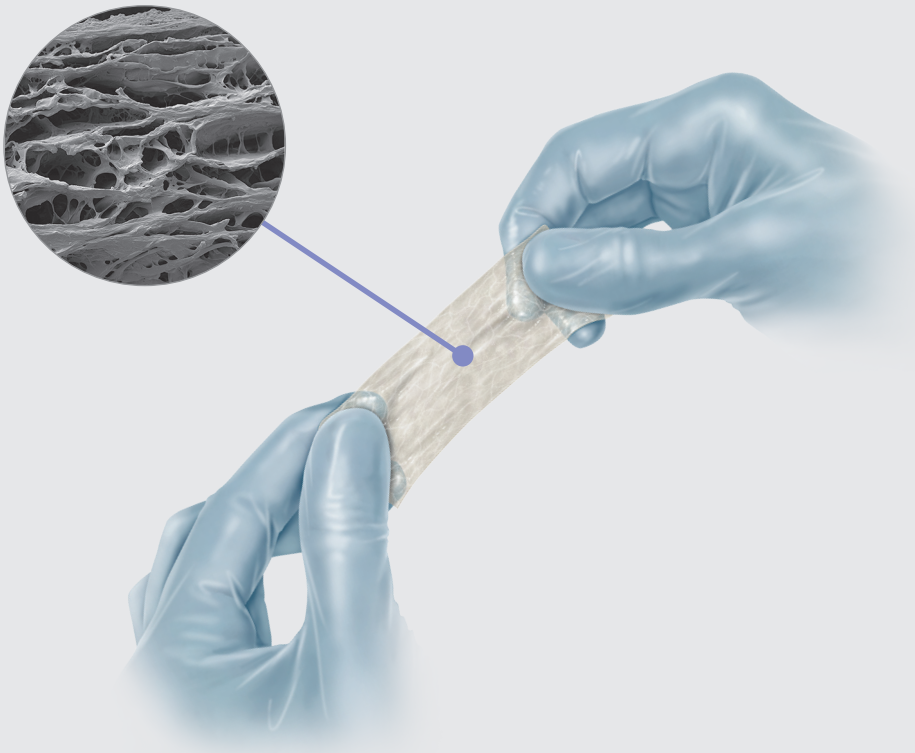
# Biodesign®

## Your biologic choice



Biodesign®

ADVANCED TISSUE REPAIR

COOK BIOTECH

cookbiotech.eu

CONTENTS

## Our history

More than 30 years ago, a Purdue University biomedical engineering team discovered the regenerative properties of porcine small intestinal submucosa (SIS).

In 1995, based on research supporting the versatility and effectiveness of SIS, Cook Biotech Inc. was founded to develop and manufacture the promising new material.

Since then, Cook Biotech has globally distributed more than 6 million SIS products.[1]

**Cook Biotech was founded in 1995 to develop and commercialise advanced tissue-repair products derived from SIS.**


**Cook Biotech Inc., Purdue Research Park, West Lafayette, Indiana.**

# A foundation of continuous improvement

**1988 - 1998** — **SIS discovered, developed**

SIS discovered as promising regenerative technology, developed into medical-grade material

**1998** — **Surgisis® released**

First international regulatory approval

**2004** — **Application-specific processing introduced**

Processing tuned to match clinical application

**2008** — **Biodesign® Hernia Graft released**

PGA stitching and perforations added. Lipids and DNA fragments removed.

**2010** — **Fistula plug improved**

First SIS fistula plug with resorbable button

**2013** — **Head & neck grafts released**

Skull-base reconstruction, sinonasal repair products receive FDA clearances

**2017** — **Regulatory clearances/ approvals expanded**

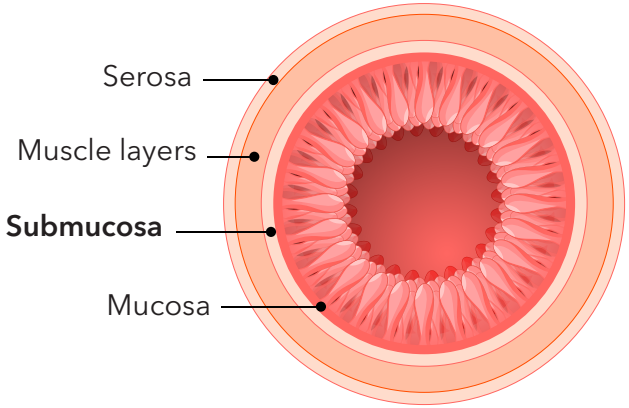
Biodesign Duraplasty Graft approved in Europe

**2020** — **New SIS formats**

Powder and liquid SIS compositions developed

# SIS technology

SIS is derived from porcine small intestinal submucosa, a naturally occurring extracellular matrix (ECM) located between the mucosal and muscular layers of the small intestine.

