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Preclinical validation of a tissue engineered product consisting in RPE derived from human embryonic stem cells disposed on human amniotic membrane in rats and non-human primates

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In developed countries, retinal degenerative diseases affecting retinal pigmented epithelium (RPE), including age-related macular dystrophy and inherited retinal diseases such as retinitis pigmentosa (RP), are the predominant causes of human blindness worldwide. Despite the scientific advances achieved in the last years, there is no cure for such diseases. In this context, we have developed a cell therapy medicinal product based on our expertise in tissue engineering and in the manipulation of pluripotent stem cells. This novel tissue engineered product (TEP) consists in RPE cells derived from clinical grade human embryonic stem cells disposed on a biocompatible substrate allowing the formation of a 3D functional sheet, suitable for transplantation. After functional validation in a rodent model of RP (Ben M'Barek et al., 2017), our purpose was to test the safety of the surgery and local tolerance in non-human primates (NHP). A specific device was developed in order to (a) embed the TEP in gelatin; (b) allow its transport in a specific medium; and (c) cut the transplant at the right format. Non-human primates (NHP, n=6) were transplanted in one eye (right eye) with the TEP in the macular region. Left eye was left untreated. Retinal integrity and functionality were assessed at different time points through eye fundus, optical-coherence tomography (OCT) and electroretinography (ERG). Inflammation was also assessed using slit lamp. At the end of the experimental period, histological analysis was performed to evaluate the correct location and integration of the TEP within the host retina. We have shown in NHP that our surgical method of implantation was safe and did not provoke any local inflammation or retinal deterioration. Morphologic and histologic studies indicated that RPE cells were integrated into the host retina and were able to interact with photoreceptors. Our results lay the foundations for clinical studies early 2019.

Biography

Christelle Monville has completed her PhD from Créteil University and Post-doctoral studies from Cardiff University. She is the current Professor at Evry's University (France). The objectives of her group (Istem, www.istem.eu) are to develop pre-clinical studies required for the development of human pluripotent stem cells cellular therapy for the treatment of a number of monogenic retinal diseases and disease modeling and drug discovery using patient-specific human induced Pluripotent Stem (hiPS). Recently, her group has successfully developed, under clinically compatible conditions, a tissue-engineered product (TEP) consisting of RPE cells derived from hESCs disposed on a biocompatible substrate. These results are supportive for the initiation of our phase I/II clinical trials to treat RP patients.

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