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Utilization of Transgenic *Bombyx mori* for Biomaterials Production - Review

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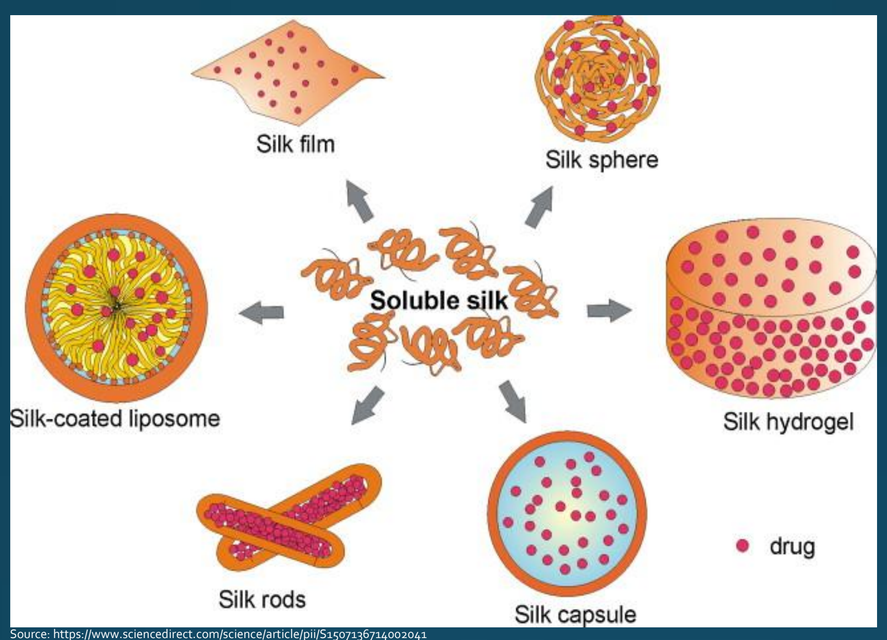
Abstract: *Bombyx mori* is one of the most studied species of Lepidoptera by the scientific community, being a permanent model organism especially for life sciences. Two major proteins named fibroin and sericin are found in silk thread used in the cocoon. Fibroin is used as a biomaterial due to the high biocompatibility, mechanical strength and biodegradability. Besides the great economic importance, over the past decade, *Bombyx mori* has received major attention as a bioreactor for large scale production of recombinant proteins. One of the greatest advantages of silkworms is the number of genes which are homologous to human genes, but also it is important to mention their short generation time and the rich genetic resource. In this article, we summarized a review of using the transgenic silkworm as a bioreactor to produce recombinant proteins. The recombinant proteins are currently used to optimize the biomaterials, which have a significant impact for the progress of human and veterinary medicine. For example, sericin hydrogels, containing human acidic fibroblast growth factor supporting wound healing, have been developed. Also, to improve cell adhesive properties, silk fibroin/hyaluronic scaffolds for human mesenchymal stem cell culture have been produced.

Introduction

Silk has been successfully used for decades in medicine as a suture material. Fibroin (fibrous protein) is the main protein derived from *Bombyx mori* cocoons and consist of a light chain (25 kDa) and a heavy chain (325 kDa) which are linked through disulfide bonds [1]. Due to silk's various biological and mechanical properties, in the past years, the scientific community has shown a great interest in using silk fibroin as a biomaterial [2]. The most important biological features of silk are the biocompatibility, versatility, water permeability and the good degree of biodegradability [3]. Also, it is important to mention the low cost and the simple processing method [2]. Owning these great advantages for medical applications, fibroin is currently used to obtain hydrogels, sponges, scaffolds, tubes, films and microspheres. Also, *Bombyx mori* exhibits a serious capacity to synthesize silk proteins in a short period, being an important tool to produce recombinant proteins that can be widely used in numerous fields [4]. Thus, transgenic silkworms can be used both to produce recombinant proteins [5] and to improve the quality of silk thread, in order to obtain biomaterials with enhanced properties [6].

Conclusions:

This review highlights the advantage of using transgenic *Bombyx mori* to produce silk with enhanced properties, with wide applications in the medical area. The aim of this review is to accentuate the importance of enhanced silk fibers and to demonstrate the progress of using silk-based biomaterials. The molecular engineering of silk opens a wide range of opportunities for its utilization, not only for the purposes mentioned above, but beyond. Due to its certain advantages, *Bombyx mori* is seen nowadays as one of the most important tools to be used as a bioreactor to produce recombinant proteins.



