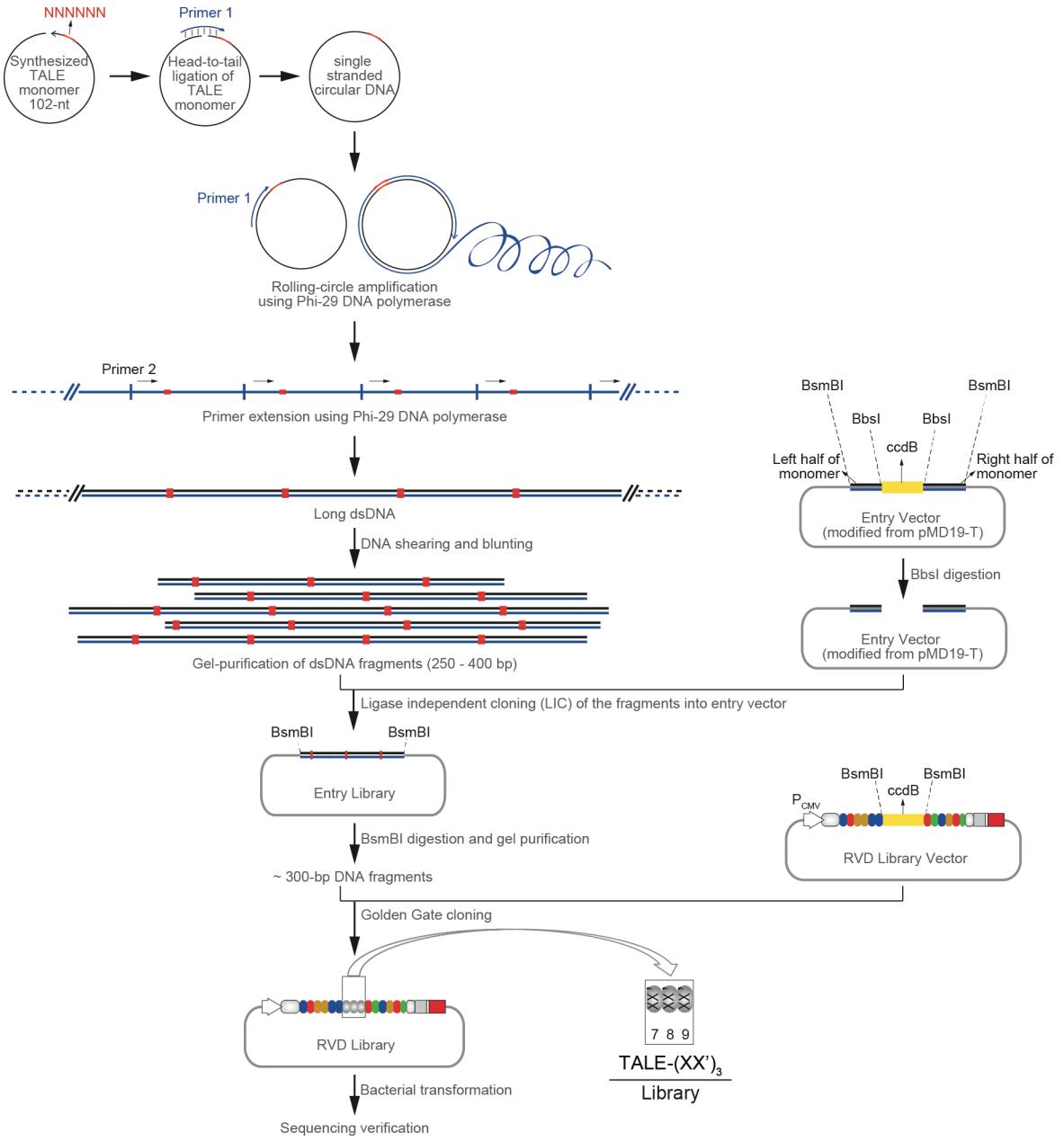

Supplementary information, Figure S2 Schematic of TALE-$(XX')_3$ library construction for novel RVD screening. A 102-nt monomer encoding a standard TALE repeat unit, containing six random nucleotides at the RVD-encoding region, was synthesized and subsequently cyclized. Rolling-circle amplification of these single-strand circular DNA templates was conducted using phi29 DNA polymerase and primer 1, and dsDNA fragments were obtained from primer extension using primer 2. After ultrasonic shearing followed by DNA blunting, 250-400 bp DNA fragments were isolated. After gel purification,

these DNA fragments were cloned into a pre-made entry vector through the LIC method. BsmBI digestion of clones in the entry library produced ~300 bp DNA fragments, which were subsequently ligated into a pre-made RVD library vector. After bacterial transformation and sequencing validation, we were able to obtain 400 types of plasmids encoding customized TALEs with three repeat modules in the middle (7^{th} to 9^{th}) carrying the variable RVDs for testing. A detailed protocol is provided in the Supplementary Methods.