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**Physical Forces, cell shapes and tissue architectures: from Aristotle to stem cells**

Cells, in their natural environment (i.e., within tissues) display remarkable social behaviors. This includes ability to read and recognize their neighboring cells and the whole environment around them, and behave accordingly. A prominent example of such "good and constructive" neighborhood relationship is the ability of cells to stop proliferating (i.e., of making copies of themselves), when they start touching each other, or the ability of stem cells to morph into a mini-organ outside of the body, in a test tube. Intrinsic and exclusive of to normal tissues is also the ability to recognize and eliminate individual tumor cells and to rapidly eliminate them.

These and other intriguing properties are not something directly encoded by our genes; rather, these represent "emergent properties" exclusive of cells physically interconnected within a tissue network. Understanding these properties requires incorporation of additional conceptual frameworks by which information on structural and architectural complexity of tissues is transmitted to their constituent cells, for patterning at all scales and over large distances.

I will discuss one of such new paradigms, namely, the roles of YAP/TAZ, two highly related transcription factors, as sensors of how cells, hard-wired within tissues, perceive themselves and their environment and communicate with it. YAP/TAZ activity is under direct control of cell's own shape and inner structure. In turn, this reflects the pattern of geometrical and mechanical strains associated to where cells are located within the global 3D tissue architecture and surrounding cells. All these inputs are essentially physical. YAP/TAZ convert all these inputs into gene expression signatures and context-dependent biological responses.