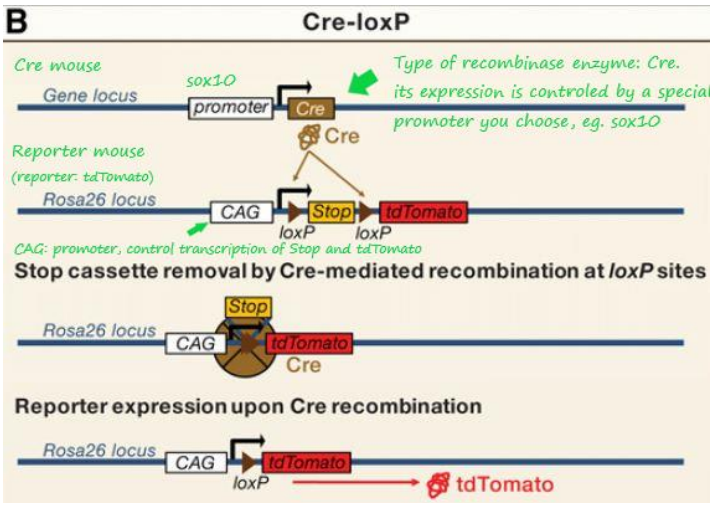
Lineage Tracing, primer. 2012 cell



Wildly used recombination systems: **Cre-loxP, FLP-FRT, Dre-Rox**

Cre, FLP and Dre are three types of recombinase enzymes.

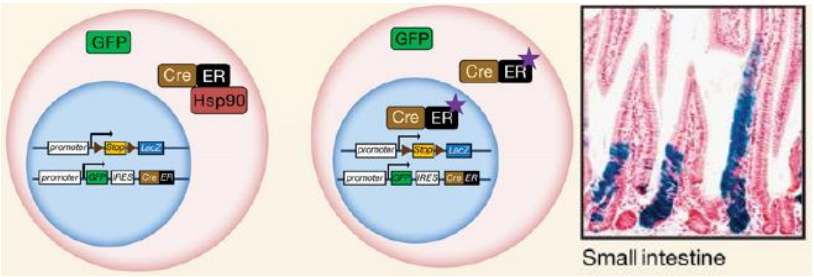
loxP, FRT, Rox are the target sequences specifically recognized by Cre, FLP and Dre, respectively.

Cre mouse: Sox10CreER^{T2}

Cre recombinase is expressed under the control of a tissue- or cell-specific promoter in one mouse line.
Sox10-Cre: Cre gene is knocked into Sox10 locus, after Sox10 promoter, so Cre expression is controlled by Sox10 promoter. Cells with Sox10 expression will also express Cre.

CreER: inducible Cre

CreER: Cre recombinase-ER fusion protein. Cre recombinase is typically fused to the human estrogen receptor (ER), In the absence of ligands, such as tamoxifen, CreER is expressed but it is inactive. It is kept in the cytoplasm by heat shock proteins (Hsp90, Figure below). Upon tamoxifen treatment, the ligand (tamoxifen) diffuses into the cell cytoplasm and binds to the ER. CreER then changes confirmation, leading to a release from its Hsp90 chaperones. Activated CreER translocates to the nucleus, where Cre can recombine (recognize and cut) the loxP sites. To prevent CreER from being activated by mouse endogenous ER ligand, more specific and sensitive mutants of CreER have been generated, such as **CreER^{T2}**.



Rosa26-CAG-tdTomato: Reporter mouse

Reporter proteins: tdTomato is one of the brightest fluorescent proteins currently available. Other common fluorescent proteins include GFP, EGFP, YFP, EYFP, RFP, CFP etc. as well as non-fluorescent proteins LacZ. The protein product of LacZ gene is β-galactosidase which will react with its substrate X-galactose and generate blue color, can be visualized without fluorescent microscope. Figure below:

In the **Rosa26-CAG**-tdTomato reporter mouse, tdTomato, together with a strong and ubiquitous promoter CAG, is knocked into the Rosa26 locus. Ubiquitous means the promoter is active in every type of tissues/cells.

Sox10CreER^{T2} X Rosa26-CAG-tdTomato:

Cre mouse cross with Reporter mouse, in their progeny, Sox10 positive cells are labeled with tdTomato. In other words, cells with tdTomato is expressing or used to express sox10.

In cells with Sox10 expression, Sox10 promoter is active and drives CreER^{T2} expression. With presence of tamoxifen, CreER^{T2} enter nuclear and cut loxP-Stop-loxP. As a result, reporter protein tdTomato is finally produced, thus labels these cells with red fluorescence. Because loxP-Stop-loxP is cut from genome DNA, this change is permanently.

In your example, R26ReYFP is likely **Rosa26-CAG-loxP-Stop-loxP-EYFP.**