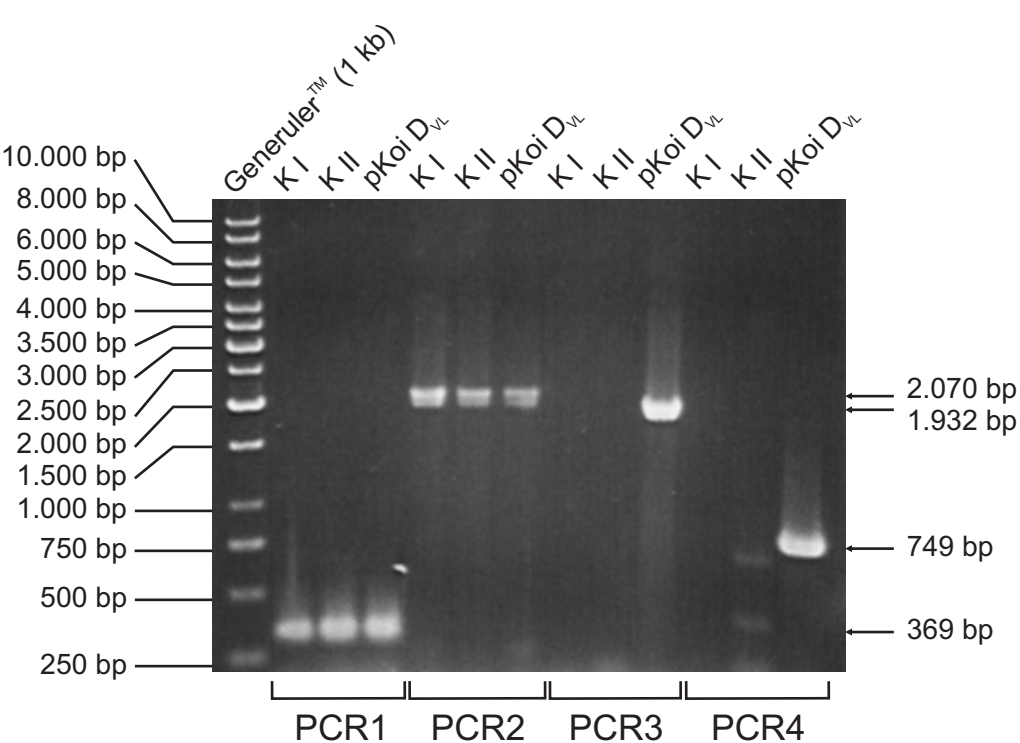
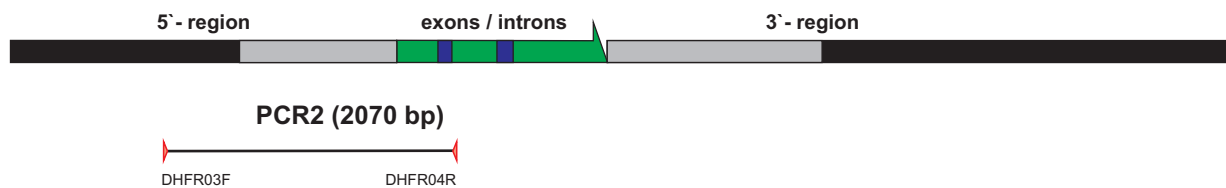
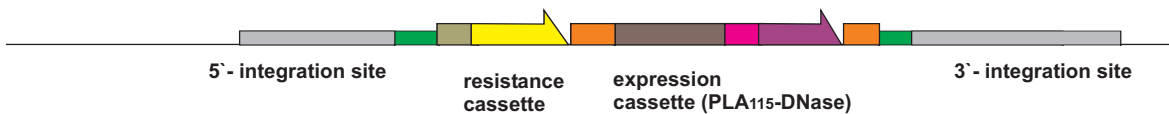




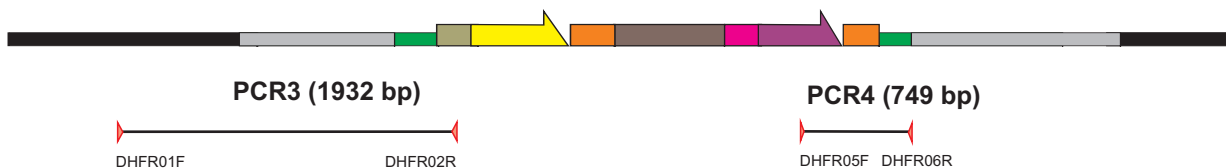
## DHFR-TS gene structure



## pKoi D<sub>vL</sub> plasmid



## DHFR-TS knock out by knock in (integration)



- |                                                                                    |                                           |                                                                                     |                                 |
|------------------------------------------------------------------------------------|-------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------|
|  | up/downstream regions of the DHFR-TS gene |  | neo resistance gene             |
|  | regions amplified for integration         |  | BTU2 terminator                 |
|  | exon of the DHFR-TS gene                  |  | MTT-1 promoter                  |
|  | intron of the DHFR-TS gene                |  | precursor sequence from PLA1    |
|  | histone promoter                          |  | sequence encoding human DNase I |