Defence hormone harnessed

Scientists at Oxford University have discovered a new way to exploit the natural reactions of the silkworm for the large-scale production of silk with bespoke qualities. This material has particular implications for the future of healthcare. **Charlotte Rogers** finds out more.

Researchers at Oxford University have investigated a new way to harness the natural defence mechanism of silkworms for the large-scale production of silks with tailor-made properties.

Professor Fritz Vollrath, and colleagues from the Oxford Silk Group at Oxford University's Department of Zoology, collected silk directly from paralysed silkworms by injecting a chemical that is naturally produced by the animal.

As the silkworm is strong and has a tendency to wiggle, the team wanted to explore the possibility that a particular hormone could paralyse the animal so as to produce a longer, more consistent silk fibre.

"The injected hemical is the exact synthetic copy of a small peptide that the worm releases itself when harmed in any way, perhaps by a bird pecking at it or a thorn poking it," Professor Vollrath explains.

In the wild silkworms produce this hormone when injured as their bodies move through hydrostatic pressure and without this self-induced paralysis they would risk their wounds 'bleeding out.'

The team's report in the journal *Biomacromolecules* concludes that, in comparison to un-paralysed silkworms, paralysis allows longer and more consistent silks to be collected by eliminating the silkworm's ability to break and alter its silk fibre. So far the Oxford Silk Group has reeled a little over 500m, but the researchers think that they should be able to reel up to 1-1.5 kilometres.

Beth Mortimer of the Oxford Silk Group, an author of the report, is interested in the way paralysis prevents the silkworms breaking the fibre, but still allows silk spinning and collection. "The direct 'forced reeling' of silk has been used in spiders for many years. However, reeling large amounts of silk directly from silkworms has not previously been possible," she adds.

Tricking the silkworm into performing its natural response to injury allows large amounts of silk to be reeled.

'The mass-rearing of genetically modified silkworms to induce paralysis 'on-demand' would be achieved by inserting the appropriate genes'

By tricking the silkworm into performing its natural response to injury the Oxford scientists show that it is possible to reel hundreds of metres of silk under full control.

The silk can be reeled through a bath before the toxic 'gum-glue' coating sericin (a protein created by silkworms) dries out, stripping it off and directly coating with a substance of choice. There is also the potential to stretch the silk whilst reeling to make it stronger or separate the two 'brin' filaments that make up the 'bave' thread.

Entomologist Dr Alex Woods, the Oxford-based medical researcher responsible for the original discovery, comments: "Importantly, this breakthrough may allow us to make high-quality silks with a variety of desirable mechanical properties in practical quantities to finally expand this exceptionally well suited biomaterial into key medical applications."

Dr Woods sees the potential for silk in eye surgery, with filaments of silk ropes being used for tendon repair and general tissue scaffold. The Oxford Silk Group also notes that the forced reeled fibres are significantly thinner than the naturally spun cocoon silks. The researchers argue that removing sericin in a more effective manner lessens the possibility of inflammatory responses associated with

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'silk' sutures that are currently available.

"This is important as it will allow immediate replacement of these sutures, but also opens silks applicability to other surgical devices," Dr Woods explains. "Even more importantly, being able to generate biomimetic silks with variable mechanical properties, for the first time in practical quantities, really makes this a viable material for the future of healthcare."

Despite the commercial opportunities for this research, a number of animal welfare and ethical issues have been raised by the fact that the scientists need to put the silkworms into an artificial state of paralysis to collect the silk.

These issues have been given serious consideration, states Professor Vollrath. "The worms will 'wake up' sometime after paralysis, as the natural enzymes that would deal with the natural peptide-hormone break down the artificial peptide copy.

"Importantly, our approach allows the moth larva to live, pupate and emerge into adulthood, while the traditional way of silk production kills the pupa inside their cocoons in order to reel from the cocoon that has not been holed by the emerging moth, which would also mean having broken threads."

Dr Woods also believes there are no animal welfare implications to the research. "Mulberry worms are totally domesticated and do not occur in the wild. They actually cannot live in the wild any longer as neither sex can really fly and both male and female moth die shortly after mating.

"Transgenic techniques are well established in a wide variety of insects now. Mass-rearing of transgenic strains and mass field release trials in the US, Brazil and Malaysia have not shown any evidence of horizontal gene transfer."

Unlike unravelling cocoons, silkworm forced reeling allows the silk properties to be modified to suit particular purposes. This has important implications for the large-scale reeling of silkworms for industrial production of environmentally-friendly fibres for use in a range of applications – from biomedical implants to super-tough composite panels.

'Paralysis allows longer and more consistent silks to be collected by eliminating the ability of the silkworm to break and alter its silk fibre'

Unlike spiders, these genetically modified silkworms can be farmed at high-densities. Subject to patent, the 'on-demand' paralysis would be achieved by inserting the appropriate genes.

"Genes can be inserted and stabilised into the genome of the silkworm (a model insect for transgenic techniques in lepidoptera)," Dr Woods states. "These genes could be under the control of known inducible promoters that respond to specific environmental criteria (such as light, temperature) at predetermined times within the animals' lifecycle."

Earlier this year the Oxford Silk Group was awarded €113, 034 by the European Research Council to aid in the development of research and pursuit of commercial opportunities. Vollrath and his team have focused on research into the biomimetic polymer structure of the silk fibre, inventing a range of novel silks that reduce reliance on Mulberry varieties, as well as looking into silk lifecycle analysis and the environmental costs/benefits of commercial production.

"The commercial implications of this process are self-evident: now we can make silks to order by manipulating the mechanical properties while at the same time adding functionality," says Professor Vollrath.

"These kinds of fibres could have highly tuned properties and be produced more sustainably than the unravelling of fibres from cocoons when the fibres are typically damaged to some extent and the boiling of the cocoons requires a lot of energy, making the process less green.

"So far there has been a great amount of interest in the research, since silk is always of interest - since 'time immemorial' when silk was worth more than its weight in gold. Nowadays the interest mainly focuses on both the medical aspects of silk and the production of sustainable materials."