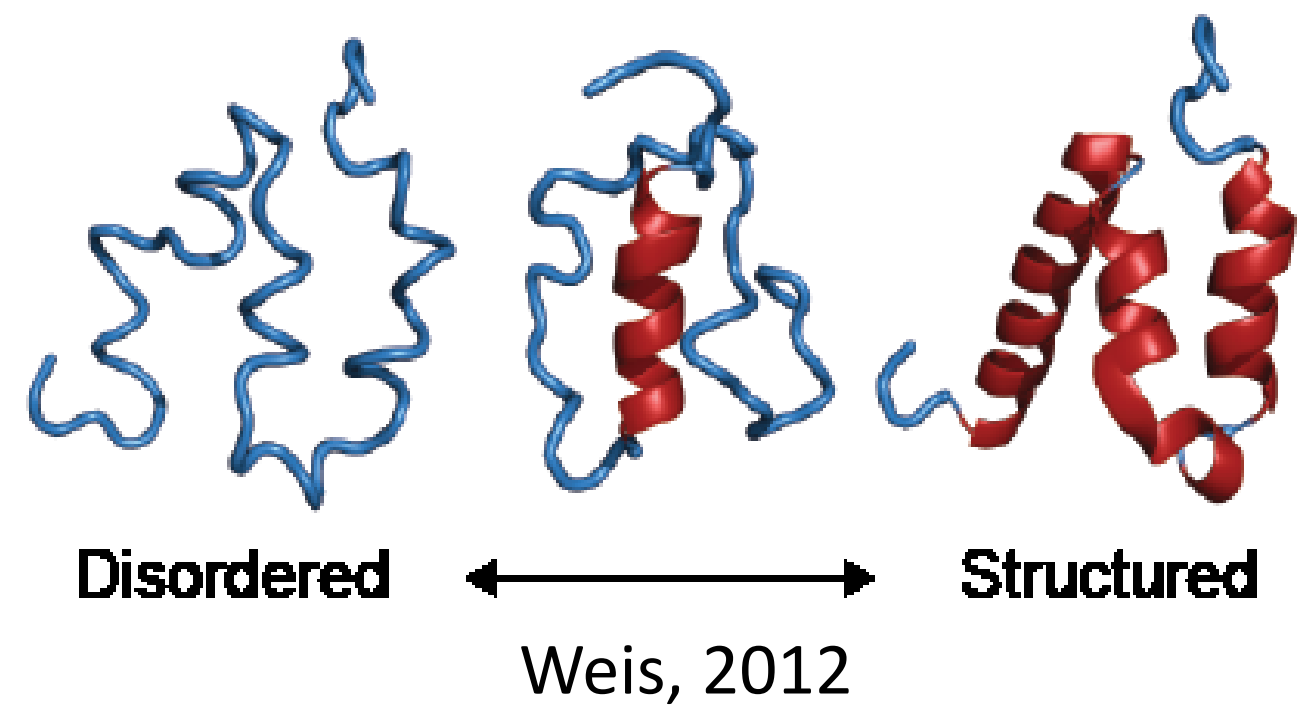


More Exquisitely Adapted Species Have Higher Structural Disorder in Vertebrate Protein Domains

