

Fibriant BV

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Nature-inspired recombinant hemostasis products

Biotech company Fibriant has developed a unique recombinant fibrinogen manufacturing platform that is able to create a range of products that offer advantages over the plasma version.

Fibrinogen, a natural blood protein, is well known for playing a key role in hemostasis, tissue repair and host defence against pathogens. What is less widely known is that fibrinogen in human blood is actually a mixture of variants, each with different functions and properties that could be harnessed to improve existing hemostatic applications or develop innovative medical products in new therapeutic areas. However, extracting individual fibrinogen variants from human donor plasma is commercially infeasible.

Fibriant, a biotech company based in Leiden, the Netherlands, has developed a unique recombinant fibrinogen manufacturing platform to take advantage of the many opportunities that fibrinogen variants offer. Using industry standard CHO expression technology and a purification process based on a proprietary affinity resin, the company is able to produce specific human fibrinogen variants—fully intact and functional—at commercially feasible production levels and cost. And because fibrinogen is often used in combination with its physiological activator thrombin, Fibriant has also developed a recombinant thrombin production process.

“Plasma versus recombinant fibrinogen is analogous to serum-derived polyclonal immunoglobulin versus recombinant monoclonal antibodies,” explained Jaap Koopman, Fibriant co-founder and CEO. “This is the first time in history that naturally occurring individual fibrinogen variants can be produced in sufficient quantity for novel applications.”

Fibriant’s lead product, RecoSeel, is the first fully recombinant fibrin sealant for use as a biodegradable and bioactive topical haemostat to stop excessive bleeding during surgery. It is based on a fibrinogen variant (selected for its optimal functional properties) and recombinant thrombin (which converts soluble fibrinogen into an insoluble three-dimensional fibrin matrix), and offers significant advantages over plasma-derived topical haemostat products, a market worth \$1.2 billion worldwide. “Recombinant thrombin is simply cheaper to produce as the amount in donor plasma is tenfold lower than our recombinant expression levels. And our recombinant fibrinogen is more stable as it is of high purity and not contaminated with plasma proteases that degrade this large sensitive protein,” said Koopman. “This facilitates the development of liquid formulations of not only RecoSeel but also injectable fibrinogen products for use in acute bleeding situations.”

RecoSeel has demonstrated robust efficacy in pig-liver bleeding models, is expected to enter clinical development in 2022, and has low development risk as US Food and Drug Administration guidelines are already available and Fibriant’s founders and technical staff have experience in developing topical hemostat products.

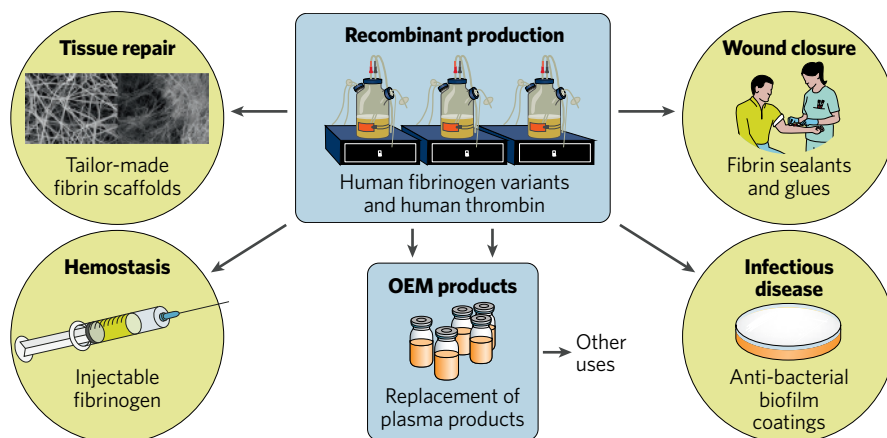


Fig. 1 | Recombinant production platform for fibrinogen variants and thrombin. The platform enables development of therapeutic end-products, as well as the supply of OEM products to companies who prefer to use recombinant fibrinogen and thrombin instead of plasma proteins. OEM, original equipment manufacturer.

Transforming natural variation into bespoke healthcare solutions

While plasma-derived fibrinogen is limited to topical and injectable hemostat products, the healthcare potential of recombinant fibrinogen is greater.

By focussing on specific variants, Fibriant can produce customized products, such as specialty sealants and matrices, coatings and injectable concentrates for use in wound closure, medical-implant biocompatibility, and treating or preventing blood loss (Fig. 1). Fibriant currently has four cell lines that each produce a specific variant and is planning to recombinantly produce up to twelve variants that are known to circulate in human blood.

A key area in Fibriant’s pipeline is host defence, with a focus on preventing and treating infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria. MRSA is known to hijack host proteins, especially circulating fibrinogen, to form biofilms on artificial surfaces or damaged tissue, enhancing its virulence and shielding the pathogen from host immunity and antibiotic treatment. However, one of Fibriant’s recombinant fibrinogen variants lacks the important pathogen-binding site; a proof-of-concept study in mice demonstrated that pre-coating medical implants with this variant reduces biofilm formation and, importantly, increases sensitivity of the biofilm-associated MRSA bacteria to antibiotic treatment.

Tissue repair is another area of future application. “The fibrin matrix also facilitates tissue remodelling and regeneration by supporting cell migration and influencing cellular phenotype,” explained Koopman. “We aim to provide tailor-made recombinant fibrin matrices with unique biochemical and biomechanical properties, for regenerative medicine applications.”

Partnering aspirations

Fibriant is looking for investors and strategic partners to help progress its pipeline and scale up Good Manufacturing Practice production of different fibrinogen variants and recombinant thrombin. The company is also keen to supply recombinant fibrinogen and/or thrombin as OEM products to other parties that would like to develop new products or replace plasma proteins in existing products.

Recombinant production offers several advantages over plasma fractionation. Product consistency and safety is higher as the need for different donors is negated, avoiding the risk of blood-borne disease transmission. Furthermore, production capacity is virtually unlimited, is unaffected by pandemics, such as COVID-19, or other global health issues that threaten blood donation, and existing import/export restrictions for plasma products do not apply, facilitating worldwide marketing.

“Individual fibrinogen variants, with their unique structure-function profiles, are an untapped healthcare resource,” said Koopman. “We believe we are the only company worldwide able to provide recombinant fibrinogen variants at commercially acceptable cost and maximise the value of this versatile molecule into customized hemostatic applications and innovative host-defence and tissue-repair products.”

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