**Supplemental Figure 1. TGFR inhibition suppresses mesenchymal features in human HCC cell lines**. TGF-driven mesenchymal phenotype HCC cell lines HLE and HLF reveal constitutively active TGF signaling and mesenchymal features, which are lost upon treatment with TGFRI/II inhibitor (LY2157299) at 48 hours as demonstrated by qRT-PCR.

**Supplemental Figure 2. AXIN2 and GLI are induced by Wnt and SHH signals in the epithelial-to-mesenchymal transition network model.** In the experimental literature GLI expression is an established marker of SHH signaling and AXIN2 expression is an established marker of canonical Wnt signaling. A) Activating SHH signaling, while keeping all other signals inactive, leads to induction of GLI in our model (1000 simulations, asynchronous update), thus supporting experimental findings. B) Activating Wnt in our Boolean model of EMT, while keeping all other signals inactive, produces AXIN2 (1000 simulations, asynchronous update).

**Supplemental Figure 3.**  **All stable motifs (feedback loops) stabilizing the TGFβ-driven EMT phenotype.**Black background represents nodes that are OFF in the EMT steady state. White background indicates nodes that are ON in the EMT steady state.

**Supplemental Figure 4. The ratio between the timescale of the slow and fast processes does not matter as long as it is significantly larger than one.** For the ranked general asynchronous updating scheme used, a range of node update probabilities for fast (signal transduction) versus slow (transcription) biological events were tested. Our results are robust to changes in update probabilities as long as the ratio of update probabilities for signal transduction to transcriptional events is significantly greater than one. An update probability ratio of 5 means that signal transduction events are five times as likely as transcription level events (left panel). An update probability ratio of 50 means that signal transduction events are fifty times as likely as transcription level events (right panel).

**Supplemental Figure 5. Exploration of alternative rules to describe nuclear localization of -catenin.**  -catenin is either localized predominantly at the membrane (-catenin\_memb node) or in the nucleus (-catenin\_nuc node), depending on Wnt signaling. One possibility to ensure this is to assume a mutual inhibition between -catenin\_memb and -catenin\_nuc (A). In this case -catenin\_nuc activity starts increasing and -catenin\_memb activity starts decreasing after four time steps. E-cadherin activity starts decreasing shortly after -catenin\_memb and decreases below 0.5 in seven time steps. A less stringent alternative is to assume that -catenin\_nuc inhibits -catenin\_memb, but not vice versa (B). In this case the decrease of the -catenin\_memb activity is still accompanied by the increase of the -catenin\_nuc activity, thus this rule also reflects the localization of -catenin. The increase of the Wnt activity is identical in both cases since Wnt is upstream of -catenin. In contrast, the inter-regulation among -catenin and E-cadherin causes a more rapid decrease in -catenin\_memb and E-cadherin activity and a more rapid increase of -catenin\_nuc activity. E-cadherin activity now decreases below 0.5 in five time steps. We used the former assumption in the model.