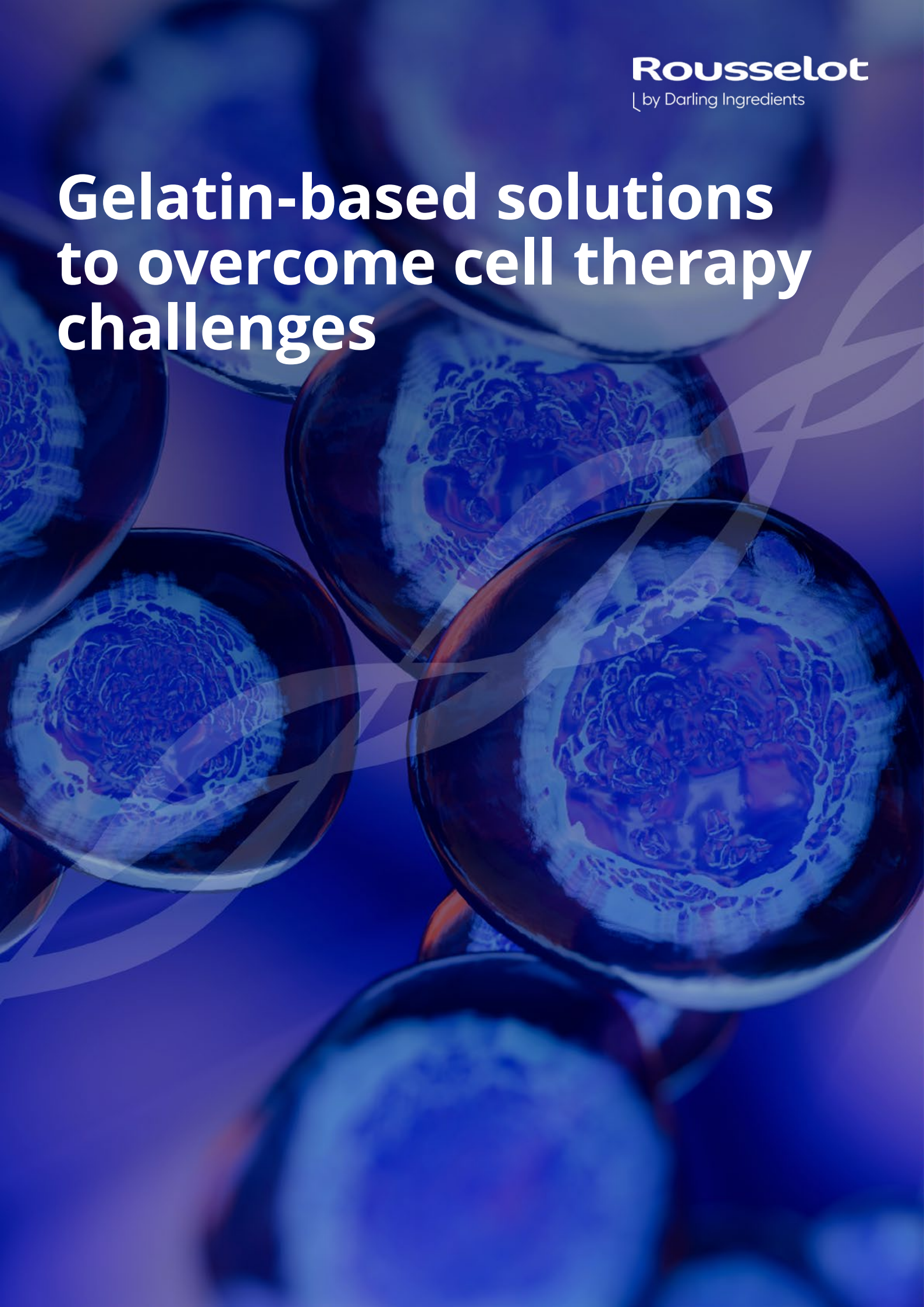


**Rousselot**

| by Darling Ingredients

# Gelatin-based solutions to overcome cell therapy challenges



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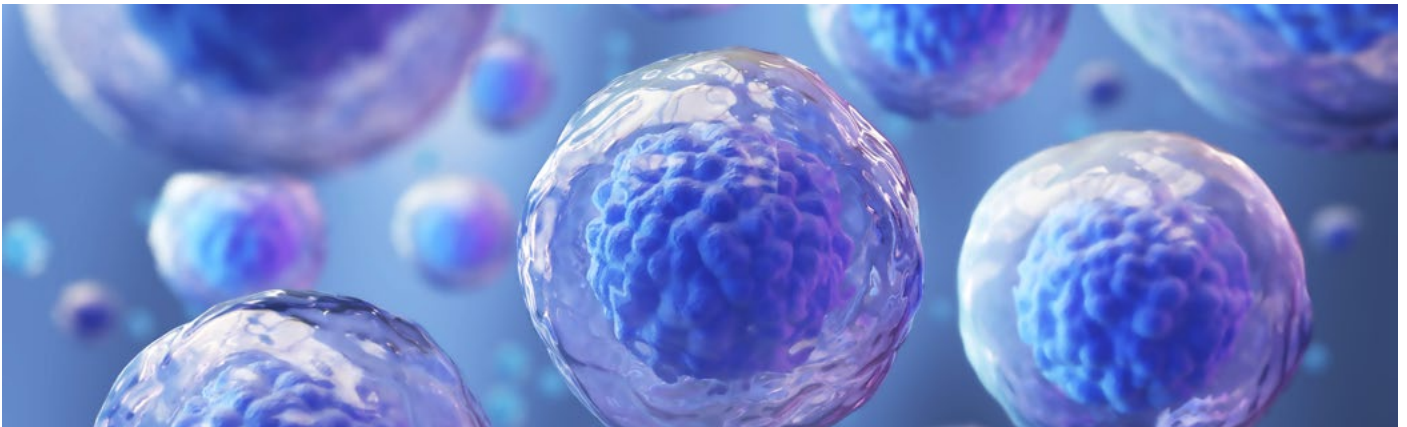
**1. Explore the promise and challenges of cell therapy**

**2. Discover common problems in cell therapy and how to overcome them**

- a. Preventing cell sedimentation
- b. Protecting cells from shear-stress-induced damage during administration
- c. Retaining cells at the site of injection
- d. Improving cell viability post-injection

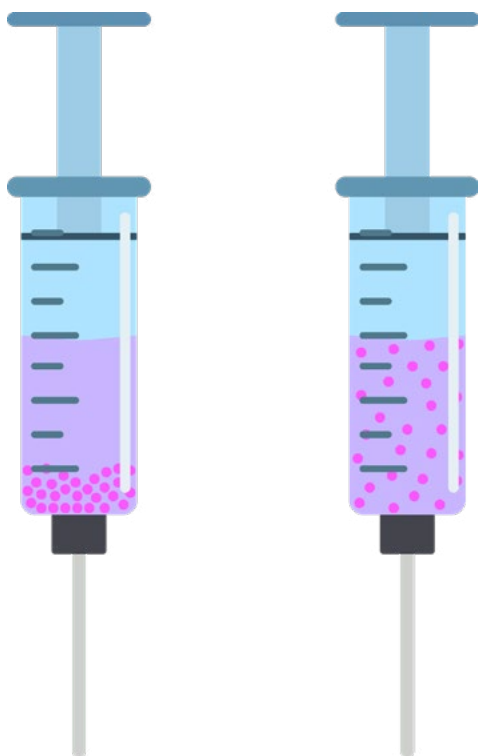
**3. Learn more about the benefits of Rousselot's gelatin-based solutions**

## Cells as medicine: the promise and challenges of cell therapy



Cell therapy is a promising and rapidly advancing field with the potential to transform medicine for a wide range of diseases and conditions. Various treatments involving therapeutic cells have received market authorization in the last decade. Most involve delivering therapeutic cells into the bloodstream, such as CAR T-cell therapies to treat blood cancers. Cell therapy also holds great promise to treat chronic conditions such as spinal cord injuries, chronic heart failure, or Parkinson's disease.

Central to successfully treating these “non-bloodstream” conditions is the effective locoregional delivery of ex-vivo cultured cells to the site of injury or disease. However, uniform delivery of therapeutic cells, retention of cells at the administration site, and maintaining high cell viability are common issues in developing effective locoregional cell therapies (Amer et al., 2017). Read on to discover how unique and customizable gelatin-based solutions are enabling researchers and clinicians to effectively deliver and retain ex-vivo cultured cells in diseased or damaged tissue sites and to help maintain high cell viability post-delivery.



