SUPPLEMENTARY ONLINE DATA

CRISPR interference: a structural perspective

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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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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 RPM 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    | Aquifex aeolicus | 2YZS | |
| Cas1    | Escherichia coli | 3NKD, 3NKE | |
| Cas1    | Pseudomonas aeruginosa | 3GG0 | |
| Cas1    | Pyrococcus horikoshii | 3PV9 | |
| Cas1    | Thermotoga maritima | 3LFX | |
| Cas2    | Bacillus halodurans | 4ES1, 4ES2, 4ES3 | |
| Cas2    | Desulfovibrio vulgaris | 3OG2 | |
| Cas2    | Pyrococcus furiosus | 3OG2 | |
| Cas2    | S. solfataricus | 2IV, 2I8E, 3EXC | Two paralogues |
| Cas2    | Thermus thermophilus | 12PW | |
| Cas3    | T. thermophilus | 3SK9, 3SKD | HD domain only |
| Cas3*   | Methanocaldococcus jannaschii | 3S4L | |
| Cas4    | S. solfataricus | 4I1C | |
| Cas5c   | Mannheimia succiniciproducens | 3KG4 | |
| Cas5c   | Bacillus halodurans | 4FRM | |
| Cas5c   | Streptococcus pyogenes | 3V1H | |
| Cas5c   | Xanthomonas oryzae | 3V2I | |
| Cas6    | E. coli | 4DO2 | |
| Cas6    | P. turgidus | 3I4H, 3P3K, 3UFC | Two paralogues |
| Cas6    | P. horikoshii | 3OJU, 3OJL, 3OJP | |
| Cas6    | S. solfataricus | 3OJU, 4I1L, 4I1M, 4I1R | Two paralogues |
| Cas6b   | T. thermophilus | 1WJ9, 2Y8N, 2Y8Y, 2Y8H, 3QRQ, 3QR0, 3QRR | |
| Cas6f   | Ps. aeruginosa | 2XLI, 2XLI, 2XLI, 4A3L, 4A3L, 4A3L | |
| Cas6f   | S. solfataricus | 3PS0 | |
| Cas10b<sup>HD</sup> | P. turgidus | 3UNG, 3UR1, 3U0Z, 4P4K | Lacking HD domain, also in complex with Cmr3 |
| Csm6    | S. solfataricus | 3OYF | |
| Csm6    | Enterococcus faecalis | 3SSU | |
| Csm6    | Streptococcus agalactiae | 3OHQ | |
| Csm6    | S. pyogenes | 3TOC, 3TVF | |
| Csm6    | Streptococcus thermophilus | 3TH | |
| Cmr3    | P. turgidus | 4H4K | In complex with Cas10b<sup>HD</sup> |
| Cmr5    | Archaeoglobus fulgidus | 20E8 | |
| Cmr5    | P. turgidus | 4GK8 | |
| Cmr5    | T. thermophilus | 209P | |
| Cmr7    | S. solfataricus | 2X30, 2X3Q | Two paralogues, Sulfolobales-specific |
| Csa3    | S. solfataricus | 3W3E | |
| Csa3    | S. solfataricus | 3ZC3 | |
| Csa3    | Acidimicrobium ferrooxidans | 4H3T | |
| Csa1    | T. thermophilus | 4AN8, 4F3E, 4E3J | |
| Csa2    | Thermotoga fusca | 4H79 | |
| Csm2    | T. thermophilus | 22CA, 4H7A | |
| Csm2    | Streptococcus thermophilus | 3ZTH | |
| Csx1    | P. turgidus | 4E3G | |
| Csx1    | S. solfataricus | 2I7 | |

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