Systems biology approach suggest new miRNAs as phenotypic stability factors in the epithelial-mesenchymal transition

Supplementary file S2
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Figures 1-2 show the stable states triggered by *in silico* perturbations listed in Table 2 of the manuscript. Each perturbation corresponds to gain of function (GoF) or loss of function (LoF) experiments. The simulations were performed using GINsim 3.0.0b. The initial conditions used in Fig. 1 were the same as used in Fig. 6 of the paper. In Fig. 2, the initial conditions correspond to the E and M (using ZEB1 level1 and SNAIL1 level1) states detailed in Table 1 of the manuscript. We analyzed cases for input ON (Fig. 1) and OFF (Fig. 2). LoF constrains the value of the respective component to 0, whereas for GoF, the value is constrained to 1 (for a Boolean variables) or to a value greater than 0 (multi-valued variables). The simulations are displayed in HTG graphs as in Figs. 3 and 6. The value of GoF for multi-valued variables are indicated between brackets. The influence of those perturbations shown in Figs. 1 and 2 on the remaining transitions of the EMT dynamics has no effect.

The results associated with the SNAIL1 self-inhibition and the miR-34/SNAIL1 circuit for low input dose are identical to Figure 1A. In other words, the bistability triggered by LoF of SNAIL1 self-inhibition for low input level is abrogated by GoF or LoF of miR-34 (Fig. 3B of the paper).

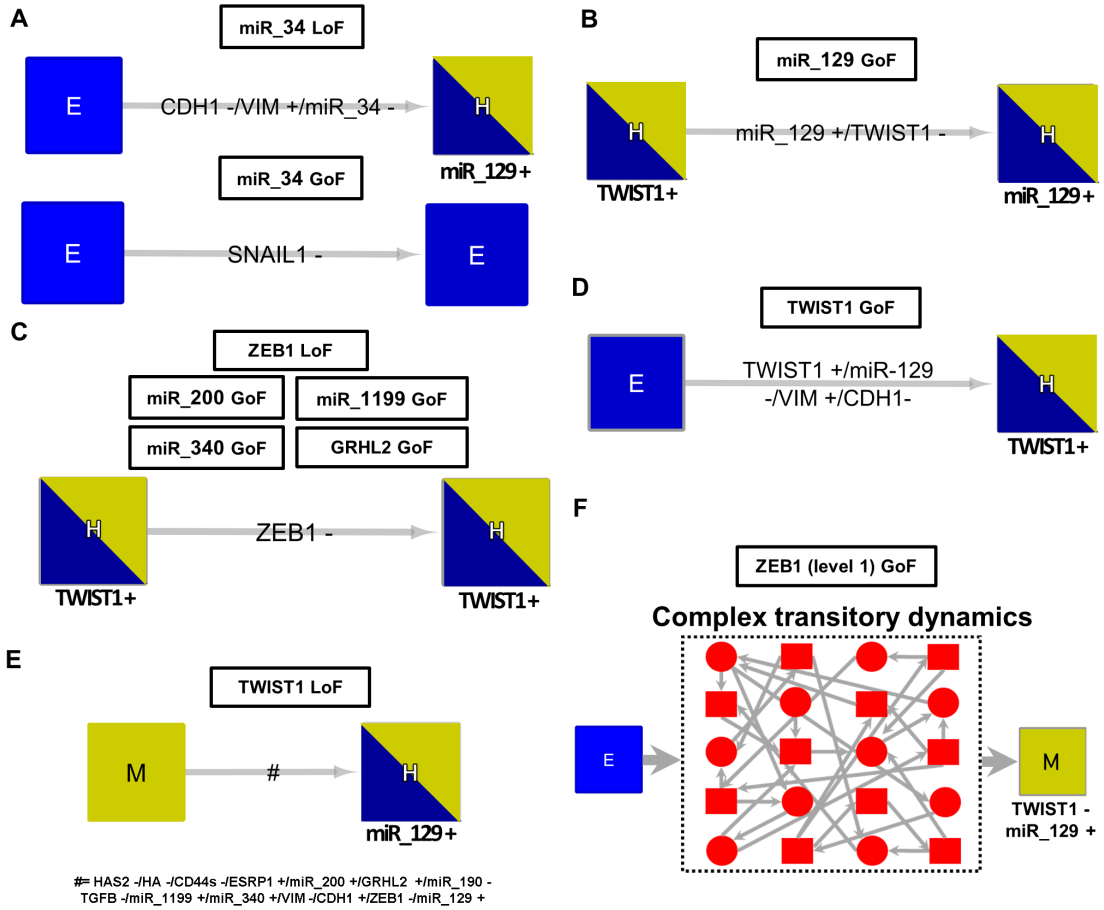

Figure 1: Analysis of perturbations for the presence of the input (level 2). Most-left states represent initial states of the simulation, whereas most-right ones denote final states. Plus and minus signs indicate that the component is increasing or decreasing its activity level, respectively. Squares and circles in red represent transient states. (A) MiR-34 LoF induces the E-to-M transition, whereas its GoF maintains the stability of the E state. (B) MiR-129 GoF induces the transition to the H state with the absence of TWIST1. (C) ZEB1 LoF or GoFs of miR-200, miR-340, miR-1199, or GRHL2 maintains the stability of the H state with the presence of TWIST1. (D) TWIST1 GoF induces the E-to-H transition. (E) LoF of TWIST1 triggers M-to-H transition with the presence of miR-129. (F) ZEB1 GoF induces the transition to the M state.