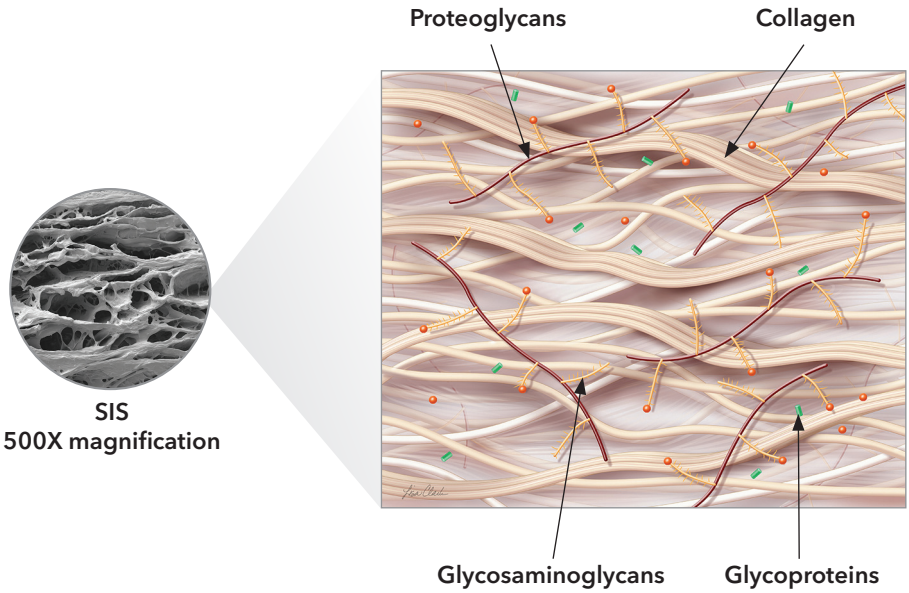



ECM is the structural and functional material that supports cells in nearly all body tissue. It serves as the structure upon which cells orient and move in response to other cells and signals and provides a healthy environment necessary for tissue maintenance and repair.[2]

Tissue-repair processes occur through the coordinated activity of cells that reside within the ECM. Because the ECM is necessary for tissue maintenance, it also plays a major role in tissue repair.[2] Without a functional ECM, the body can no longer support normal cellular processes, and tissue repair fails to progress.[3]

# Complex composition

SIS is a naturally occurring ECM that contains collagen, glycosaminoglycans, proteoglycans, and glycoproteins.[4]




These components create an environment that allows cells in the body to secrete growth factors and replicate.[5,6]

## The Biotech Process™

Cook Biotech designs and continuously improves proprietary processing methods to adapt SIS for specific clinical applications.

The result of the Biotech Process is variations of SIS that are optimised for application-specific requirements, such as strength and biochemical specifications.

Cook Biotech obtains SIS material from the intestine in a manner that removes all viable cells but leaves the naturally fibrous and porous nature of the matrix behind.[4]

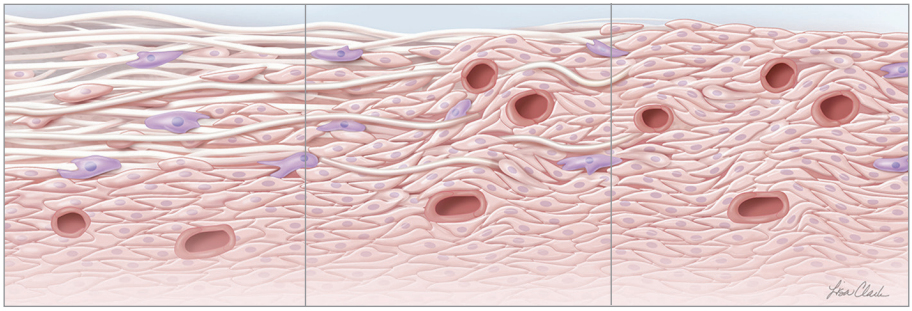
**SIS is carefully processed and meticulously crafted into Biodesign® tissue-repair products designed for specific clinical applications.**

The complex architecture and composition of the ECM are retained, providing not only the structural collagen framework but also the natural non-collagenous ECM components that are essential for cell interaction, function, and growth.[4,5]

Each product is then meticulously crafted to meet global quality standards with SIS material that was processed specifically for the product's clinical application.

