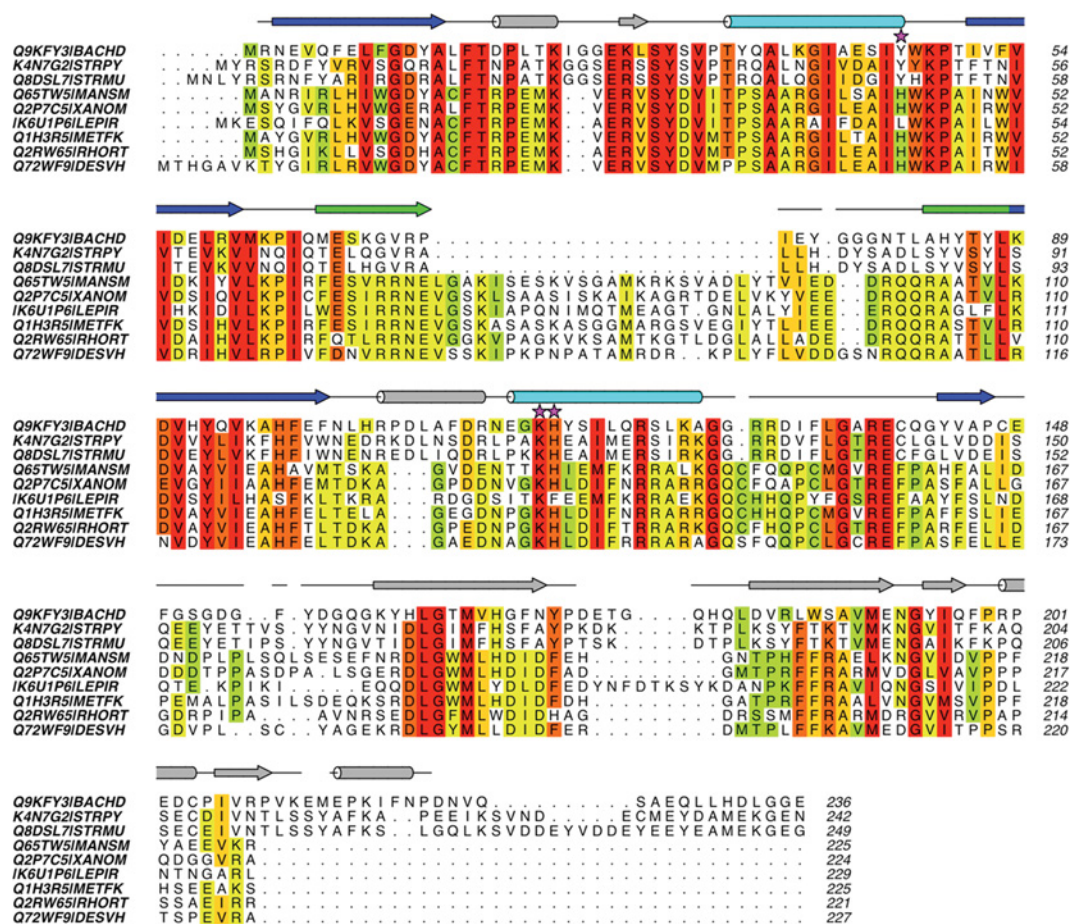


# SUPPLEMENTARY ONLINE DATA

## CRISPR interference: a structural perspective

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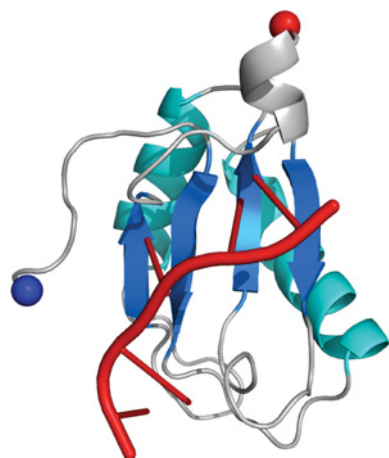
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**Figure S1** Sequence alignments of Cas5c proteins

Sequence similarity is shaded from red (highest) to green (lowest). The secondary structure elements of BhCas5c are shown above the alignments and are coloured according to Figure 3 of the main text. Gaps in the elements represent disordered residues. The catalytic residues of BhCas5c are indicated by magenta stars.