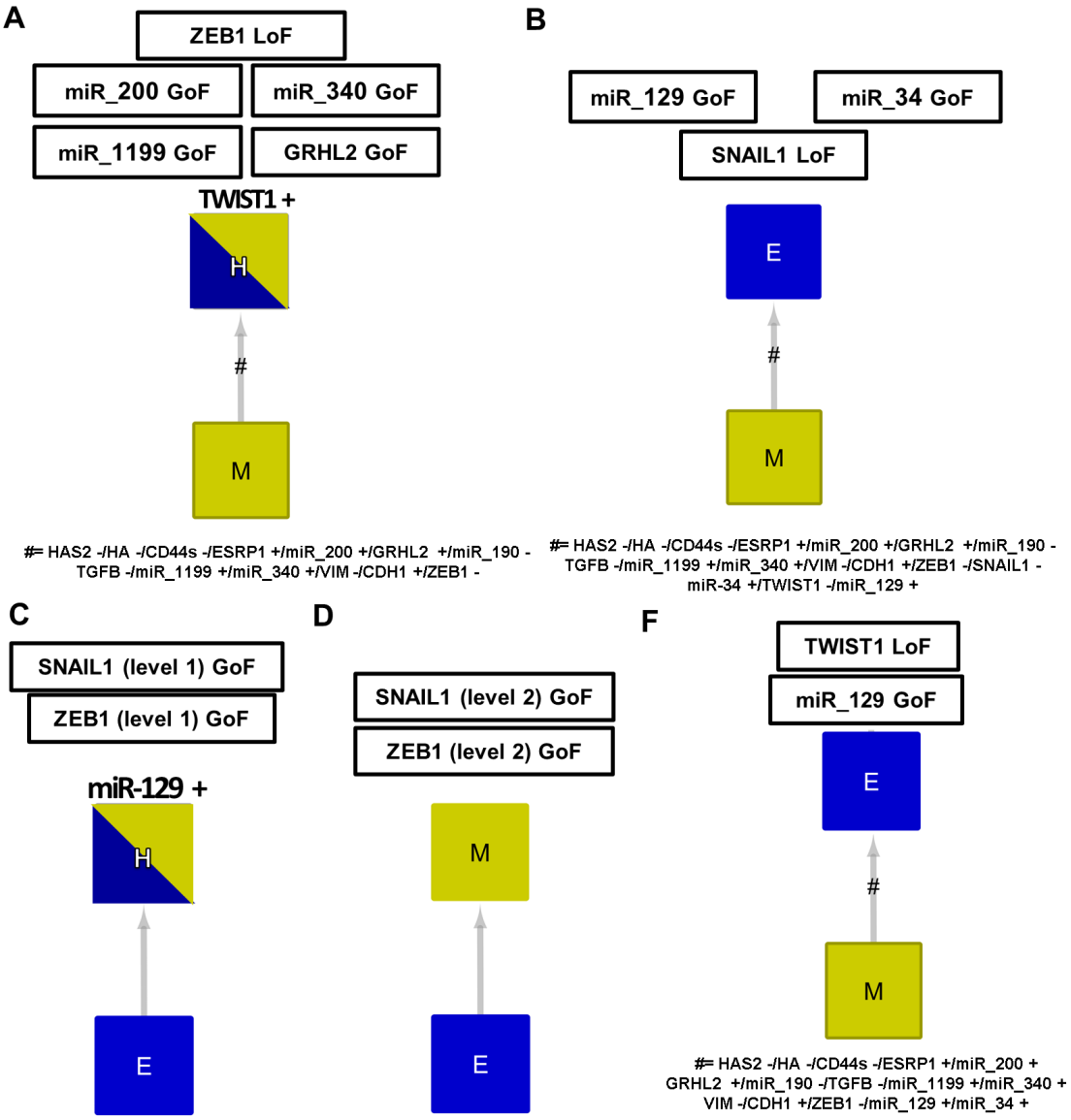

Figure 2: Analysis of perturbations for the absence of the input. Bottom states represent initial condition, whereas top ones denote final states. The remaining information are displayed as Fig. 1 of the present supplementary material. Those labels of the transition that are not shown can be found in Fig. 1. (A) The M-to-H is induced by LoFs of ZEB1, miR-200, miR-340, miR-1199, or GRHL2. (B) The M-to-E transition is triggered by GoFs of miR-129 or miR-34 or SNAIL1 LoF. (C) The transition to the H from the E state is induced by SNAIL1 GoF (level 1) or ZEB1 GoF (level 1). (D) The E-to-M transition is triggered by SNAIL1 GoF (level 2) or ZEB1 GoF (level 2). (F) The transition to the E from the M state is induced by TWIST LoF or miR-129 GoF.