OXFORD BIOMATERIALS LTD

A METHOD OF SPINNING SPIDER-LIKE SILK, THE 'HOLY GRAIL' OF BIO MATERIALS

OXFORD BIOMATERIALS LTD
KEY DATA: FACT FILE

Technology
Spider-like silk material

Established
2002

Type
Spinout vehicle

Location
Oxford

Employees
20 (group basis)

Funding
Self-funded

CEO
Dr David Knight
Together with Professor Fritz Vollarth of Oxford University, he co-founded Oxford Biomaterials in 2002. In his academic career Knight has been head of department, reader and visiting professor at several European universities. He has numerous publications in the field of biomaterials, especially silk and collagen, and is the author of 25 patents.

Oxford Biomaterials Limited

Spider silk is known to have amazing properties but up to now it has been impossible to produce in commercial quantities. Oxford Biomaterials has found a way to source and process a silk from certain species of Wild Silkworms to give a fibre with a strength, weight for weight, greater than steel, and a toughness matching that of Kevlar. On top of this, it is biocompatible, non-toxic, cell binding, and therefore can be applied to a variety of medical as well as non-medical applications.

OXFORD BIOMATERIALS LTD

A METHOD OF SPINNING SPIDER-LIKE SILK, THE 'HOLY GRAIL' OF BIO MATERIALS (CONTINUED)

Commercial silkworm cocoons

Silkworms reeling

The principal inventors of the process and co-founders of Oxford Biomaterials Ltd (OBM) are Professor Fritz Vollrath and Dr David Knight. The company's technology has grown out of their long standing interest in structural biomaterials, and in particular a shared interest in how spiders spin silk, based initially on Dr Knight's work studying the way that cartilaginous fish spin egg cases from a collagenous silk.

BACKGROUND

Their collaboration started in 1998, at Aarhus University, where Professor Vollrath was Professor of Zoology. In 2000, Professor Vollrath took a chair at Oxford's Department of Zoology where Dr Knight followed him. Here Professor Vollrath headed up the prestigious silk research group while David Knight focused on inventing and patenting discoveries via an Oxford University spinout, Spinox Ltd, the company which eventually mutated into Oxford Biomaterials Ltd.

SPINNING INSIGHT

The difference between spider and silkworm silk is due largely to the way in which the spider spins its silk. The initial focus of Vollrath and Knight's collaboration therefore lay in finding a way to mimic the way the spider does this. By 2001 they had developed sufficient understanding to set up Spinox in order to develop a "biomimetic spinning machine". This required finding a way to extrude silk monofilaments from a concentrated aqueous solution of silk proteins obtained directly from spiders or silkworms.

Spinox published an initial report of its progress in the prestigious journal Nature. Their findings intrigued a German venture capital company, Technostart, which contacted them to discuss an investment. This eventually led to the sale of Spinox's bio-mimetic spinning IP and to the formation of a new company, in Germany,

THE SILKWORM

A silkworm is the larva, or caterpillar, of the domesticated silkmoth, Bombyx mori. It is completely domesticated, and does not occur naturally in the wild. The practice of breeding silkworms for the production of raw silk originated at least 5,000 years ago, starting in China, from where it spread to Korea, Japan, and later to India and the West. In contrast, wild silks are obtained from other species of silkworm (Wild Silkworms) that breed in the wild.

SPIDER SILK

Spider silk is a natural fibrous protein, a group which also encompasses collagen (for example in tendons, ligaments and bone), and keratin (nails and hair). These structural proteins all form strong materials but spider silk's properties are exceptional. For example, it is said to be six times stronger than steel, weight for weight, and five times tougher than Kevlar. By way of illustration, a Boeing 747 could be stopped in flight by a single pencil-width strand, at least so it is claimed.

OXFORD BIOMATERIALS LTD

A METHOD OF SPINNING SPIDER-LIKE SILK, THE 'HOLY GRAIL' OF BIO MATERIALS (CONTINUED)

SPIDREX® SILK SOLUTIONS

The Spidrex® material is obtained by thoroughly but gently removing the unwanted silk gum from the natural silk filaments. This yields a highly pure and undegraded fibroin, which is an immensely large long chain protein, and the principal structural component of silk. The fibroin filaments are then dissolved under mild conditions and carefully refolded under proprietary conditions to produce concentrated solutions of Spidrex® silk solutions. These can be formed into a wide range of materials or combined with specially cleaned domesticated or wild Spidrex® silk fibres.

Spin'tec Engineering GmbH, which has since developed the device into a much more sophisticated version.

SPIDREX® SILK SOLUTIONS

The Oxford collaborators then turned to look for a simpler way to make spider silk, which would not require using spiders, not least because spiders are difficult to farm (because they turn to cannibalism if too closely confined). After a "trawl" of databases on moth silks they found a species with a very similar amino acid sequence to spider silk, and with mechanical properties, which after proprietary cleaning and subsequent treatment, approach those of spider silk. They named these "Spidrex® silk filaments", and set about developing advanced methods for dissolving and refolding the protein using commercial domesticated and wild silk fibres to produce their Spidrex® silk solutions [see Side Box].

