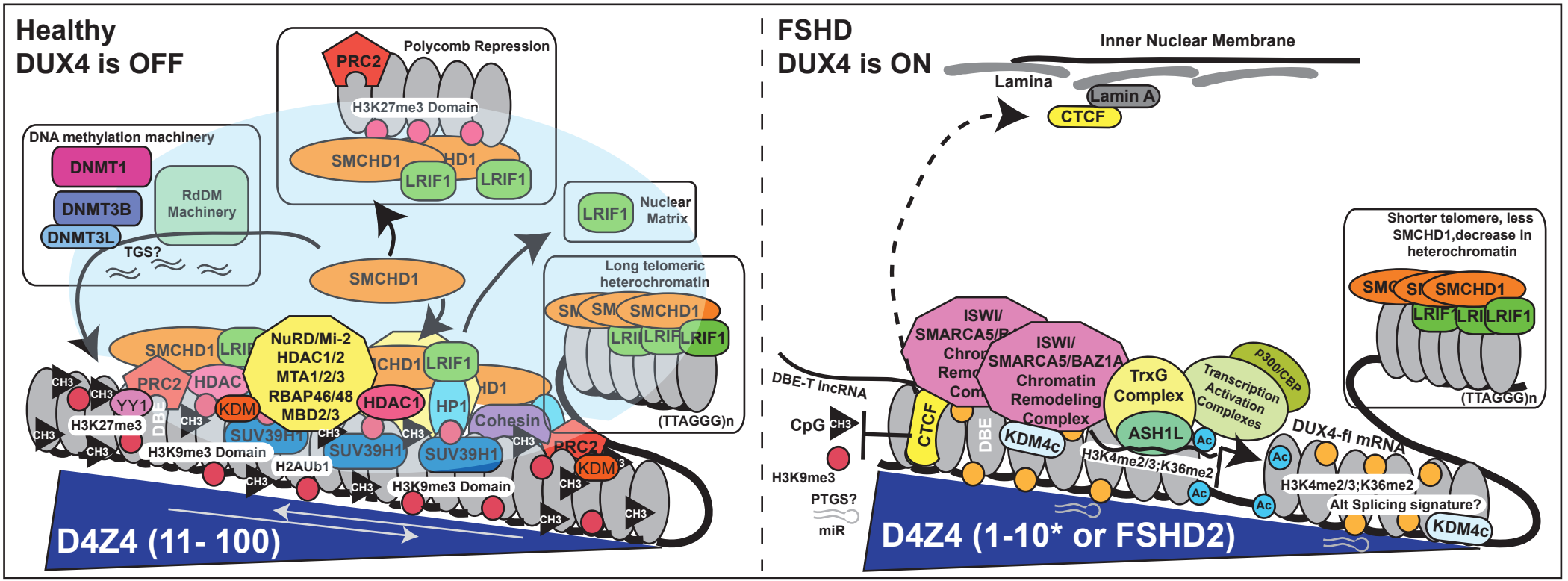
Model for FSHD1

FSHD1 and FSHD2 are caused by genetic changes that affect epigenetic repression of the chromosome 4 D4Z4 array resulting in aberrant expression of the *DUX4* gene from within the array.



(Left panel) Healthy-sized D4Z4 arrays are recognized by the cell's mlecular machinery to be transcriptionally silenced (OFF) in skeletal muscle cells and thus recruit transcriptional repressor proteins and establish an OFF epigenetic state. (Right panel) However, in FSHD1, the contraction of the D4Z4 array to less than 11 repeat units results in the D4Z4 array escaping recognition for transcription repression and the repressive proteins normally found on the expanded (healthy-sized) D4Z4 arrays are not recruited and the pathogenic *DUX4* gene is able to become expressed.