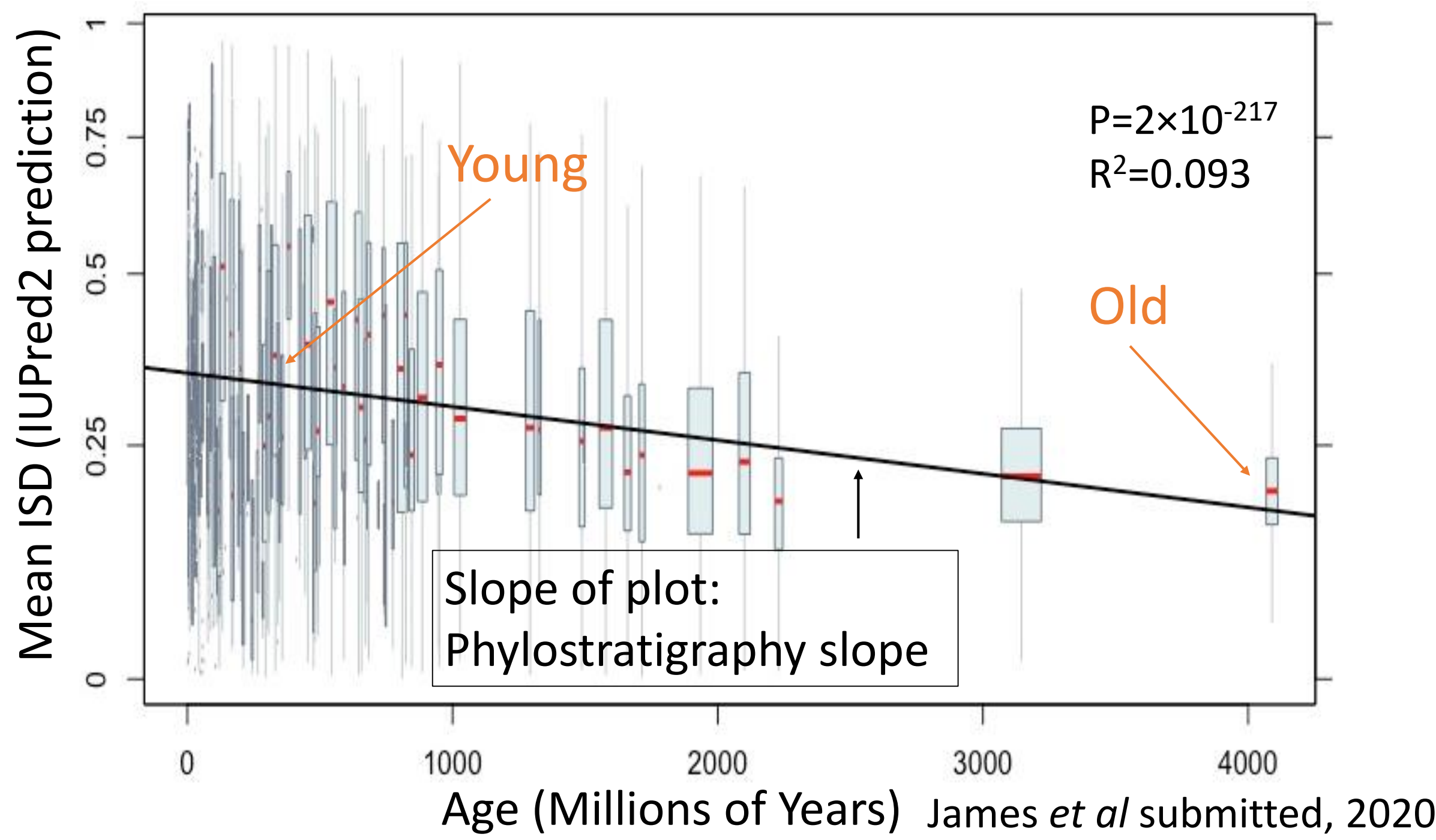
Catherine Weibel*, Jennifer James, Sara Willis, Paul Nelson, Joanna Masel
University of Arizona, Departments of Physics and Mathematics



1 Intrinsic Structural Disorder (ISD) describes the degree of conformational freedom of protein structures; linked with protein folding and aggregation (Foy *et. al*, 2019)



Work done in the Masel lab has found that old protein domains have lower ISD than young protein domains



