Creating a protein chimera to study regulation of muscle diversity.

Body muscles are made of many individual super-cells, called muscle fibers, that have distinct properties and determine every individual's strength and endurance. Initially all muscle fibers have identical characteristics, but become differentiated into specific types in adults. The mechanism of such transition is not well understood, despite its obvious importance for shaping human physicality.

Remarkable conservation of the muscle tissue enables us to use fruit flies to study the mechanisms of muscle fiber diversity. We hypothesized that the transcription factor Mef2 acts as a molecular switch that activates structural genes in embryos, but then suppresses the very same genes in adults.

To test our hypothesis, we have designed and cloned Mef2::VP16, a chimeric protein that contains the DNA-binding domain from Mef2 and the transactivation domain from Herpes Simplex Virus. We are going to test Mef2::VP16 in flies with the Act57B reporter. Act57B is ubiquitously expressed in all embryonic muscles, but then becomes restricted to a limited set of muscles in adults. If our hypothesis is correct, the flies expressing Mef2::VP16 will reactivate Act57B activity in the muscles where it is normally not expressed, confirming the repressive action of Mef2 transactivation domain and its regulatory role in adult muscles.

Since Mef2 is a conserved factor that is involved in muscle regulation in vertebrates and humans, we believe that our study will uncover a new conserved mechanism that underlies muscle tissue diversification.