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A model for genetic and epigenetic regulatory networks identifies rare pathways for transcription factor induced pluripotency MAXIM ARTYOMOV, MIT, ALEX MEISSNER, Broad Institute, ARUP CHAKRABORTY, MIT — Most cells in an organism have the same DNA. Yet, different cell types express different proteins and carry out different functions. This is because of epigenetic differences; i.e., DNA in different cell types is packaged distinctly, making it hard to express certain genes while facilitating the expression of others. During development, upon receipt of appropriate cues, pluripotent embryonic stem cells differentiate into diverse cell types that make up the organism (e.g., a human). There has long been an effort to make this process go backward – i.e., reprogram a differentiated cell (e.g., a skin cell) to pluripotent status. Recently, this has been achieved by transfecting certain transcription factors into differentiated cells. This method does not use embryonic material and promises the development of patient-specific regenerative medicine, but it is inefficient. The mechanisms that make reprogramming rare, or even possible, are poorly understood. We have developed the first computational model of transcription factor-induced reprogramming. Results obtained from the model are consistent with diverse observations, and identify the rare pathways that allow reprogramming to occur. If validated, our model could be further developed to design optimal strategies for reprogramming and shed light on basic questions in biology.

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