

Supplementary information, Table S5.

RVDs targeting multiple bases.

RVDs targeting two bases

| Category | RVDs | A | T | C | G |
|----------|------|----|----|----|------|
| A/T | SG | + | + | - | - |
| A/C | HC | ++ | - | ++ | - |
| | KC | ++ | - | ++ | - |
| | NC | + | - | + | - |
| | KS | ++ | - | + | - |
| A/G | HN | ++ | - | - | ++++ |
| | NN | ++ | - | - | ++++ |
| T/C | HA | - | + | + | - |
| | KA | - | ++ | + | - |
| | KP | - | ++ | + | - |
| | FS | - | + | + | - |
| T/G | KF | - | + | - | + |
| | SN | - | + | - | + |
| | RQ | - | + | - | ++++ |
| | GR | - | + | - | + |
| C/G | KR | - | + | - | +++ |
| | HQ | - | - | + | +++ |
| | KQ | - | - | + | ++ |
| | QR | - | - | + | ++ |
| | YR | - | - | + | ++++ |

RVDs targeting four bases

| Category | RVDs | A | T | C | G |
|----------|------|-----|----|-----|-----|
| A/T/C/G | RH | + | + | + | +++ |
| | LQ | + | ++ | + | + |
| | VR | + | + | + | ++ |
| | CS | + | + | + | + |
| | RT | + | + | + | ++ |
| | RV | +++ | ++ | +++ | ++ |

Note:

The ranges of fold induction of EGFP reporter for RVDs in TALE-(XX')₃ are indicated as follows:

| | |
|------|---------|
| - | < 6 |
| + | 6 - 12 |
| ++ | 12 - 18 |
| +++ | 18 - 24 |
| ++++ | ≥ 24 |

RVDs targeting three bases

| Category | RVDs | A | T | C | G |
|----------|------|------|----|-----|------|
| A/T/C | RL | + | ++ | + | - |
| | MS | + | + | + | - |
| | TT | + | + | + | - |
| A/T/G | TC | ++ | + | - | + |
| | MH | + | + | - | + |
| | LR | + | + | - | ++ |
| | SS | + | + | - | + |
| A/C/G | RC | + | - | ++ | + |
| | CR | + | - | + | +++ |
| | HS | ++ | - | ++ | ++++ |
| | NS | ++++ | - | + | ++++ |
| | HT | ++ | - | + | + |
| | KT | + | - | + | ++ |
| | NT | ++++ | - | + | ++++ |
| | HV | ++ | - | + | + |
| | KV | ++++ | - | +++ | +++ |
| | NV | ++ | - | + | + |
| T/C/G | FQ | - | + | + | + |
| | NA | - | ++ | + | + |
| | RN | - | + | + | ++++ |

SUPPLEMENTARY REFERENCES

1. Zhang, F. et al. Efficient construction of sequence-specific TAL effectors for modulating mammalian transcription. *Nature biotechnology* **29**, 149-153 (2011).
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3. Boussif, O. et al. A versatile vector for gene and oligonucleotide transfer into cells in culture and in vivo: polyethylenimine. *Proc Natl Acad Sci U S A* **92**, 7297-7301 (1995).
4. Mussolino, C. et al. A novel TALE nuclease scaffold enables high genome editing activity in combination with low toxicity. *Nucleic acids research* (2011).