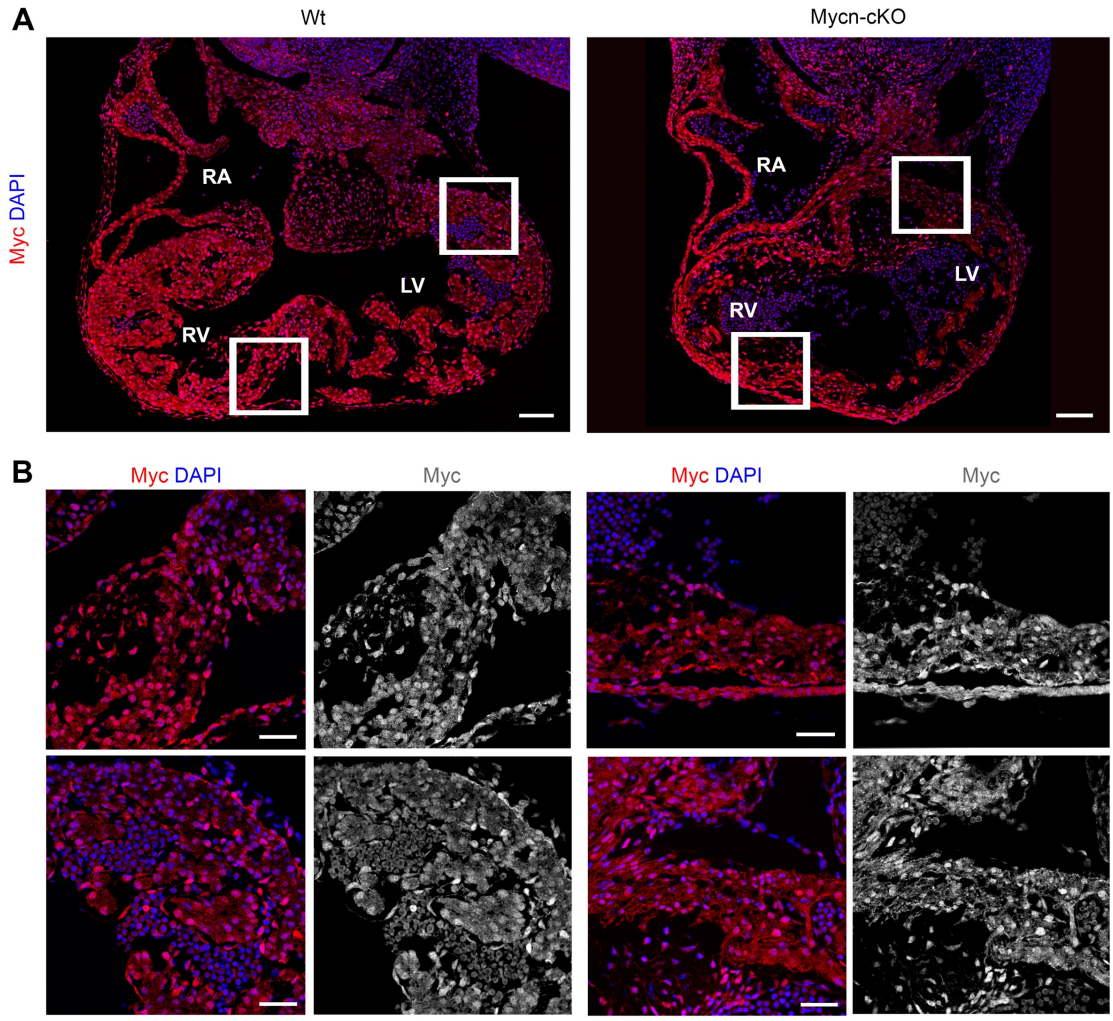

Figure S1. Myc antibody staining in *Mycn*-deficient hearts. A. Confocal images showing Myc antibody staining in sections of a E10.5 WT heart (left) and Mycn-cKO (right). **B**. Magnification of boxed areas in A. WT heart is shown on left panels and Mycn-cKO on right panels. Greyscale images of antibody staining are shown in both cases. Bar 100 μm in A and 50 μm in B. LV: Left ventricle, RV: Right ventricle, RA: Right atria, LA: Left atria,

