

**Table S3. Categorization into known, semi-novel, and novel motifs****A. Categorizing 100 randomly chosen motifs (%)**

<b>100 Random Motifs</b>	<b>Non- Domain Signatures</b>	<b>Domain Signature</b>	<b>Totals</b>
Known	15	3	18
Semi-novel	39	8	47
Novel	26	9	35
<i>Totals</i>	80	20	100

**B. Categorizing all ~6900 motifs (%)**

<b>All motifs</b>	<b>Non Domain Signatures</b>	<b>Domain Signature</b>	<b>Totals</b>
Known } Semi-novel }	42	12	55
Novel	36	10	45
<i>Totals</i>	78	22	22

(A) 100 randomly chosen motifs were analyzed by hand and categorized into one of three classifications: known, semi-novel, and novel. Known motifs are those that match previously identified motifs in the literature in both sequence and biological context; semi-novel motifs are those that match a previously identified motif in sequence but not in biological context; novel motifs are those that do not match any previously identified motif. Motifs with a positive overlap Z-score were considered to be domain signatures. (B) All ~6,900 motifs found in this study were automatically classified into one of two categories: known/semi-novel if they matched a previously identified motif, and novel otherwise. Motifs with a positive overlap Z-score were considered to be domain signatures.