# Tissue remodelling

SIS provides a natural scaffold that allows the body to restore itself through the complex natural process of tissue remodelling. Tissue remodelling involves the **recruitment** of cells, the **renewal** of tissue composition, and the **reinforcement** of structural tissue architecture.[7] As the body heals, SIS is gradually remodelled and integrated into the body, leaving behind organised tissue that provides long-term strength.[8-10]



## Recruit

**Immediately after implantation, the remodelling process starts when the body's inflammatory and progenitor cells populate the matrix and release cytokines and growth factors that recruit collagen-secreting fibroblasts.[11,12] In this phase, SIS acts as a scaffold material to support the population of the ECM with patient-derived cells.**

## Renew

**As remodelling progresses, host macrophages and fibroblasts in the newly populated matrix work together to renew the tissue through the complementary processes of phagocytosis, collagen deposition, and angiogenesis (blood vessel formation).[13] In this phase, SIS is gradually replaced by the patient's own tissue and cells.**

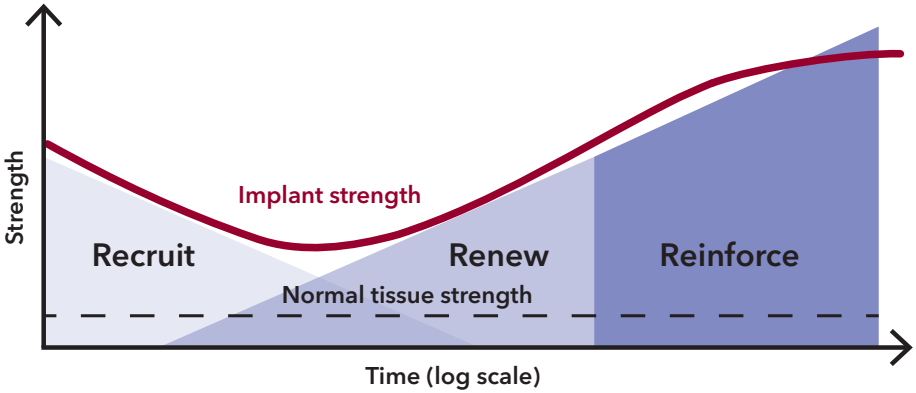
## Reinforce

**Over time, the resident fibroblasts secrete cytokines and growth factors to signal reinforcement of the deposited tissue through the processes of additional collagen deposition and maturation, resulting in a strong, repaired tissue.[5,8-10] In this phase, SIS is no longer needed as the patient's own collagen has gradually matured into a stable structure that has long-term strength but is entirely the patient's.[8-10]**

**Not all products or indications are available in all jurisdictions.**

Recruitment of cells, renewal of tissue composition, and reinforcement of structural tissue architecture result in mature, organised, strong tissue that can withstand the natural physiological forces it encounters.[14]

**Biodesign® graft remodelling**

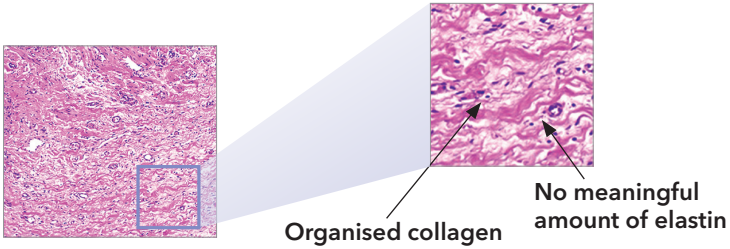



**Not all products or indications are available in all jurisdictions.**

## Non-dermis, non-cross-linked

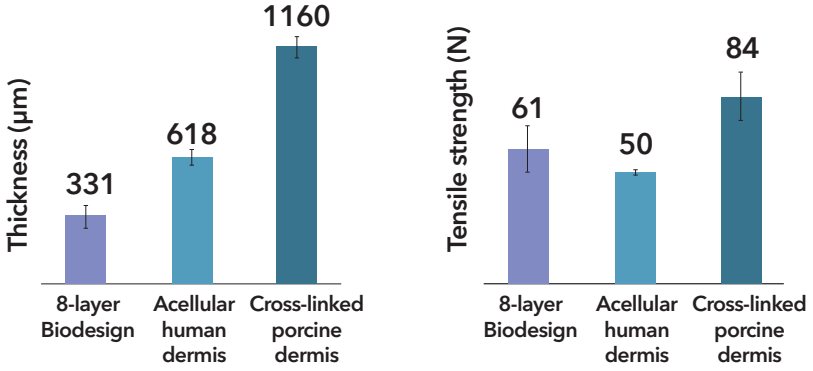
Because Biodesign® products are not manufactured from dermis, they contain no meaningful amount of elastin.[15] Dermis-based biologic grafts contain high amounts of elastin. Studies attribute higher rates of failure to higher elastin levels in some clinical applications.[16,17]

