

The M project --- Mechanical, Metabolism, Mitochondria and Muscles ---

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We are studying molecular mechanisms how cells sense and respond to physical forces. In this project, we have identified several regulatory factors that shuttle from cytoplasm to nucleus in immediate response to mechanical stimuli, such as stretch and shear stress. We have also found that this shuttling response maintains homeostasis of blood circulation, cardiac/skeletal muscles and even metabolism. Our data suggest that these regulatory factors and their associated proteins could be good protein targets of novel drugs (exercise mimetics) for sarcopenia, diabetes, obesity, etc.

As a different approach, we are isolating target proteins for small compounds that exert exercise pill-like effects, by exploiting a powerful method we used to isolate a target of thalidomide (*Science* 327, 1345, 2010).

By combining these two different approaches, namely mechanobiology and chemical biology, we are trying to pave a way to combat with frailty, especially from a viewpoint of physical activities and metabolism/obesity.