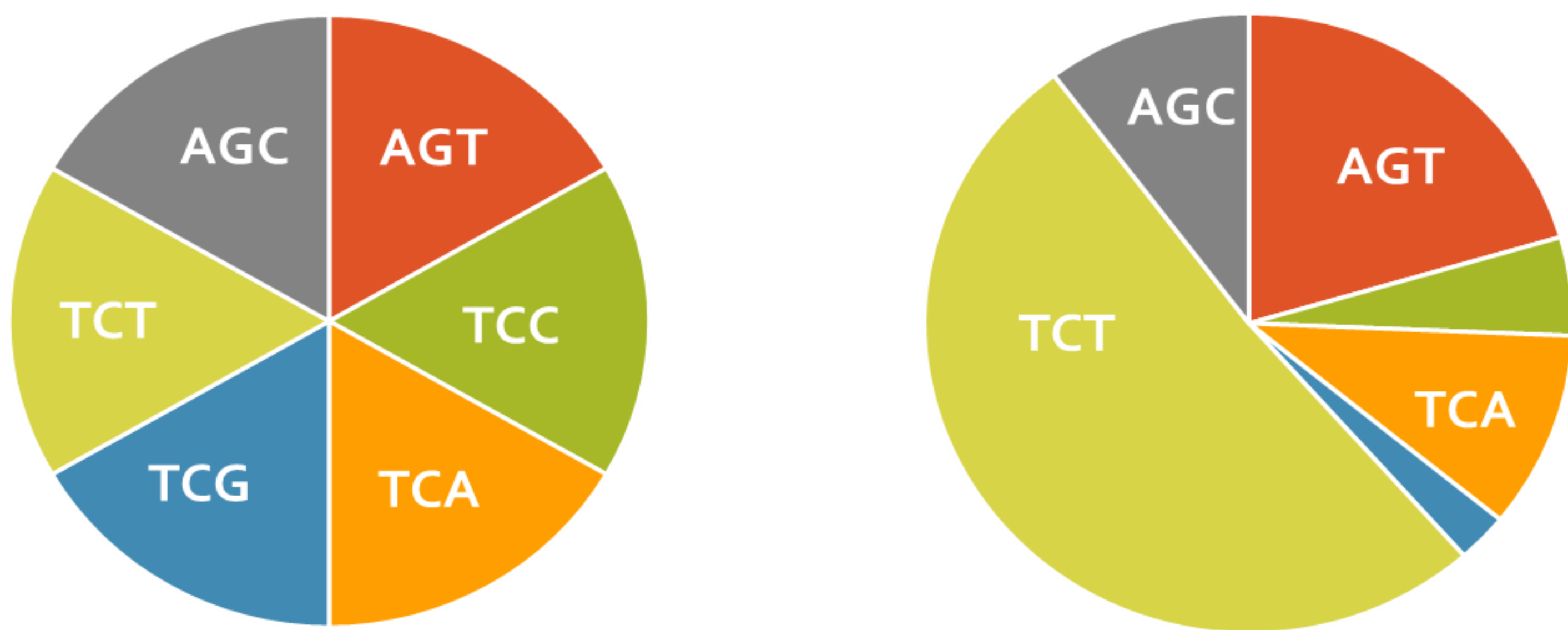
This implies the potential for an **arrow of time** for disorder trends in protein evolution

Do species with more effective selection prefer protein domains with more or less ISD ?