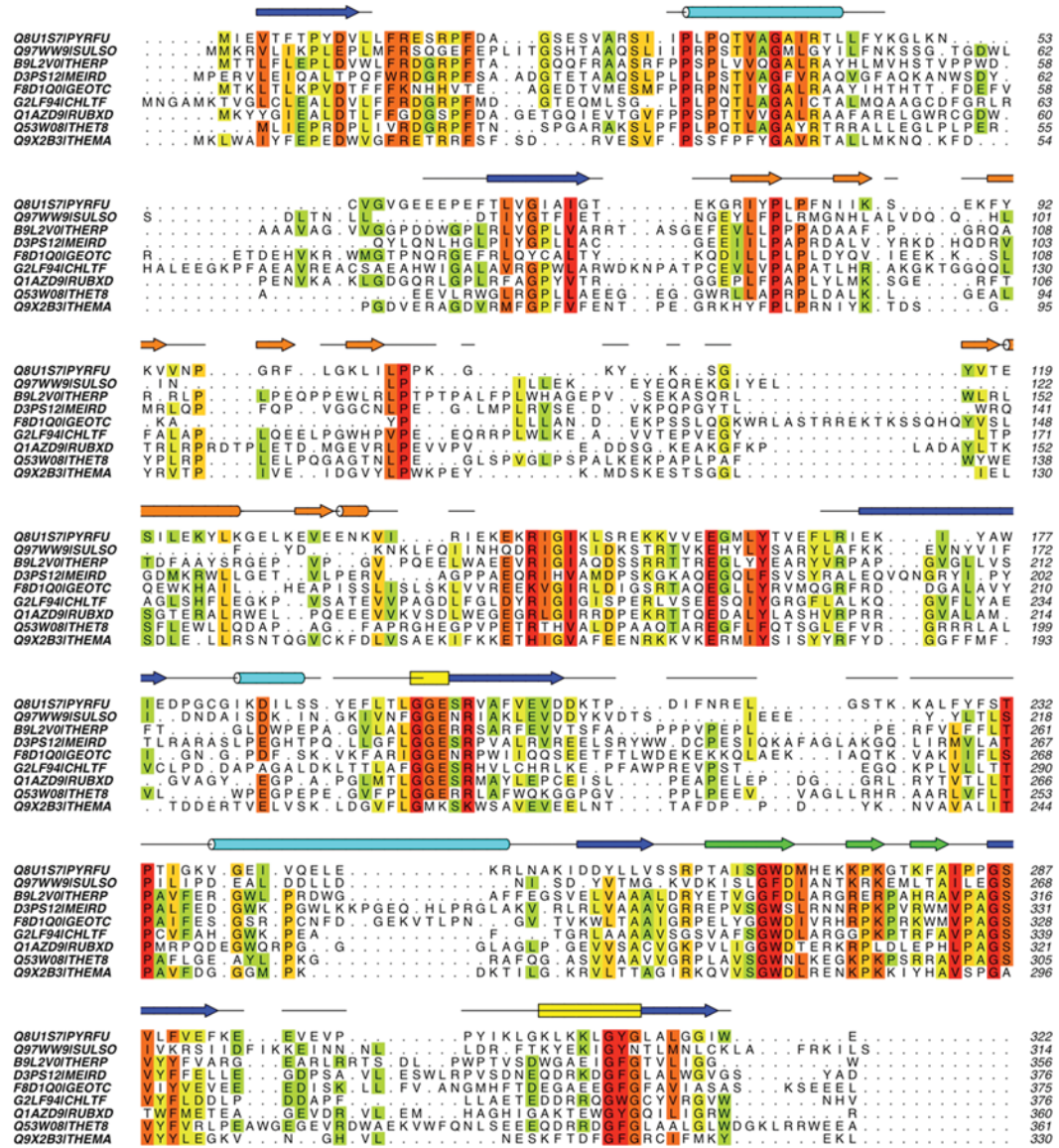
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RNP1 K/R-G-F/Y-G/A-F/Y-I/L/V-X-F/Y  
RNP2 I/V/L-F/Y-I/V/L-X-N/L