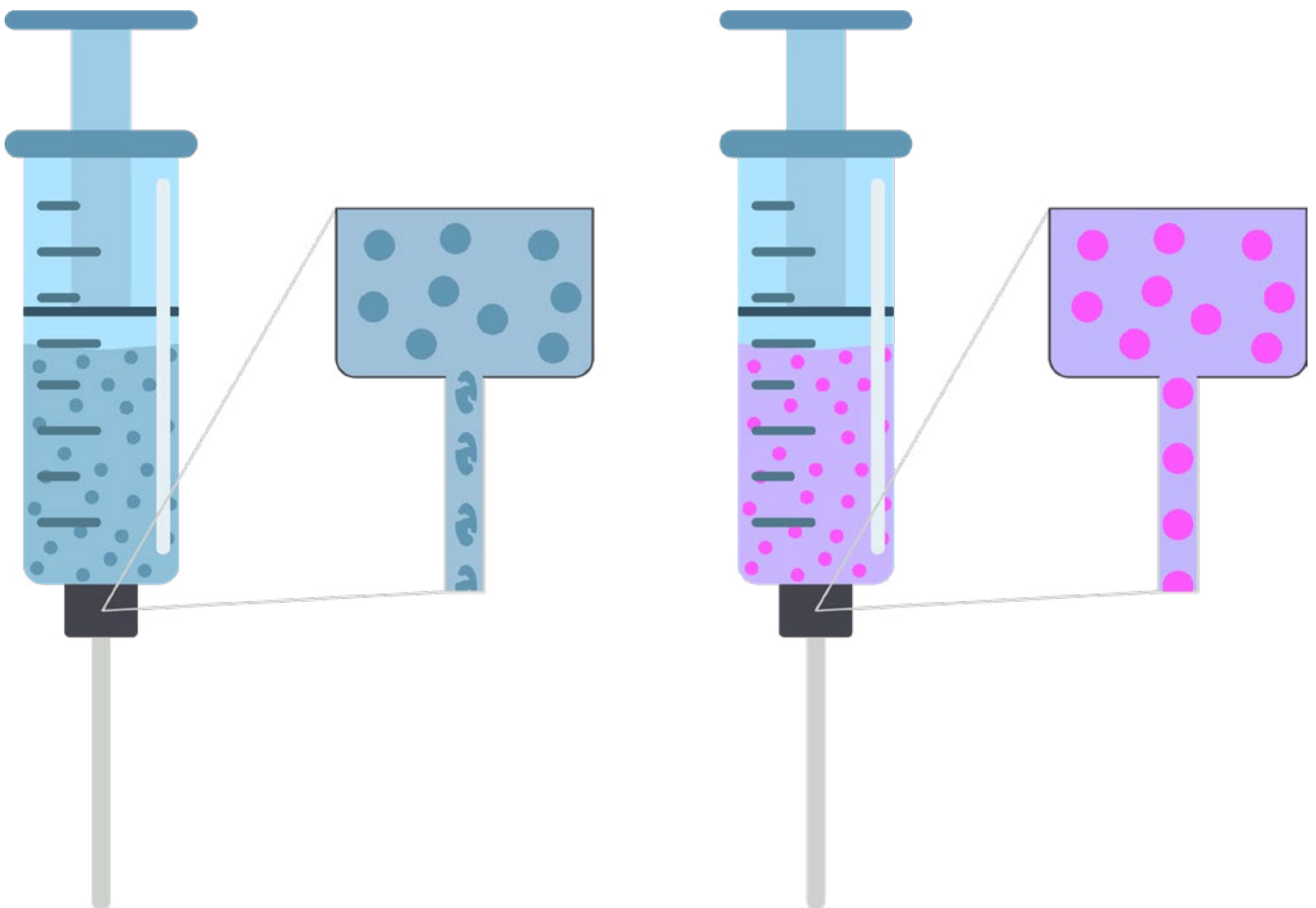
### Preventing cell sedimentation

During the transportation of therapeutic cells from the production site to the patient, cells tend to sediment in the vial or syringe. This not only affects cell viability, but also causes inconsistent dosing. Non-uniform cell doses can create hotspots of therapeutic cells that could cause serious adverse effects. Hydrogels can prevent this sedimentation, thereby helping to achieve uniform dosing.

Left: cell aggregation and sedimentation in a syringe. Right: use of hydrogels can help to prevent sedimentation of cells.