Biodesign grafts are designed to maintain strength throughout the remodelling process, so there is no need for chemical cross-linking.[10] Some cross-linked grafts have been associated with chronic inflammation and encapsulation.[18]




## Thin but strong

Even though Biodesign grafts are typically thinner than dermis-based grafts, the average tensile strength of Biodesign is comparable to the average strength of either an acellular human dermal graft or a cross-linked porcine dermal graft.[19,20]




**Not all products or indications are available in all jurisdictions.**

Because Biodesign® grafts are thin yet strong, they offer significant advantages to grafts made from thicker materials.

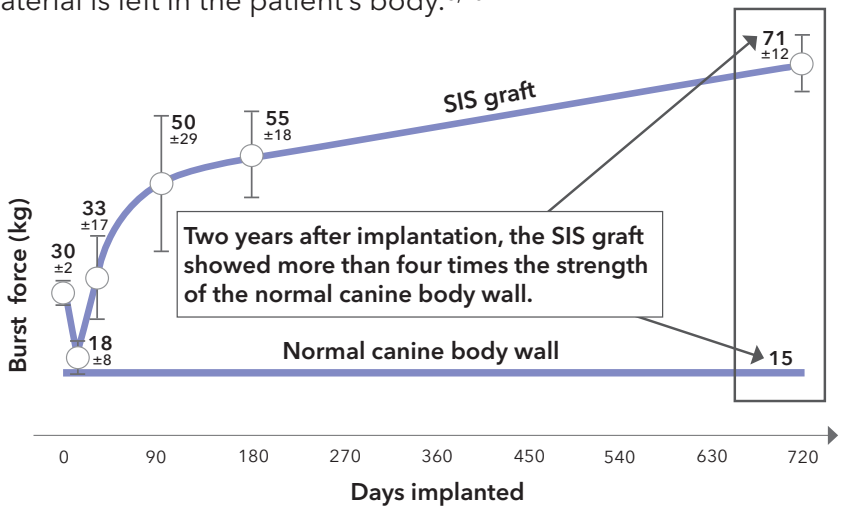
- They can be quickly hydrated, in a minute or less, using sterile saline or lactated Ringer's solution.
- They can easily be secured to the adjacent tissues using a suture, tack, or staple.
- They can easily be placed through a laparoscopic port during a laparoscopic operation.

## Long-term strength

Preclinical data have shown long-term strength as SIS remodels.[10]

Not only is the material strong at the time of implant, it is designed to exceed the strength of the recipient's tissue during the time it is being remodelled into vascularised tissue.

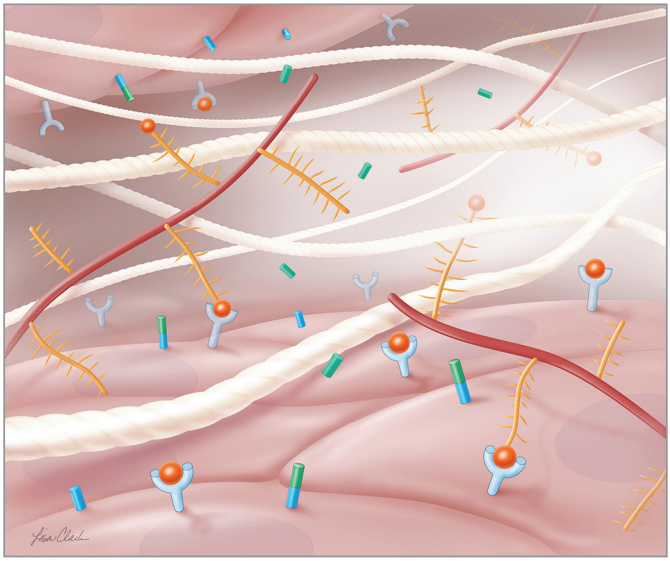
When tissue repair and remodelling are complete, the resulting tissue is stronger than that which was implanted. No permanent material is left in the patient's body.[8,10]




**Not all products or indications are available in all jurisdictions.**

# Site-specific remodelling

Biologic grafts made from natural tissues, when processed correctly for clinical use, have unique properties that are not found in synthetic materials, bioabsorbable materials, or highly processed and cross-linked graft materials.