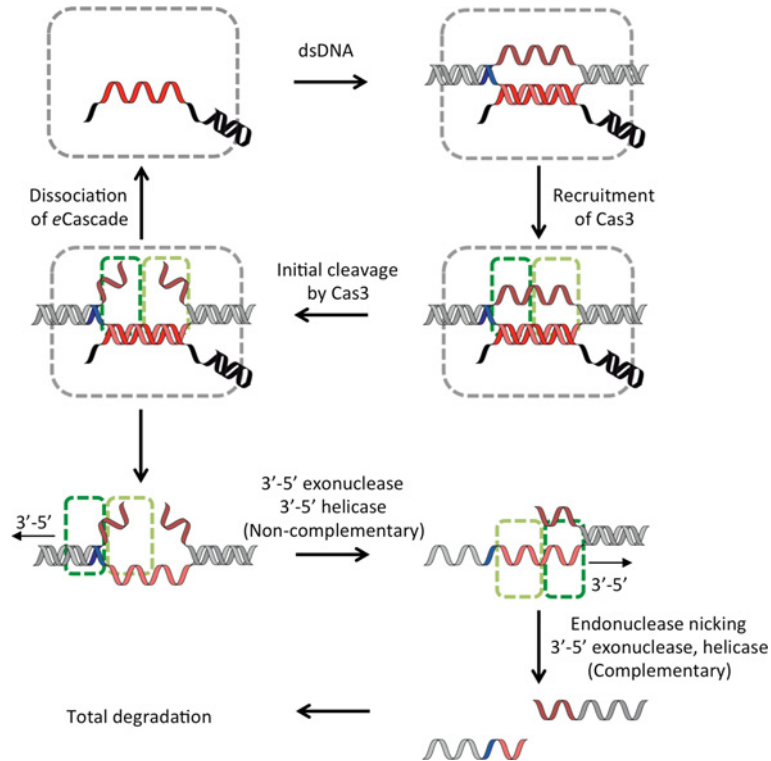
**Figure S2 The structure of U1A spliceosomal protein, a typical RRM protein, in complex with RNA (red) (PDB code 1URN)**

For clarity, the unbound RNA hairpin is not shown. The two RRM RNA-binding consensus sequences are shown beneath the structure. The RRM domain is coloured in the same manner as the RAMP domain in the main text.



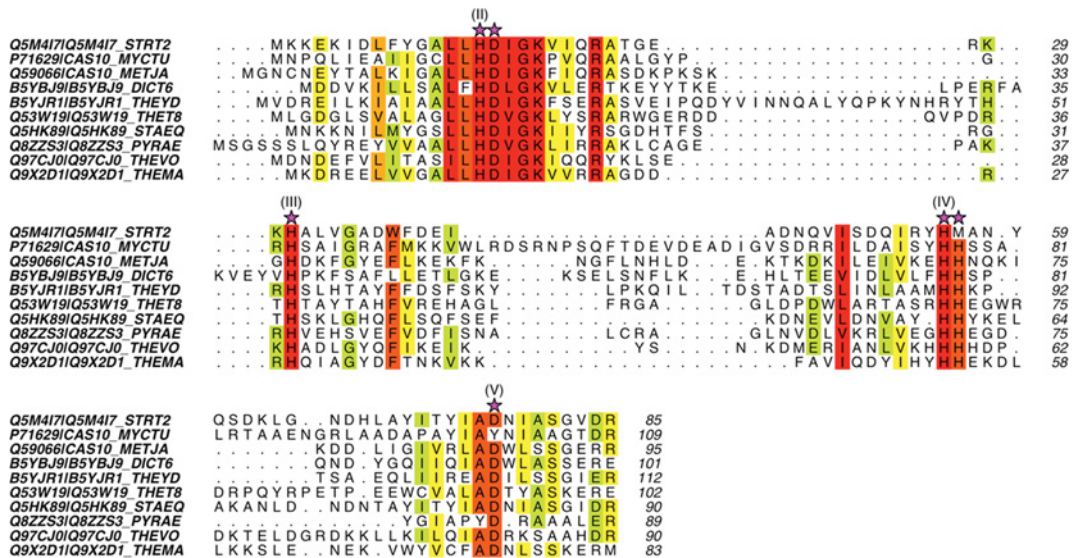
**Figure S3** Sequence alignment of Cmr3 proteins

Sequence similarity is shaded from red (highest) to green (lowest). The secondary structure elements from PfuCmr3 are shown above and coloured according to Figure 8 of the main text.



