1. What mechanisms determine the number of cells that belong to stage 4?

The mechanisms that determine the number of cells in stage 4 are as follows:

* Direct differentiation into stage 4: This corresponds to the transcriptional activity of MyoD (in stage 3), which promotes myogenin expression in stage 4. The change in myogenin expression results from strain effects signaling molecules (S) that cause MyoD to bind to the myogenin promoter, increasing myogenin expression and transitioning cells into stage 4.
* Direct differentiation from stage 4 to stage 5: The combination of free myogenin in Stage 4 and the action of strain-related signaling molecules causes myogenin to bind to the myosin heavy chain (MHC) promoter, increasing the gene expression of MHC, which leads to the formation of more mature muscle cells.
* Cell death in stage 4.

1. What mechanisms determine the number of cells that belong to stage 3?

The mechanisms that determine the number of cells in stage 3 are as follows:

* Symmetric differentiation: number of daughter cells returning to the current state after division (self-renewal)
* Asymmetric differentiation: the number of daughter cells resulting from the division and differentiation from the previous stage 2 and resulting in the transcription factor MyoD reaching a threshold necessary for further differenationtaion (MyoD+).
* Direct differentiation into stage 4 corresponding to the transcriptional activity to MyoD promoting myogenin expression in stage 4.
* Cell death in stage 3

1. What mechanisms determine the number of cells that belong to stage 5?

The mechanisms that determine the number of cells in stage 5 are as follows:

* Direct Differentiation from stage 4 to stage 5: This process is driven by myogenin activity in stage 4. Strain-related signaling molecules enhance this process by promoting myogenin’s binding to the myosin heavy chain (MHC) promoter, increasing MHC expression and forming more mature muscle cells.
* Cell death in stage 5

1. What biological mechanism is behind the effect of strain on myogenic differentiation?

The effect of strain on myogenic differentiation is primarily mediated by a strain-induced molecule S, which represents mechanotransduction effects such as integrin-mediated FAK activation and involvement of the Rho pathway.

When strain is applied, it promotes the production of S, which modulates the activity of transcription factors such as MyoD and myogenin. This modulation enhances the binding of MyoD to the myogenin promoter, leading to increased myogenin expression and then MHC expression, promoting the progression of myogenic differentiation.

1. What are the differences between the mechanisms of cell differentiation in stages 2 and 5?
2. What are the differences between the mechanisms of cell differentiation in stages 3 and 5?