**The natural ECM, when retained in its complex arrangement of matrix proteins and associated factors, can provide the key components needed to restore damaged tissues to their natural state.[6,21]**

These unique properties allow the naturally occurring biologic graft to completely integrate with the recipient's tissues and cells to ultimately form a vascularised, highly organised tissue structure that resembles the native tissue structure and architecture.[8,10]

As a result of this site-specific remodelling process, **no permanent material is left behind.**[8,10]

**Not all products or indications are available in all jurisdictions.**

A key concern when implanting any material into the body is how it will react and what may go wrong. Because no Biodesign® material is left behind after site-specific remodelling is complete, complications that may be common when synthetic materials are implanted, such as **erosion, encapsulation, and prolonged inflammation, are minimised**.[12]

### Immune response

SIS-derived biologic grafts have been shown to be accepted by the body's immune system and do not lead to a rejection response.[22] They do not cause the activation of the complement cascade, nor are they acutely rejected following implant.[22] They are associated with a Th2-dominant lymphocyte response (a response associated with transplant acceptance[23]) that does not adversely affect the patient's ability to overcome viral or bacterial infections,[24,25] and have also been associated with an M2 macrophage phenotype response[26] – a macrophage phenotype that promotes immunoregulation, tissue repair, and constructive tissue remodelling.[27]

### Pain or discomfort

Two clinical studies have shown that SIS-derived biologic grafts are associated with **lower incidence of pain or discomfort** when compared to polypropylene mesh in inguinal hernia repair.[28,29] (Cook Biotech's inguinal hernia product is not currently available in Europe.)

### Erosion, encapsulation, inflammation

Additionally, because Biodesign is designed to fully integrate with the patient's surrounding tissues, numerous studies in a variety of clinical applications have shown a reduced risk of erosion, encapsulation, and prolonged inflammation as compared to synthetic materials.[8, 30-32]

**Not all products or indications are available in all jurisdictions.**

## Studied and proven

The technology behind Biodesign® tissue-repair products is supported by more than 1,600 total publications. More than 600 publications describe clinical use. Ten publications have more than five years of follow-up data.

**36**
Clinical RCTs

**> 1,600**
Published articles

**> 600**
Clinical publications

**10**
Articles with more than five years of follow-up

Publications focused on SIS and its applications continue to grow. These numbers are accurate as of September 2020.

**Not all products or indications are available in all jurisdictions.**

# Key clinical evidence

## Abdominal wall reconstruction with components separation and mesh reinforcement in complex hernia repair

Nockolds CL, Hodde JP, Rooney PS. Abdominal wall reconstruction with components separation and mesh reinforcement in complex hernia repair. *BMC Surg.* 2014;14:25.

## The use of porcine small intestinal submucosa as a prosthetic material for laparoscopic hernia repair in infected and potentially contaminated fields: Long-term follow-up

Franklin ME Jr, Treviño JM, Portillo G, Vela I, Glass JL, González JJ. The use of porcine small intestinal submucosa as a prosthetic material for laparoscopic hernia repair in infected and potentially contaminated fields: Long-term follow-up. *Surg Endosc.* 2008;22(9):1941-1946.

## Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial

Oelschlager BK, Pellegrini CA, Hunter JG, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. *J Am Coll Surg.* 2011;213(4):461-468.

## Porcine small intestinal submucosa (SIS) myringoplasty in children: a randomized controlled study

D'Eredita RD. Porcine small intestinal submucosa (SIS) myringoplasty in children: a randomized controlled study. *Int J Pediatr Otorhinolaryngol.* 2015;79(7):1085-1089.

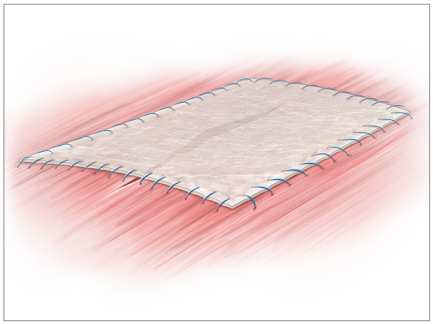
## Ventral herniorrhaphy: experience with two different biosynthetic mesh materials, Surgisis and Alloderm

Gupta A, Zahriya K, Mullens PL, Salmassi S, Keshishian A. Ventral herniorrhaphy: experience with two different biosynthetic mesh materials, Surgisis and Alloderm. *Hernia.* 2006;10(5): 419-425.