2 Effectiveness of selection is reflected in **synonymous codon usage**

Codon Nonadapted Serine

Codon Adapted Serine



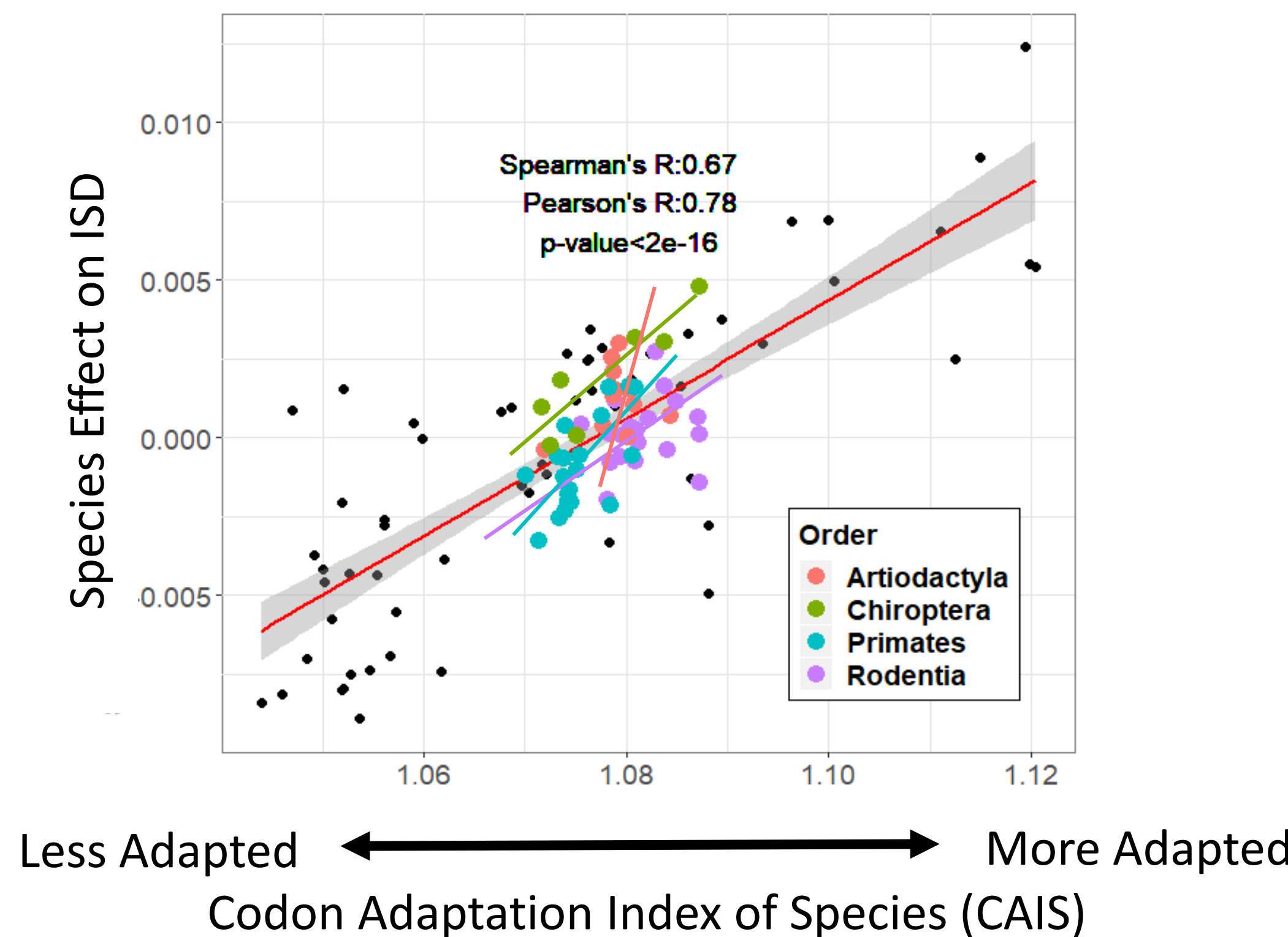
We designed a metric that is comparable between species, Codon Adaptation Index of Species (CAIS). It controls for GC content and amino acid composition.

