



**Figure S3.** Protein families containing candidate RBPs with significant sequence similarity display less variable UV-crosslinking efficiencies than higher-order protein classes. (A–E), Analytical summary: protein-specific UV-crosslinking efficiencies were  $\log_{10}$  normalized and adjusted by subtracting the average  $\log_{10}(\%CL)$  value of all candidate RBPs (total) or only those within their own protein class (e.g., InterPro families) for graphical purposes (E). Levene’s test for equality of variances detected a significant difference in %CL variability between total candidate RBPs and InterPro homologous superfamilies (A),  $F(1, 2550) = 145.42$ ,  $P < .001$ ; total candidate RBPs and Pfam clans (B),  $F(1, 2187) = 94.71$ ,  $P < .001$ ; InterPro homologous superfamilies and InterPro families (C),  $F(1, 1575) = 47.47$ ,  $P < .001$ ; Pfam clans and Pfam families (D),  $F(1, 1345) = 25.67$ ,  $P < .001$ . Summary of statistical test results included as part corresponding Source Data in the provided Source Data file. Complete list of %CL ranked InterPro and Pfam IDs, including those mapped to less than 3 candidate RBPs containing estimated UV-crosslinking efficiencies, were included as part of Supplemental Table S3.