## Porcine small intestine submucosal graft for endoscopic skull base reconstruction

Illing E, Chaaban MR, Riley KO, Woodworth BA. Porcine small intestine submucosal graft for endoscopic skull base reconstruction. *Int Forum Allergy Rhinol.* 2013;3(11):928-932.

**Not all products or indications are available in all jurisdictions.**



## Biodesign® 4-Layer Tissue Graft

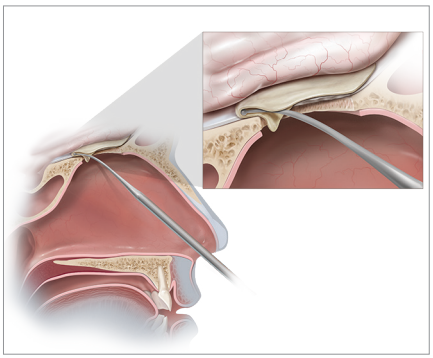
Used for implantation to reinforce soft tissue. Indicated for use in chordee correction, Peyronie's disease treatment, and urethral repair.

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G58004 | SLH-4S-2X3-2 | 2 x 3 |
| G58005 | SLH-4S-3.5X5-2 | 3.5 x 5 |
| G58006 | SLH-4S-4X7-2 | 4 x 7 |
| G58007 | SLH-4S-7X10-2 | 7 x 10 |
| G58008 | SLH-4S-7X20-2 | 7 x 20 |

## Biodesign® Dural Graft

Used as a dura substitute for repairing dura mater

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G57557 | C-DUR-2X3-2 | 2 x 3 |
| G57558 | C-DUR-4X7-2 | 4 x 7 |
| G57559 | C-DUR-7X10-2 | 7 x 10 |
| G57560 | C-DUR-7X20-2 | 7 x 20 |



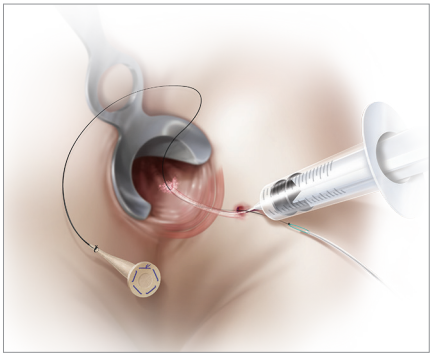
## Biodesign® Duraplasty Graft

Used as a dura substitute for the repair of dura mater

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G57553 | ENT-CBD-1X2-2 | 1 x 2 |
| G57554 | ENT-CBD-2.5X2.5-2 | 2.5 x 2.5 |
| G57555 | ENT-CBD-5X5-2 | 5 x 5 |
| G57556 | ENT-CBD-7X8.5-2 | 7 x 8.5 |

Illustrations by Lisa Clark

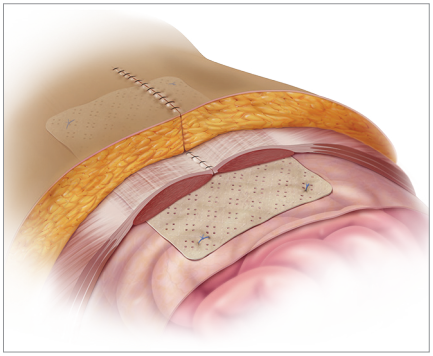
**Not all products or indications are available in all jurisdictions.**



## Biodesign® Fistula Plug Set

Used for implantation to reinforce soft tissue for repair of anorectal fistulas

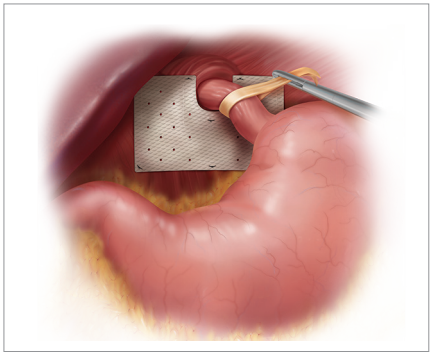
| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G46374 | C-FPS-0.2-2 | 0.2 |
| G46372 | C-FPS-0.4-2 | 0.4 |
| G46373 | C-FPS-0.7-2 | 0.7 |



## Biodesign® Hernia Graft

Used for implantation to reinforce soft tissues where weakness exists during ventral hernia repair

