Chitosan scaffold cellularized for colorectal tissue regeneration in swine model

Denost Q, Buscail E, Pontallier A, Bareille R, Montembault A, Delmont S, Siadous R, Durant M, Rullier E, Laurent D, Bordenave L
(France)
New surgical tool for colorectal surgery in electives indications

**Prerequisites**

1. Tissue sample
2. In vitro Cells culture
3. Cells seeded on scaffold
4. Cells proliferation
5. Transplantation

**Perspectives**

- Anastomosis reinforcement
- Rectal wall defect treatment
  - Pelvic fistula
  - Endoanal local excision
# Colorectal Tissue engineering

## Current status

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Scaffold</th>
<th>Cells</th>
<th>Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutter, 1996</td>
<td>Human Collagen</td>
<td>-</td>
<td>Rats</td>
</tr>
<tr>
<td>Oh, 2002</td>
<td>ePTFE</td>
<td>-</td>
<td>Dogs</td>
</tr>
<tr>
<td>Grikscheit, 2002</td>
<td>PLLA-PGA tube</td>
<td>Organoid Units</td>
<td>Rats</td>
</tr>
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<td>Rats</td>
</tr>
<tr>
<td>Nocca, 2002</td>
<td>Bovin Collagen</td>
<td>-</td>
<td>Pigs</td>
</tr>
<tr>
<td>Ueno, 2007</td>
<td>SIS*</td>
<td>-</td>
<td>Rats</td>
</tr>
<tr>
<td>Hoeppner, 2009</td>
<td>SIS*</td>
<td>-</td>
<td>Pigs</td>
</tr>
</tbody>
</table>

*SIS = Small intestine submucosa
Preliminary experimental works

**Scaffold selection**

Colorectal tissue engineering: comparative study between porcine Small Intestinal Submucosa (SIS) and chitosan hydrogel patches.
Denost Quentin\(^1,2,3\), Adam Jean-Philippe\(^1,2,3\), Montembault Alexandra\(^4\), Bareille Reine\(^2,3\), Siadous Robin\(^2,3\), Delmont Samantha\(^3\), Rullier Eric\(^1\), David Laurent\(^4\), Bordenave Laurence\(^2,3\).

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**Cells delivery system**

Composite Chitosan-Fibrin glue in a preliminary in vitro study for colorectal tissue engineering application.
Arnaud Pontallier\(^1,2,3\), Alexandra Montembault\(^4\), Robin Siadous \(^2,3\), Reine Bareille\(^2,3\), Eric Rullier\(^1\), Laurent David\(^4\), Laurence Bordenave\(^2,3\), Quentin Denost\(^1,2,3\)
The aim of this study was to demonstrate the interest of scaffold cellularization for colorectal tissue engineering.
### Methods

<table>
<thead>
<tr>
<th>Operative procedure</th>
<th>Euthanasia (8 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1</strong></td>
<td></td>
</tr>
<tr>
<td>Implantation of scaffold (2x3 cm) without cells</td>
<td>n=10</td>
</tr>
<tr>
<td><strong>Group 2</strong></td>
<td></td>
</tr>
<tr>
<td>Fat tissue harvested</td>
<td></td>
</tr>
<tr>
<td>Implantation of scaffold (2x3 cm) seeded by autologous SVF</td>
<td>n=10</td>
</tr>
</tbody>
</table>
Methods
Clinical outcomes

Weight evolution

Acellular scaffold

Cellularized scaffold
Graft area outcomes

Macroscopic assessment

Acellular scaffold

Cellularized scaffold
Graft area outcomes

Microscopic assessment

HES staining
## Graft area outcomes

### Fibrosis ratio

#### Acellular scaffold

#### Cellularized scaffold

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groupe A (N=9)</th>
<th>Groupe B (N=10)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Médiane (min-max)</td>
<td>Médiane (min-max)</td>
<td></td>
</tr>
<tr>
<td>Rapport</td>
<td>0.55 (0.22-1.00)</td>
<td>0.13 (0.00-0.95)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

* test des rangs de Wilcoxon
Graft area outcomes

Immunochemistry

Alpha actine

Caldesmon

Smooth muscle cells
Our data confirmed in a large animal model the healing effect of chitosan on colorectal tissue.

Scaffold cellularization by autologous SVF allowed to obtain:

- a better control of inflammation
- an ad integrum colorectal tissue engineered
Circular chitosan scaffold

- Diameter: 25 mm; Length: 20 mm
- 3 pigs
- Euthanasia scheduled July 31th

Weight of pigs

![Graph showing weight of pigs over time.](image)
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