Proteins as Parents

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So that we can move, and so that our heart beats, we need proteins with special mechanical properties, "molecular springs", which give our tissues the necessary strength and take care of elasticity and tensibility.

Such proteins are also interesting as building blocks for novel high-tech materials because the natural materials often outperform the artificial: One only has to think about the highly elastic and extremely tear-proof spider dragline silk. Molecules with defined mechanical properties are especially needed for the assembly of nanotechnological devices. A team from the University of British Columbia (Vancouver, Canada) succeeded in producing proteins with new mechanical properties through the combination of two "parent" protein fragments.

The research group of Hongbin Li chose two different titin domains from heart muscle for their experiments. Titin, a giant molecule, is responsible for controlling the passive tension of our muscles and also pulls them together again after an extension. Depending on the type of muscle, there are differences: The titin found in heart muscle is less tensile than that found in skeletal muscle and it gives the heart the necessary stability to resist the pressure of the inflowing blood.

As the parent generation, the scientists chose two globular titin domains called I27 and I32, whose mechanical properties have already been intensively researched. Both are similarly built and are composed of the protein segments A, A’, as well as B to G. The researchers interchanged several fragments of the genes that encode I27 and I32 ("DNA shuffling"). Genetically they produced four different protein "children":

an I27 with the A'/G strands from I32, an I32 with A'/G from I27, an I27 with C, D, and E from I32, and also an I32 with the C, D, and E strands from I27.

The mechanical properties of all the proteins were investigated with atomic force microscopy. To do this, one end of the protein chain was attached onto a solid support and the other end was adsorbed onto the tip of the atomic force microscope. When the tip is gradually pulled away from the support, the protein elongates and the force increases until the protein finally unfolds. The resultant force–extension curves characterize the mechanical properties of the proteins. It turned out that all children show different mechanical characteristics to their parents. It was previously thought that the specific arrangement of the A'/G section was critical for the mechanical stability of the domain, whereas other parts of the domain, including the C, D, and E strands, only played a less-significant role. This opinion must now be revised.

Li hopes that this exciting new application of the powerful recombination technique in the field of protein mechanics will open a new way to tailor proteins' mechanical properties.

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