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G57513 | C-SLH-8H-10X10-2 | 10 x 10 |
| G57514 | C-SLH-8H-13X15-2 | 13 x 15 |
| G57515 | C-SLH-8H-13X22-2 | 13 x 22 |
| G57516 | C-SLH-8H-20X20-2 | 20 x 20 |
| G57517 | C-SLH-8H-20X30-2 | 20 x 30 |



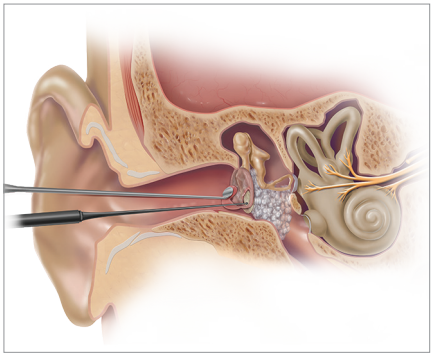
## Biodesign® Hiatal Hernia Graft

Used for implantation to reinforce soft tissues where weakness exists, during hiatal hernia repair

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G58002 | C-PHR-7X10-2 | 7 x 10 |
| G58003 | C-PHR-7X10-U-2 | 7 x 10 |

Illustrations by Lisa Clark

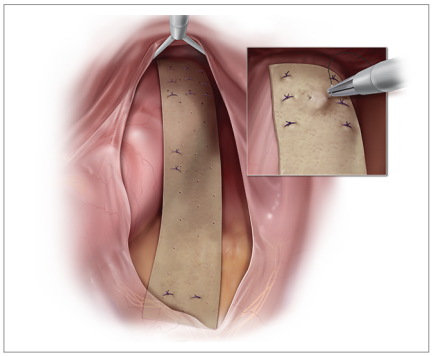
**Not all products or indications are available in all jurisdictions.**



## Biodesign® Otologic Repair Graft

Used as grafting material for tympanic membrane perforation closure

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G58271 | ENT-OTO-0.4-0.6-2 | 0.4 & 0.6 (diameter) |
| G58272 | ENT-OTO-0.6-0.9-2 | 0.6 & 0.9 (diameter) |
| G58273 | ENT-OTO-2.5X2.5-2 | 2.5 x 2.5 |
| G58274 | ENT-OTO-5X5-2 | 5.0 x 5.0 |



## Biodesign® Rectopexy Graft

Used to support/reinforce soft tissue in surgical procedures for open and laparoscopic repair of rectal prolapse/rectal intussusception

| Order Number | Reference Part Number | Size cm |
|---|---|---|
| G58011 | C-BRG-7X20-2 | 7 x 20 |

