

## Osaka University Team Does World's First Successful iPS Cell-Derived Corneal Transplant

A team of researchers led by Osaka University Professor Koji Nishida has successfully treated an eye disease patient by transplanting artificially-cultured corneal cells derived from induced pluripotent stem cells, or iPS cells, the research team announced on August 29.

The corneal transplant operation using iPS cells is the first of its kind in the world, the researchers say. Given the dearth of corneal donations, the success is viewed as a step toward regenerative medicine for corneal disease.

The patient who underwent the transplant surgery is a woman in her 40s who had almost no vision because of what is technically called “corneal epithelial stem cell deficiency (CESCD).” It is a disease that causes corneal opacity due to an impediment posed to the epithelium, which is on the outermost part of the cornea.

The surgery was performed at the Osaka University Hospital on July 25. The patient was discharged from the hospital on August 23.

### Follow-up Checks to Determine Long-term Success

Professor Nishida said in a news conference: “The operation was finished without incident and there occurred no rejection responses at all. The patient would say she was nearly blind before the transplant, but after the operation, she seemed very happy, saying she now could see things well. From now on, we will continue monitoring to confirm whether her current condition can be maintained.”

There are an estimated 1,000 CESCD patients in Japan. The cornea is a transparent membrane about 11 millimeters across and .5 millimeters in thickness at the center of the eye. Its role is that of a lens for seeing things. When it gets walleyed, one has his or her visual strength lowered, bringing a risk of blindness.

Up to now, corneal transplantation has been the only available remedial procedure for CESCD. Transplant therapy, however, has been plagued by such intractable problems as chronic shortages of cornea donors and many cases of rejection reactions after corneal grafting.

Many rejection reactions tend to occur within one year after a cornea or another organ is transplanted from one individual to another. The iPS cell-derived cells used by Professor Nishida and his team, in contrast, can be produced with stable quality and they have considerably lesser risks of rejection responses compared to cornea transplantation, according to the researchers.

The group of Osaka University researchers plan to verify the safety and efficacy of the iPS corneal transplant procedure by close monitoring of the patient over the coming year, followed by one more year of followup checks.

[GO TO THE NEXT PAGE]

## Looking Toward Practical Use in 5 to 6 Years

The Osaka University team made corneal cells using iPS cells that Kyoto University's Center for iPS Cell Research and Application had created and stockpiled by using blood collected from robust donors with the type of blood that has a history of low immunorejection, meaning there is a low possibility of the foreign matter producing a rejection reaction in the patient.

The corneal cells were cultivated and then processed into a thin circular sheet measuring .05 millimeters in thickness before being transplanted. The researchers say there is a possibility of the iPS-derived treatment method being put into practical use in five to six years, if things proceed smoothly.

Professor Nishida noted, "There are many things not known yet about medical treatment using iPS cells, and we have only conducted the first operation."

He quickly added a note of optimism, saying, "If the safety and effectiveness of the iPS cell-derived transplant is substantiated, prospects of applying our method to patients to whom cornea transplantation is considered unsuitable will be increased, while at the same time eliminating the problem of a dearth of [corneal] donors."

Cells made for transplant purposes from iPS cells are accompanied by risks of becoming cancerous, but Professor Nishida's team, through experiments on animals, has shown that their iPS-derived cells do not cause malignant alterations. In recognition of the test results, the Health, Labor and Welfare Ministry gave the go-ahead to the research team's clinical studies in March 2019.

The breakthrough accomplished by the Osaka University team is the third successful example of regenerative medicine operations in Japan based on iPS-derived cell technology. Earlier operations were conducted by the government-backed Riken institute, which transplanted retina cells into a patient with age-related macular degeneration, and by Kyoto University, which used iPS-cell transplants in the treatment of a Parkinson's disease patient.

Source: **Osaka University Team Does World's First Successful iPS Cell-Derived Corneal Transplant**  
<https://japan-forward.com/osaka-university-team-does-worlds-first-successful-ips-cell-derived-corneal-transplant/>

## i P S 角膜を移植、大阪大が世界初

人工多能性幹細胞（i P S 細胞）から作った目の角膜の細胞を患者に移植する手術を実施したと、大阪大の西田幸二教授らのチームが 29 日、発表した。i P S 細胞を使った角膜移植は世界初で、手術は成功したという。提供者が不足している角膜の病気の再生医療に向けた一歩となる。

移植手術を受けたのは、角膜の最も外側の上皮という部分に障害が生じて角膜が濁る「角膜上皮幹細胞疲弊症」という病気で視力をほぼ失った 40 歳代の女性患者。大阪大付属病院で 7 月 25 日に手術を行い、先週退院した。

角膜上皮幹細胞疲弊症の国内患者数は推定で 1000 人程度。角膜移植が唯一の治療法だが、提供者が慢性的に不足し、拒絶反応も多いなどの課題があった。術後の 1 年間で安全性と有効性を確認した後、さらに 1 年間の追跡調査を行う。

会見した西田教授は「手術は問題なく終了し、拒絶反応も起きていない。患者はほぼ見えない状態だったが、現在はよく見えると喜んでいて。今後は、この状態が維持されるかどうかを確認していく」と話した。

角膜は目の中央にある直径約 11 ミリ、厚さ約 0.5 ミリの透明な膜で、物を見る際のレンズの役割を担う。濁ると視力が低下し、失明につながる。

チームは、拒絶反応が起きにくい免疫タイプを持つ健常者の血液から京都大が作って備蓄している i P S 細胞を使って、角膜の細胞を作製。培養して厚さ 0.05 ミリの円形のシート状に加工し、移植した。

i P S 細胞から作った移植用の細胞はがん化の懸念があるが、チームは動物実験でがん化しないことを確認。厚生労働省が 3 月、臨床研究の実施を承認していた。

i P S 細胞を使う再生医療研究は理化学研究所などが目の網膜の病気、京大がパーキンソン病でそれぞれ移植を実施しており、今回が 3 つ目の病気となった。

出典: i P S 角膜を移植、大阪大が世界初

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