## Protecting cells from shear-stress-induced damage during administration

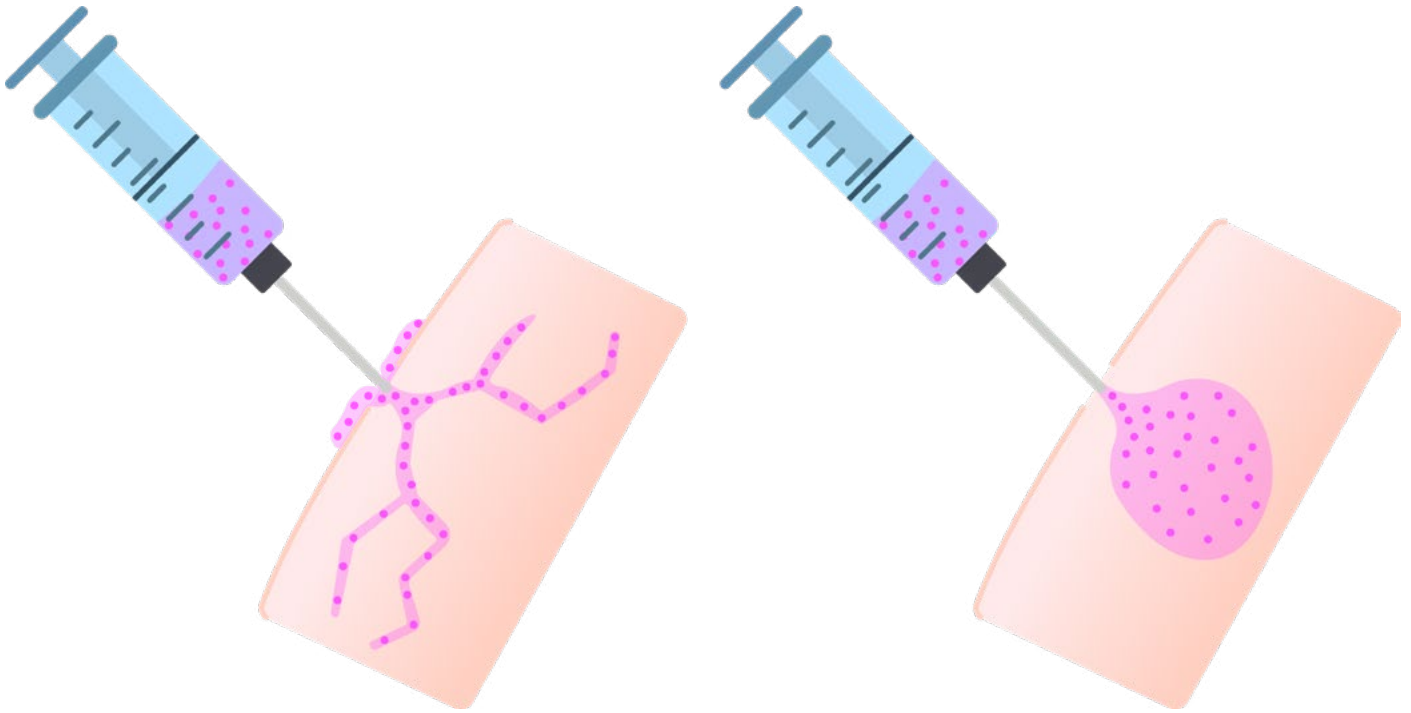
Cells can be damaged when they are forced through an injection device, affecting their ability to survive and function after transplantation. The mechanical force on the cell surface as it flows through the confined space of a needle is called shear stress. Even low levels of shear stress can significantly affect cells, activating molecular cascades and altering cell viability and function. Shear thinning liquids protect cells during injection. When passing through small orifices such as narrow gauge needles, shear thinning liquids provide a shear band and shield the cells from damage due to shear stress.



Left: cells damaged in a syringe due to shear stress. Right: shear thinning liquids protect cells from damage during injection.