**Figure S4 Schematic diagram of dsDNA degradation by Cas3 in the type I-E system**

Repeats are shown in black, protospacers and spacers in red, PAMs in blue and DNA in grey. The Cas3 HD domain is represented by a light green dotted line, the Cas3 helicase domain in dark green and eCascade by a grey line.



**Figure S5 Sequence alignments of the HD domains of Cas10a**

The putative HD superfamily sequence motifs are highlighted with magenta stars and the motif number is indicated.

**Table S1** Details of all of the crystal structures of Cas proteins available at the time of writing

Protein	Organism	PDB code(s)	Notes
Cas1	<i>Aquifex aeolicus</i>	2YZS	
Cas1	<i>Escherichia coli</i>	3NKD, 3NKE	
Cas1	<i>Pseudomonas aeruginosa</i>	3GOD	
Cas1	<i>Pyrococcus horikoshii</i>	3PV9	
Cas1	<i>Thermotoga maritima</i>	3LFX	
Cas2	<i>Bacillus halodurans</i>	4ES1, 4ES2, 4ES3	
Cas2	<i>Desulfovibrio vulgaris</i>	3OQ2	
Cas2	<i>Pyrococcus furiosus</i>	2IOX	
Cas2	<i>S. solfataricus</i>	2IVY, 2I8E, 3EXC	Two paralogues
Cas2	<i>Thermus thermophilus</i>	1ZPW	
Cas3	<i>T. thermophilus</i>	3SK9, 3SKD	HD domain only
Cas3''	<i>Methanocaldococcus jannaschii</i>	3S4L	
Cas4	<i>S. solfataricus</i>	4IC1	
Cas5c	<i>Mannheimia succiniciproducens</i>	3KG4	
Cas5c	<i>Bacillus halodurans</i>	4F3M	
Cas5c	<i>Streptococcus pyogenes</i>	3VZH	
Cas5c	<i>Xanthomonas oryzae</i>	3VZI	
Cas6	<i>E. coli</i>	4DZD	
Cas6	<i>P. furiosus</i>	3I4H, 3PKM, 3UFC	Two paralogues
Cas6	<i>P. horikoshii</i>	3QJJ, 3QJL, 3QJP	
Cas6	<i>S. solfataricus</i>	3ZJV, 4ILL, 4ILM, 4ILR	Two paralogues
Cas6e	<i>T. thermophilus</i>	1WJ9, 2Y8W, 2Y8Y, 2Y9H, 3QRP, 3QRQ, 3QRR	
Cas6f	<i>Ps. aeruginosa</i>	2XLI, 2XLJ, 2XLK, 4AL5, 4AL6, 4AL7	
Cas7	<i>S. solfataricus</i>	3PS0	
Cas10b <sup>dHD</sup>	<i>P. furiosus</i>	3UNG, 3UR3, 4DOZ, 4H4K	Lacking HD domain, also in complex with Cmr3
Csm6	<i>S. solfataricus</i>	3QYF	
Csn2	<i>Enterococcus faecalis</i>	3S5U	
Csn2	<i>Streptococcus agalactiae</i>	3QHQ	
Csn2	<i>S. pyogenes</i>	3TOC, 3V7F	
Csn2	<i>Streptococcus thermophilus</i>	3ZTH	
Cmr3	<i>P. furiosus</i>	4H4K	In complex with Cas10b <sup>dHD</sup>
Cmr5	<i>Archaeoglobus fulgidus</i>	2OEB	
Cmr5	<i>P. furiosus</i>	4GKF	
Cmr5	<i>T. thermophilus</i>	2ZOP	
Cmr7	<i>S. solfataricus</i>	2XVO, 2X5Q	Two paralogues, <i>Sulfolobales</i> -specific
Csa3	<i>S. solfataricus</i>	2WTE	
Csa5	<i>S. solfataricus</i>	3ZC4	
Cse1	<i>Acidimicrobium ferrooxidans</i>	4H3T	
Cse1	<i>T. thermophilus</i>	4AN8, 4F3E, 4EJ3	
Cse2	<i>Thermobifida fusca</i>	4H79	
Cse2	<i>T. thermophilus</i>	2ZCA, 4H7A	
Csn2	<i>Streptococcus thermophilus</i>	3ZTH	
Csx1	<i>P. furiosus</i>	4EOG	
Csx1	<i>S. solfataricus</i>	2I71	

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