3 We extracted how a given protein domain is different depending on which species it is found in



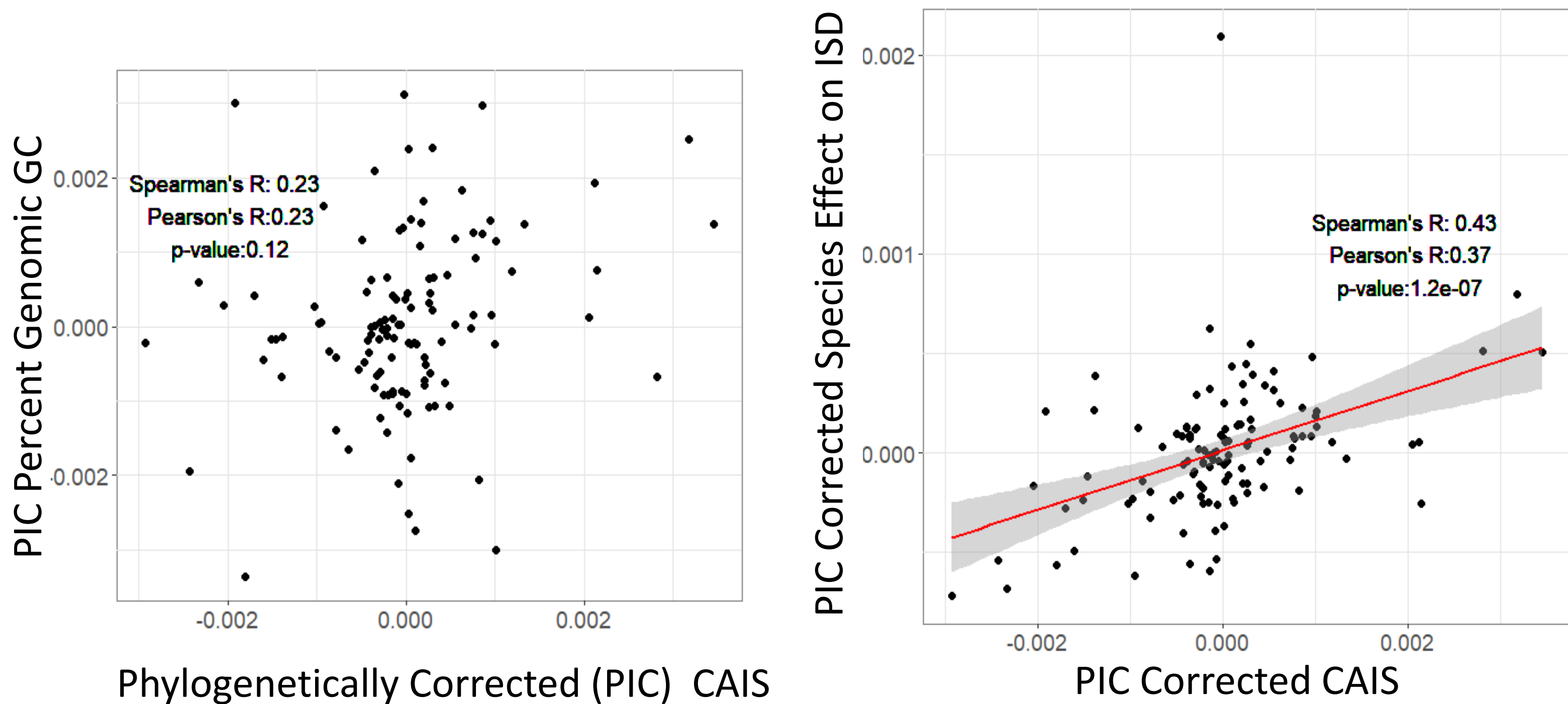
We ran linear models with species as fixed effect and Pfam as random effect to calculate a species-specific disorder metric

