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'Jumping gene' may contribute to a premature aging syndrome

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Scientists have identified a fusion protein that may contribute to Cockayne syndrome, a devastating disease characterized by developmental defects, neurodegeneration, severe wasting, and premature aging. The study is described in an article published March 21 in the open-access journal *PLoS Genetics*.

Genetic defects in certain DNA repair factors like the CSB protein have been known for some time to cause premature aging, but the reasons are still unclear. Most cases of Cockayne syndrome (CS) are caused by recessive mutations in the CSB gene, yet some individuals with inherited mutations that cause complete loss of the CSB protein are nearly unaffected. The implication is that CS is not caused solely by loss of functional CSB protein, but by continued expression of CSB-related proteins or protein fragments.

The University of Washington researchers, led by Alan Weiner, had been investigating the normal function of the CSB gene when co-author John Newman stumbled across hints that the human CSB gene harbored a previously unsuspected guest. The guest was a "domesticated" PiggyBac transposon – a formerly selfish "jumping gene" that had settled into the CSB gene over 40 million years ago before marmosets diverged from humans. As a result, the CSB gene began making two equally abundant products – the normal CSB protein, and a fusion protein in which the beginning of the CSB protein was fused to the DNA transposase encoded by the PiggyBac element. Interestingly, the fusion protein continued to be expressed in almost all CS patients, but not in the

individual who was unaffected by a complete loss of the CSB protein.

The conserved fusion protein is clearly advantageous for the human species in the presence of the CSB protein, but potentially devastating for individuals in the absence of the CSB protein. As Newman remarks, "The discovery of the fusion protein complicates an already complicated situation. Now we have a whole new set of questions to answer."

Citation: Newman JC, Bailey AD, Fan H-Y, Pavelitz T, Weiner AM (2008) An Abundant Evolutionarily Conserved CSB-PiggyBac Fusion Protein Expressed in Cockayne Syndrome. PLoS Genet 4(3): e1000031. doi:10.1371/journal.pgen.1000031 (www.plosgenetics.org/doi/pgen.1000031)

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