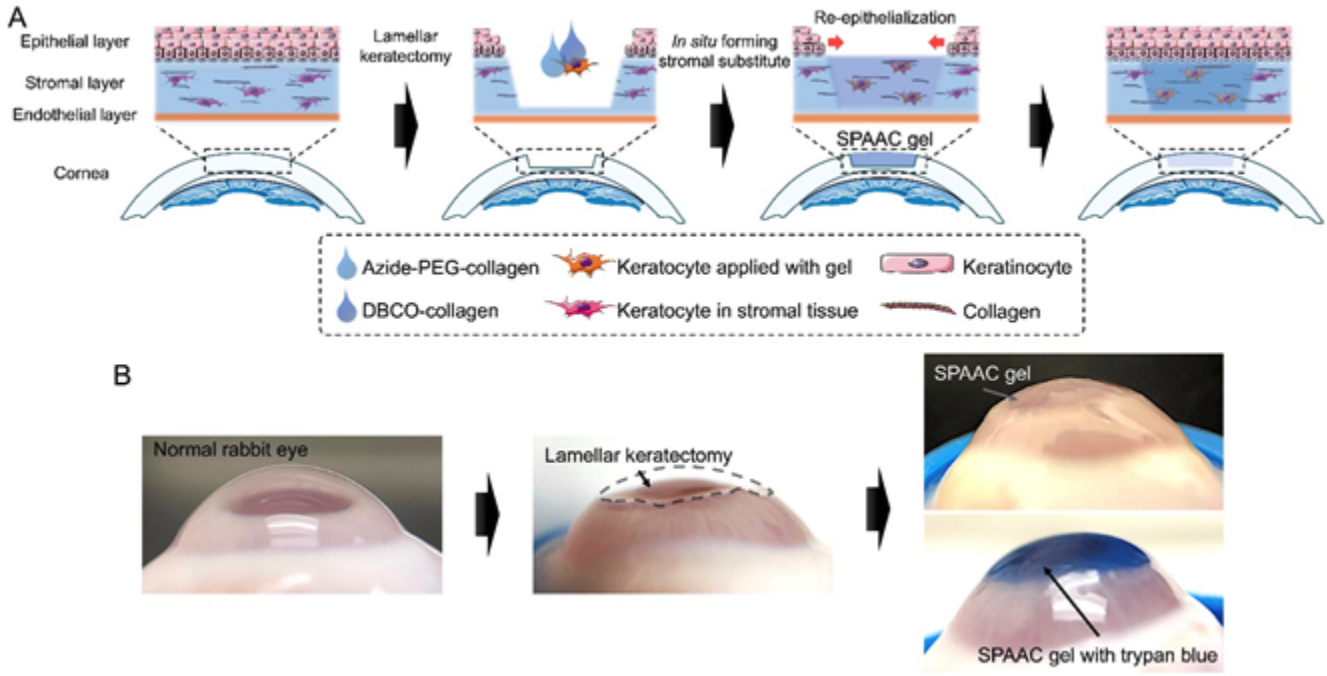
Docket #: S18-196

Gel scaffold for corneal wound healing and tissue engineering

Researchers in Prof. David Myung's laboratory have developed a bio-compatible, crosslinking gel that can be used for in situ repair of damaged cornea or as a three-dimensional scaffold for keratocyte-keratinocyte tissue culture. This click chemistry technology uses bio-orthogonal SPAAC (strain-promoted azide-alkyne cycloaddition) crosslinking to provide a corneal stromal substitute based on collagen type I. The viscous injectable material could be safely applied to a wounded cornea where it reacts to form a gel scaffold able to promote tissue repair without sutures or a human donor. The gel recapitulates the thickness and smooth, continuous surface of the cornea so it can be used as a three-dimensional acellular scaffold or a scaffold that encapsulates cultured cells (keratocytes). In research applications, the scaffold could be used for three-dimensional tissue culture to synthesize lamellar substitutes or to study keratocyte-keratinocyte interactions. In wound healing applications, this technology is a promising candidate for in situ lamellar and defect reconstruction of corneal stromal tissue in cases of deep corneal ulcers to rapidly stabilize wounds or to replace a section of the cornea.



SPAAC gel performance in organ culture model *of sutureless in situ-forming anterior lamellar keratoplasty. (A) Schematic of lamellar keratectomy and SPAAC gel treatment with keratocyte as an in situ-forming corneal stromal substitute. (B) Photographs of rabbit corneal tissue with lamellar keratectomy and SPAAC gel application.*

Stage of Research

The inventors have characterized the transparency and mechanical properties of the crosslinked gel (transmittance: 84.58 +/- 1.44%; storage modulus: 112.03 +/- 3.94 Pa). Using a rabbit cornea organ culture model, they demonstrated that the SPAAC gels promoted multi-layer re-epithelialization as well as good apposition and adherence to the host tissues.

Applications

- **Ocular wound healing:**
  - injectable, in situ-forming scaffold to fill, stabilize and regenerate deep corneal wounds, particularly in patients where the risks and morbidities associated with penetrating the globe are high (e.g., keratoplasty for deep ulcers or severe thinning)
  - in vitro system for synthesizing cellular or acellular lamellar substitutes

    - delivery vehicle for therapeutic factors that aid in wound healing
- **Tissue scaffold for ophthalmologic research** - three-dimensional in vitro model system for studying keratocyte-keratinocyte interactions within corneal tissue

Advantages

- **Minimally-invasive:**
    - administered at the point of care by injection with no sutures
    - no need for human donor
- **Bio-compatible:**
    - non-toxic SPAAC (strain-promoted azide-alkyne cycloaddition) crosslinking relies on bio-orthogonal click-chemistry that is compatible with living tissue
    - gel scaffold integrates with surrounding tissues
    - gel reacts in water and ambient conditions with no external catalyst and produces no side products
- **Transparent matrix** - crosslinked collagen gel has transmittance of 84.58 +/- 1.44%, enabling corneal wound healing applications

Publications

- Lee, H. J., Fernandes-Cunha, G. M., Na, K. S., Hull, S. M., & Myung, D. (2018). Bio-Orthogonally Crosslinked, In Situ Forming Corneal Stromal Tissue Substitute. *Advanced healthcare materials*, 1800560.

Patents

- Published Application: WO2020006255
- Published Application: 20210244659
- Issued: 12,036,314 (USA)

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