Gene editing technique allows silkworms to produce spider silk

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An analysis of transformed cocoons. Morphology of the WT-1, FibH+/-, FibH-/-, WT-2, MaSp1+/-, and MaSp1+/+ cocoons. Scale bar represents 1 cm. Credit: Jun Xu

A team of researchers affiliated with several institutions in China has succeeded in using a gene editing technique to get silkworms to produce spider silk. In their paper published in *Proceedings of the National Academy of Sciences*, the group describes the technique they used and the quality of the silk produced.

In recent years, scientists have discovered that the unique attributes of spiker silk make it useful in a number of applications. One group found, for example, that it could be used to create micro-capsules for delivering cancer drugs. Another found that it could be used to repair damaged nerves, and yet another found it could make bulletproof vests stronger. Thus, biological researchers have sought ways to produce spider silk commercially, but have come up short. Efforts to farm them like silkworms have failed due to the erratic nature and aggressive behavior of spiders. And efforts to genetically alter other critters have come up short, as well. In this new effort, the researchers tackled the latter approach and report that they have found a way to succeed where others have failed.

Rather than using the more familiar CRISPR gene editing technique, the researchers chose instead to use an editing technique called TALEN—it is a method that uses so-called "molecular scissors" to operate on DNA. Using the technique, the team replaced one part of a silkworm genome with a snippet from a golden orb-web spider to produce a spider-silk making silkworm.

The researchers report that their efforts resulted in silkworms able to produce silk that was a mixture of that normally produced by the silkworm and the spider. Testing showed that the silk was 35.2 percent spider, which was a big improvement over the work of other teams, which were only able to achieve approximately 5 percent. The newly improved silk was also ready for use as spun by the silkworms, as opposed to results obtained by other teams. The researchers note that the process also allows for creating custom silks depending on need. They suggest their technique lends itself very well to mass production, making it a viable option for future applications.

More information: Jun Xu et al. Mass spider silk production through targeted gene replacement inBombyx mori, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1806805115

Abstract
Spider silk is one of the best natural fibers and has superior mechanical properties. However, the large-scale harvesting of spider silk by rearing spiders is not feasible, due to their territorial and cannibalistic behaviors. The silkworm, Bombyx mori, has been the most well known silk producer for thousands of years and has been considered an ideal bioreactor for producing exogenous proteins, including spider silk. Previous attempts using transposon-mediated transgenic silkworms to produce spider silk could not achieve efficient yields, due to variable promoter activities and endogenous silk fibroin protein expression. Here, we report a massive spider silk production system in B. mori by using transcription activator-like effector nuclease-mediated homology-directed repair to replace the silkworm fibroin heavy chain gene (FibH) with the major ampullate spidroin-1 gene (MaSp1) in the spider Nephila clavipes. We successfully replaced the ~16-kb endogenous FibH gene with a 1.6-kb MaSp1 gene fused with a 1.1-kb partial FibH sequence and achieved up to 35.2% chimeric MaSp1 protein amounts in transformed cocoon shells. The presence of the MaSp1 peptide significantly changed the mechanical characteristics of the silk fiber, especially the extensibility. Our study provides a native promoter-driven, highly efficient system for expressing the heterologous spider silk gene instead of the transposon-based, random insertion of the spider gene into the silkworm genome. Targeted MaSp1 integration into silkworm silk glands provides a paradigm for the large-scale production of spider silk protein with genetically modified silkworms, and this approach will shed

light on developing new biomaterials.