Protein Hydrogels to Examine Emergent Mechanical Properties of Striated Muscle

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Striated muscle is a natural biomaterial with remarkable properties: it is strong, elastic and capable of self-healing. Proper function of striated muscle depends on its mechanical properties. Single-molecule approaches have shown that the passive elasticity of muscle is determined by the mechanics of specific cytoskeletal proteins in cardiomyocytes, such as titin. Due to the complexity of muscle architecture, these characteristics have proven tough to recapitulate, and there are no models that can predict macroscopic mechanic behaviour directly from the mechanical properties of constituent proteins. Therefore, it remains a challenge to synthesize materials that possess the properties of biological muscles.
In this work, we propose a bottom-up approach to produce protein hydrogels that recapitulate the basic passive elastic properties of muscle. This approach will allow to examine direct correlations between the mechanical properties of the constituent proteins and those of the resulting hydrogels. To generate the hydrogels, we use engineered polyproteins based on titin domains whose mechanical properties can be probed by single-molecule Atomic Force Microscopy. Proteins are subsequently crosslinked through photocatalytic tyrosine oxidation. Hydrogel stiffness is measured using a custom-built stretching device. Working with single-point mutants of the constituent polyproteins, we will be able to determine how changes in the nanomechanical properties of the protein building blocks translate into macroscopic changes in hydrogel stiffness.
Thanks to this strategy, it will be possible to translate the mechanical properties of proteins to higher order arrangements. In addition, these protein hydrogels are an initial step in the establishment of versatile biomaterials that mimic the mechanical properties of muscle, with promising potential in tissue engineering.