## Retaining cells at the site of injection

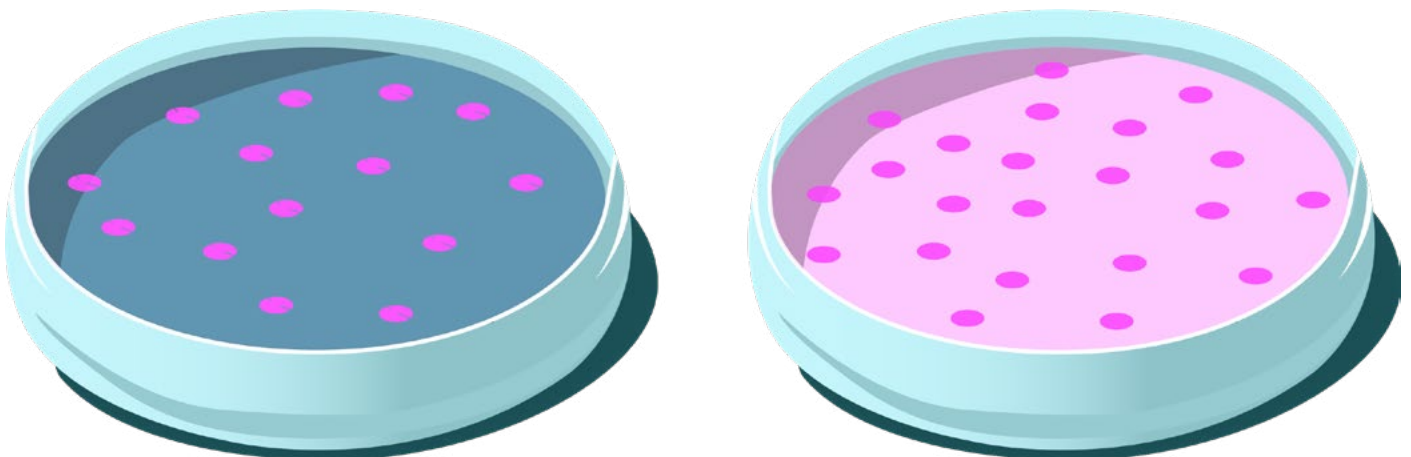
Another significant challenge in locoregional cell therapy is the retention of therapeutic cells at the injection site. Typically, less than 5% of injected cells remain at the target site shortly after injection. Blood vessels or lymphatic vessels could carry cells away, tissue pressure can squeeze the cells out, or the cell suspension can flow back via the needle access point. A shear-thinning gel or flowable gelatin paste can help improve cell retention at the injection site by preventing the cells from flowing away.



Left: cells flowing away from the injection site. Right: cells remaining within the flowable gelatin paste.

## Improving cell viability post-injection

Once delivered to the target site, considerable cell loss may still occur due to cell death or removal by the immune system. Some cells may undergo programmed cell death (anoikis), which occurs when cells detach from the surrounding extracellular matrix due to the loss of anchorage-dependent survival signals. Gelatin hydrogel inherently contains RGD cues, a specific sequence of amino acids – arginine (R), glycine (G), and aspartic acid (D) – that is commonly found in proteins within the extracellular matrix, which facilitate cell adhesion. In addition, high-density gelatin has the advantage of temporarily protecting the cells from macrophages.



Left: image of dying, detached cells in a hostile environment. Right: healthy cells protected by gelatin hydrogel.

## The benefits of Rousselot's gelatin-based solutions

At Rousselot, we offer various customizable, medical-grade, gelatin-based solutions for locoregional therapeutic cell delivery, including gelatin-based shear-thinning hydrogels. Gelatin has a long history of use in biomedical applications. Compared to other hydrogel materials, the immune system does not recognize gelatin as a foreign body, and it can be made to biodegrade within hours or within weeks after injection. Additionally, Rousselot's X-Pure gelatins meet the purity and regulatory requirements for use in clinical products.

## Rousselot's STITCH, a Shear-Thinning Injectable Cell Therapy Hydrogel with Proven Biocompatibility

1. STITCH leverages an FDA-approved medical device formulation, ensuring safety and biocompatibility for seamless integration.
2. Optimized Cell Viability (>85%): Our hydrogel maintains superior cell viability, ensuring the functionality of transplanted cells both in vitro and in vivo.
3. Localized Matrix Support: With its shear-thinning properties, STITCH remains in place post-delivery, providing essential matrix support and preventing flow-back through the needle tract.
4. Prevention of Sedimentation: STITCH's viscosity prevents cell sedimentation, guaranteeing uniform cell distribution and integration post-injection.

## Get in touch

Contact us to find out more about STITCH and our other gelatin-based solutions for therapeutic cell delivery.

## References

Amer, M. H., Rose, F., Shakesheff, K. M., Modo, M., & White, L. J. (2017). Translational considerations in injectable cell-based therapeutics for neurological applications: concepts, progress and challenges. *NPJ Regen Med*, 2, 23. <https://doi.org/10.1038/s41536-017-0028-x>