ALTERNATIVES

The Spidrex® filament approach contrasts with electro-spinning, which is another method of making the scaffolds for cell attachment (electro-spinning uses a high voltage electric field to pull out tiny filaments from a polymer solution). According to Knight the drawback of electro-spinning in this application is that it subjects polymers to only small strains, which results in relatively weak fibroin fibres. The porous sponges, and the larger strains of Spidrex®, on the other hand, mimic the spinning process in natural spider and silkworm spinning, which helps to align the fibroin molecules and cause them to link together with hydrogen bonds to form stronger and tougher materials.

In the field of medical materials, Spidrex® competes mainly with collagen, and synthetic resorbable polymers, such as PLA. Knight says Spidrex® is highly competitive with them in terms of biocompatibility, mechanical strength, resilience, and tuneable resorption time. It is also often cheaper than medical grade implantable manmade polymers. Further advantages claimed are that it avoids the risks of disease transmission and ethical objections involved in the use of collagen derived from cows, pigs or human cadavers.

APPLICATIONS

As a new super-material, Spidrex® can be processed in a wide number of ways to form tough sheets, coatings, porous sponges, tubes, gels, and nano- and micro-spheres. It can also be combined with specially-cleaned Spidrex® silk fibres to form immensely tough and resilient composite materials entirely constructed from silk.

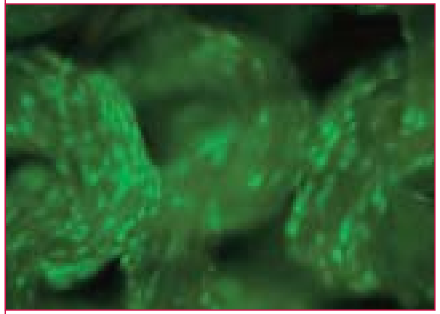
It is particularly good as a medical material because both fibre and materials formed from the silk solution are biocompatible and allow many types of mammalian cells to attach, grow and multiply. The surfaces of these materials can be chemically modified in numerous ways for different biomedical applications; also the time the material takes to be reabsorbed by the body can be tuned.

BIOMEDICAL

It is the biomedical applications which therefore to date have been seen as the most promising. Vollrath, Knight and their collaborators discovered that Spidrex® filaments could bind cells to surfaces because they are naturally decorated with multiple copies of a tripeptide (arginine-glycine-aspartic acid, known as RGD for short). RGD is also found on the surface of the structural protein, fibronectin. This protein is found in all multi-celled animals where it plays an important part in binding cells together and enabling them to communicate with one another by means of mechanical signals. Silk fibroin resembles fibronectin not only in its possession of multiple copies of RGD but also in its detailed three dimensional structure. Thus one of the first applications of

OXFORD BIOMATERIALS LTD

A METHOD OF SPINNING SPIDER-LIKE SILK, THE 'HOLY GRAIL' OF BIO MATERIALS (CONTINUED)



Tenocyte cell adhesion on Spiderx®

Spiderx® suture

NEUROTEX LTD - Neurotex draws on the expertise of Professor John Priestley, Head of Neuroscience at Queen Mary's School of Medicine and Dentistry. His initial studies have shown Spidrex® to be highly supportive of directed nerve growth with low immune-toxicity. The likelihood therefore is that the research will lead to treatment for damaged nerves which require a scaffold support to grow back. The eventual goal is to repair damaged spinal cords, which is much more difficult as the nerve does not grow back naturally.

Spidrex® has the advantage that it is highly biocompatible and has the ability to guide the migration of regenerating nerve cell processes and supporting (Schwann) cells.

SUTUROX LTD - The company was formed to address the need for a suture which is slowly absorbed, and provides long term support to the healing process. Together with Pearsalls Ltd., the UK's largest independent suture manufacturer, they have developed a range of absorbable Spidrex® Sutures which Suturox intends to market. The material is claimed to provide an excellent substrate for mammalian cell adhesion, while sequence characteristics make it chemically malleable and initial trials show that it is biocompatible and can be rendered pyrogen-free.

There is a major commercial opportunity because of concerns over prion disease from collagen-based sutures and adverse patient reactions from PLLA sutures which have resulted in product withdrawal.

Spidrex® silk filaments has been as a scaffold for binding cells, for example in nerve repair.

SPINOUT PLATFORM

After Oxford Biomaterials was set up in 2003 the two founders went on to establish three separately funded joint venture companies to develop the material for specific fields of use. They believe the advantage of this structure for investors is that it prevents funds from being diverted into other, more speculative projects; it also makes it less likely that the equity holding of OBM, the parent company, is extensively diluted by multiple investment rounds; and it gives OBM more control over the background IP.

The role of Oxford Biomaterials as the parent company is to manage the platform technologies and to initiate new IP, which it licenses to its joint venture companies on a non-exclusive basis. The founders continue to work on the development and commercialisation of new inventions, such as a patented silk reeling process which would improve silk quality and extend commercial production to a much wider range of silkworm species than the eight or so currently exploited commercially.

EXPLOITATION

Two of the three joint venture companies - Neurotex and Suturox - are described in the side bars, while the most advanced of the three, Orthox Ltd is described in the next section. David Knight meanwhile is extremely engaged in a variety of sustainability projects around the world aimed at the production of environmentally-friendly material from silkworms. This extends beyond medical materials to applications in sustainable energy production, which Knight says are too new still to be publicly discussed. ■

www.oxfordbiomaterials.com