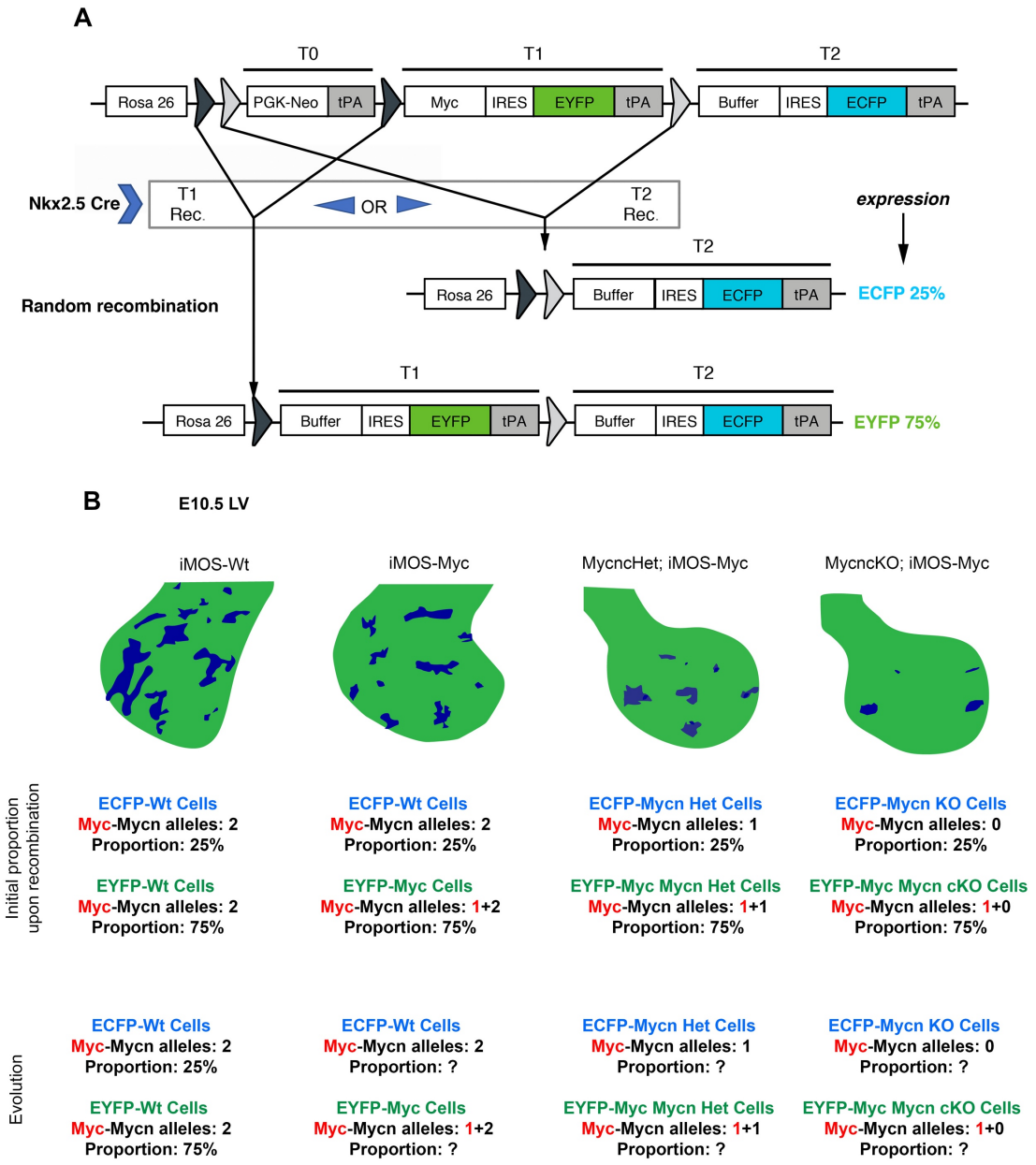

Figure S2. Summary of the iMOS-mosaic system and the different genetic combinations used in this work. **A.** Schematic of the *iMOS*$^{T1\text{-}Myc}$ allele. The system consists of three cassettes knocked-in to the *Rosa26* locus that can be excised by Cre recombination at random due to two pairs of LoxP sites. When the T0 cassette is excised, T1 is expressed and the cell and its progeny will be labelled in EYFP and overexpress Myc (EYFP-Myc). When T2 recombination takes place both T0 and T1 are excised leading to the expression of T2 (ECFP-WT) in the resulting cell and its progeny. Due to the distances between the lox sites and the Cre efficiency, the proportions of each cell type upon recombination is 75:25 (EYFP:ECFP), as determined experimentally in several tissues. Upon Cre-recombinase exposure, the system thus generates two labelled cell populations at random but reproducible frequencies. **B.** Schematics of E10.5

LV showing the two labelled cell populations in iMOS-WT, iMOS-Myc, MycnHet;iMOS-Myc and MycncKO;iMOS-Myc embryos. Below the images, the proportions and corresponding allele ratio for Myc and Mycn of each cell type is shown. At initial timepoints the relative proportion of EYFP and ECFP proportions is 75:25. In iMOS-Wt this is maintained because no cell population has a competitive advantage over the other. When an imbalance in Myc and Mycn alleles between neighbouring cells is implemented due to the iMOS system and the conditional deletion of Mycn, these proportions vary with developmental progression. Green and blue colours represent the EYFP and ECFP cell populations, respectively.

Table S1. Observed and expected frequencies of adult mice of the different genotypes

Genotype	Adult mice	Observed frequency	Expected frequency
WT	20	0.266	0.25
cHet-Myc	38	0.506	0.50
cKO-Myc	18	0.240	0.25