4 Well-adapted species have higher ISD

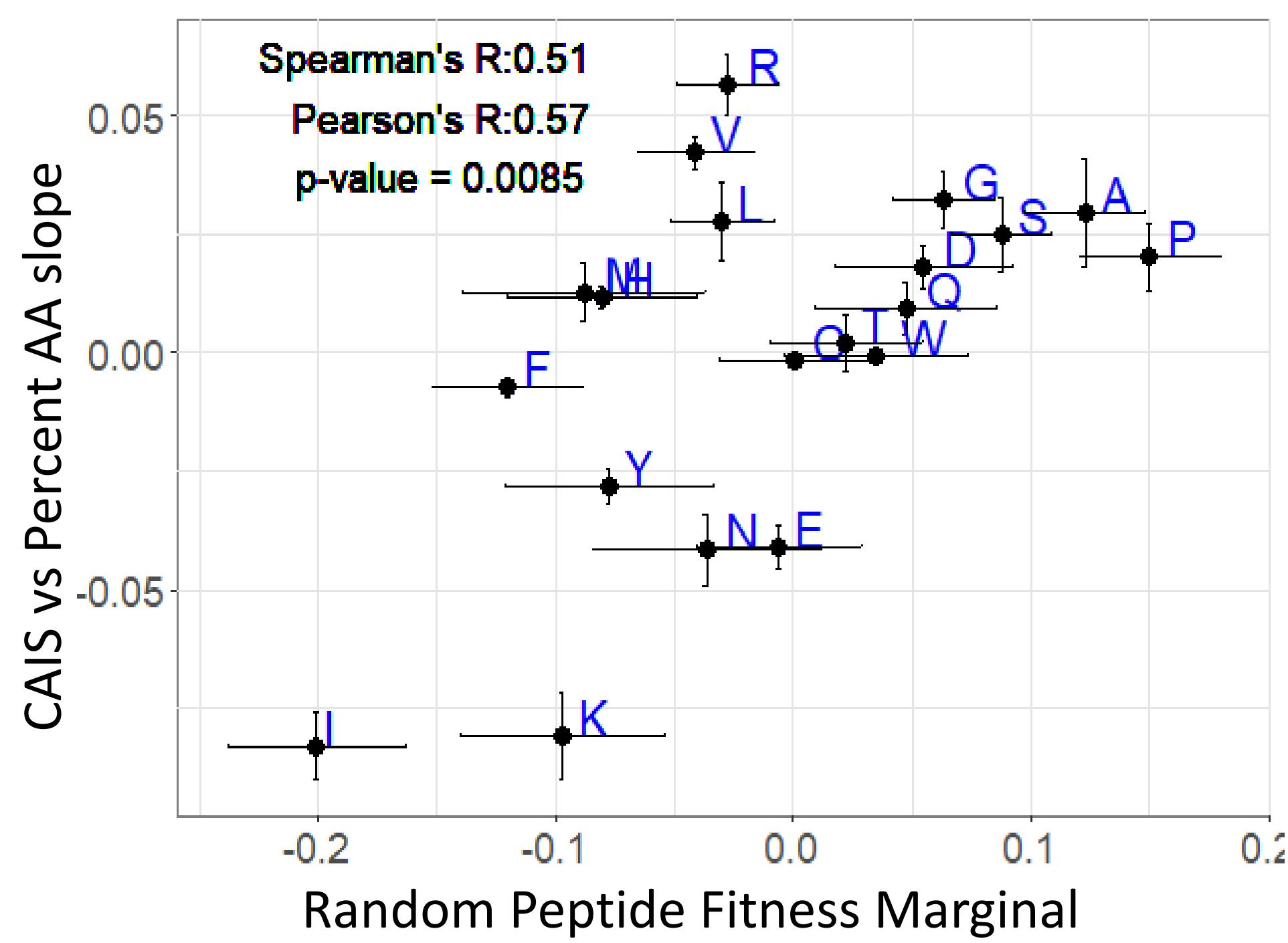


Data vulnerable to Simpson's Paradox, pseudoreplication and phylogenetic confounding; solved by using Phylogenetic Independent Contrasts (PIC)

PIC analysis confirms: Well-adapted species have higher ISD and CAIS is uncorrelated with genomic GC content



5 Species with more effective selection have protein domains that are enriched in less deleterious random peptides in *E. coli* (Marginal Effects from Kosinski *et. al*, in prep.)



Relationships between domain age and amino acid composition found in James *et. al* 2020 **cannot be explained** by variations in effectiveness of selection of species