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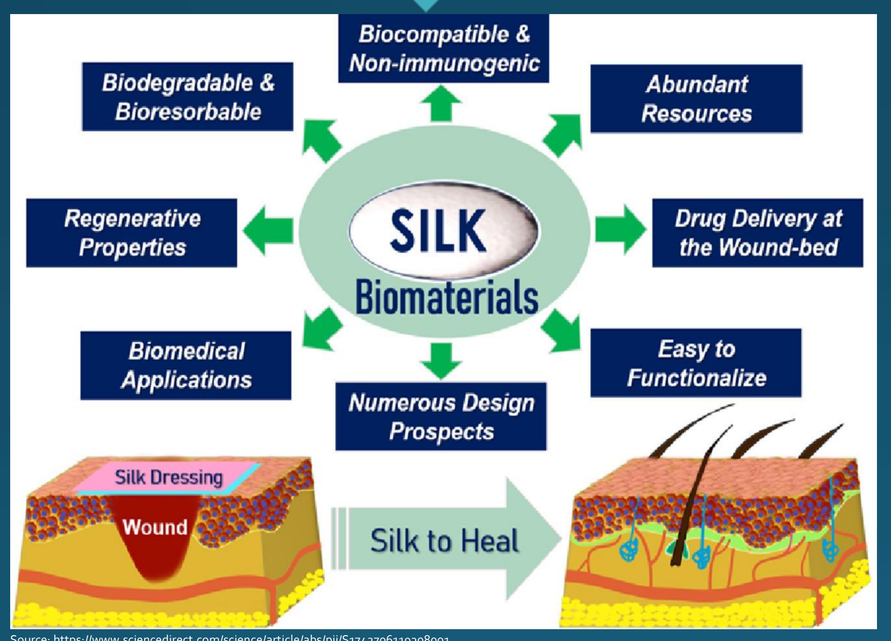

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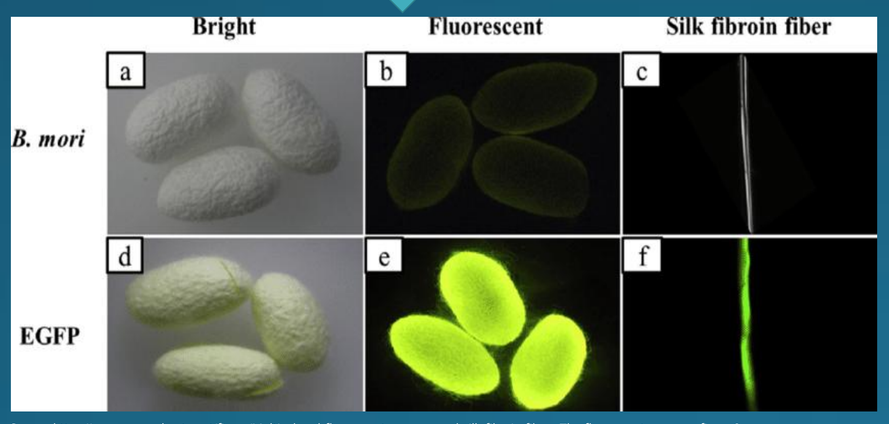

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Bombyx mori as a bioreactor

As the need for recombinant proteins is constantly increasing, there are numerous bioreactors, specifically bacteria, yeast or mammalian cells, which have been used for this purpose. The major drawbacks when choosing an expression system to be used, are the cost of purification process and the posttranslational modification which differ between organisms. Thus, the bioreactor dictates the possibility of using a certain organism to produce target proteins [7]. At this point, *Bombyx mori*, is one of the best choices regarding the production of recombinant proteins, due to the low feeding cost, the short generation time, the rich genetic resource and the posttranslational modifications [8]. For this purpose, the silk synthesis system is exploited. The large amount of silk proteins produced by the silk gland is the most important aspect to be considered for choosing this kind of expression system to obtain the target proteins. There is wide range of recombinant proteins which have been obtained by using transgenic silkworms, specifically the thyroid hormone receptor, collagen, fibronectin or lactoferrin [5, 6, 8].

Enhanced silk fibers

Fluorescent silk fibroin has numerous applications in the bioimaging area and has been developed for the first time by using the piggyBac transposon based vector. This kind of transgenic fibroin can be used as a tool for drug controlled release or as a biosensor tool for bioimaging. There are studies that showed that the solution form of fluorescent silk fibroin could operate approximately one year after it was subcutaneously inserted. Another study described the fluorescent silk fibroin as a successful tool for cancer detection [9]. By using the silk expression system Zhu et al., [10] transformed *Bombyx mori* to produce modified silk with enhanced mechanical strength and elasticity. Wen et al. [11] also used *Bombyx mori* as a bioreactor and *piggyBac* as a vector, to produce recombinant spider silk in cocoons. After analyzing the mechanical strength of recombinant silk, the results showed that it is lower than the strength of native spider silk, thus there are some aspects which need to be improved. Wang et al. [12] also reported the success of genetically engineered silk fibers. They engineered silk in order to enhance its properties, particularly the cell-proliferation and the anti-inflammatory activities.

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