Illustrations by Lisa Clark

**Not all products or indications are available in all jurisdictions.**

1. Internal Cook Biotech document: D00278582.
2. Clause KC, Barker TH. Extracellular matrix signaling in morphogenesis and repair. *Curr Opin Biotechnol*. 2013;24(5):830-833.
3. Daley WP, Peters SB, Larsen M. Extracellular matrix dynamics in development and regenerative medicine. *J Cell Sci*. 2008;121(Pt 3):255-264.
4. Hodde J, Janis A, Ernst D, Zopf D, Sherman D, Johnson C. Effects of sterilization on an extracellular matrix scaffold: Part I. Composition and matrix architecture. *J Mater Sci Mater Med*. 2007;18(4):537-543.
5. Nihsen ES, Johnson CE, Hiles MC. Bioactivity of small intestinal submucosa and oxidized regenerated cellulose/collagen. *Adv Skin Wound Care*. 2008;21(10):479-486.
6. Hodde J, Janis A, Hiles M. Effects of sterilization on an extracellular matrix scaffold: Part II. Bioactivity and matrix interaction. *J Mater Sci Mater Med*. 2007;18(4):545-550.
7. Turner NJ, Badylak SF. Biologic scaffolds for musculotendinous tissue repair. *Eur Cell Mater*. 2013;25:130-143.
8. Franklin ME Jr, Trevino JM, Portillo G, Vela I, Glass JL, Gonzalez JJ. The use of porcine small intestinal submucosa as a prosthetic material for laparoscopic hernia repair in infected and potentially contaminated field: Long-term follow-up. *Surg Endosc.* 2008;22(9):1941-1946.
9. Stelly M, Stelly TC. Histology of CorMatrix bioscaffold 5 years after pericardial closure. *Ann Thorac Surg*. 2013;96(5):e127-e129.
10. Badylak S, Kokini K, Tullius B, Whitson B. Strength over time of a resorbable bioscaffold for body wall repair in a dog model. *J Surg Res*. 2001;99(2):282-287.
11. Badylak SF, Park K, Peppas N, McCabe G, Yoder M. Marrow-derived cells populate scaffolds composed of xenogeneic extracellular matrix. *Exp Hematol*. 2001;29(11): 1310-1318.
12. Hodde J. Extracellular matrix as a bioactive material for soft tissue reconstruction. *ANZ J Surg*. 2006;76(12):1096-1100.
13. Badylak SF. The extracellular matrix as a scaffold for tissue reconstruction. *Semin Cell Dev Biol*. 2002;13(5):377-383.
14. Frantz C, Stewart KM, Weaver VM. The extracellular matrix at a glance. *J Cell Sci*. 2010;123(24):4195-4200.
15. Hiles M, Record Ritchie RD, Altizer AM. Are biologic grafts effective for hernia repair?: a systematic review of the literature. *Surg Innov.* 2009;16(1):26-37.
16. Gupta A, Zahriya K, Mullens PL, Salmassi S, Keshishian A. Ventral herniorrhaphy: experience with two different biosynthetic mesh materials, Surgisis and Alloderm. *Hernia*. 2006;10(5):419-425.
17. Kissane NA, Itani KMF. A decade of ventral incisional hernia repairs with biologic acellular dermal matrix: What have we learned? *Plast Reconstr Surg*. 2012;130(5 Suppl 2):194S-202S.
18. Novitsky YW, Rosen MJ. The biology of biologics: basic science and clinical concepts. *Plast Reconstr Surg.* 2012;130(5 Suppl 2):9S-17S.
19. Internal Cook Biotech document: 00-107.
20. Internal Cook Biotech document: 02-063.
21. Swinehart IT, Badylak SF. Extracellular matrix bioscaffolds in tissue remodeling and morphogenesis. *Dev Dyn*. 2016;245(3):351-360.
22. Raeder RH, Badylak SF, Sheehan C, Kallakury B, Metzger DW. Natural anti-galactose alpha1,3 galactose antibodies delay, but do not prevent the acceptance of extracellular matrix xenografts. *Transpl Immunol*. 2002;10(1):15–24.
23. Bach FH, Ferran C, Hechenleitner P, et al. Accommodation of vascularized xenografts: expression of "protective genes" by donor endothelial cells in a host Th2 cytokine environment. *Nat Med*. 1997;3(2):196–204.

24. Allman AJ, McPherson TB, Badylak SF, et al. Xenogeneic extracellular matrix grafts elicit a TH2-restricted immune response. *Transplantation*. 2001;71(11):1631–1640.
25. Allman AJ, McPherson TB, Merrill LC, Badylak SF, Metzger DW. The Th2-restricted immune response to xenogeneic small intestinal submucosa does not influence systemic protective immunity to viral and bacterial pathogens. *Tissue Eng*. 2002;8(1):53–62.
26. Badylak SF, Valentin JE, Ravindra AK, McCabe GP, Stewart-Akers AM. Macrophage phenotype as a determinant of biologic scaffold remodeling. *Tissue Eng Part A*. 2008;14(11):1835-1842.
27. Martinez FO, Sica A, Mantovani A, Locati M. Macrophage activation and polarization. *Front Biosci*. 2008;13:453-461.
28. Bochicchio GV, Jain A, McGonigal K, et al. Biologic vs. synthetic inguinal hernia repair: 1-year results of a randomized double-blinded trial. *J Am Coll Surg*. 2014;218(4):751-757.
29. Ansaloni L, Catena F, Coccolini F, Gazzotti F, D'Alessandro L, Pinna AD. Inguinal hernia repair with porcine small intestine submucosa: 3-year follow-up results of a randomized controlled trial of Lichtenstein's repair with polypropylene mesh vs. Surgisis Inguinal Hernia Matrix. *Am J Surg*. 2009;198(3):303-312.
30. Smart NJ, Pathak S, Boorman P, Daniels IR. Synthetic or biological mesh use in laparoscopic ventral mesh rectopexy – a systematic review. *Colorectal Dis*. 2013;15(6): 650-654.
31. Albayati S, Morgan MJ, Turner CE. Laparoscopic ventral rectopexy for rectal prolapse and rectal intussusception using a biological mesh. *Colorectal Dis*. 2017;19(8):857-862.
32. Oelschlager BK, Pellegrini CA, Hunter JG, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. *J Am Coll Surg*. 2011;213(4):461-468.

For information on contraindications, precautions, and potential complications, see product IFUs.

For clinical enquiries: Biodesign@CookBiotech.com.

COOK BIOTECH

cookbiotech.eu