Reduced corneal nerve fiber length in prediabetes and type 2 diabetes: The Maastricht Study

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Results: We show effective abrogation of HSV-1 replication by targeting gRNAs to essential viral genes. Simultaneous targeting of HSV-1 with multiple gRNAs completely abolished the production of infectious particles from human cells. The CRISPR/Cas9 system was active at limiting replicating virus, but appeared ineffective at targeting a latent HSV-1 infection. However, virus replication upon HSV-1 reactivation from latency was efficiently abrogated.

Conclusion: Our studies indicate that the CRISPR/Cas9 system can be effectively targeted to herpesvirus genomes as a potent prophylactic and therapeutic anti-viral strategy that may be used to impair viral replication in vivo.

Reduced corneal nerve fiber length in prediabetes and type 2 diabetes: The Maastricht Study

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Purpose: In individuals with diabetes, injury to the corneal nerve fibers predisposes to delayed corneal epithelial healing, reduced corneal sensitivity, and corneal erosion. We investigated to what extent a reduction in corneal nerve fiber length (CNFL) is present in individuals with prediabetes or type 2 diabetes (DM2) compared with individuals with normal glucose metabolism (NGM).

Methods: This study was performed as part of The Maastricht Study, an observational prospective population-based cohort study. Using composite images acquired by corneal confocal microscopy, we assessed total CNFL per mm^2 in the subbasal nerve plexus of the cornea in 165 participants (mean age 58 ± 8 years, 44% men, 110 NGM, 25 prediabetes, 30 DM2). Multivariable linear regression was used to assess the association between CNFL and glucose metabolism status, adjusted for age and sex.

Results: In individuals with prediabetes [$\beta = -1.53$ mm/mm^2 (95% CI -3.36 to 0.29), p = 0.10] and in individuals with DM2 [$\beta = -1.78$ mm/mm^2 (95% CI -3.52 to -0.04), p = 0.045], CNFL was reduced as compared with individuals with NGM after adjustment, with a significant linear trend of CNFL reduction with severity of glucose metabolism status (p trend = 0.02).

Conclusion: Major part of the reduction in CNFL observed in individuals with DM2 was already found in individuals with prediabetes. This may result in a delayed corneal healing and an increased risk for corneal complications after surgery.

Long term survival of repeated corneal transplantations – a Dutch registry study

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Purpose: The cornea is the most commonly transplanted tissue worldwide and in the Netherlands. Fuchs' Endothelial Dystrophy (FED) and Pseudophakic Bullous Keratopathy (PBK) are the leading indications for corneal transplantation in the Western world. Although endothelial keratoplasty (EK) revolutionized the surgical treatment of both conditions, graft failure remains a major societal challenge. In the current study we set out to determine and compare re-graft survival based on primary indication and surgical technique.

Methods: Nonrandomized treatment comparison with national registry data (NOTR). All consecutive patients undergoing re-graft for FED or PBK following a previous Penetrating Keratoplasty (PK) or EK between 1994 and 2015 were analyzed, with a maximal follow-up of 5 years. Graft survival was analyzed using Kaplan-Meier survival curves, Log-rank test and Cox regression analysis.

Results: A total of 335 re-grafts were analyzed (re-PK $n = 178$, re-EK $n = 105$, EK after PK, $n = 18$ and PK after EK, $n = 34$). We found a significant increase in the number of re-grafts between 1994 and 2015 (p < 0.001). Post-hoc analysis showed the number of re-grafts did not change between 1994 and 2006 (p = 0.16), but significantly changed between 2007 and 2015 (p = 0.002). Overall 5-year re-graft survival was 60%, and was higher for FED vs. PBK [77% vs. 43%, p = 0.001] but did not differ between re-PK vs. re-EK [52% vs. 79%, p = 0.08]. Univariable Cox regression analysis showed similar two-year re-graft survival for FED vs. PBK [94% vs. 86%, HR 0.46, 95% CI 0.2–1.04, p = 0.06] and re-PK vs.re-EK [90% vs. 92%, HR 1.04, 95% CI 0.42–2.57, p = 0.94], higher two to five-year re-graft survival for FED vs. PBK [77% vs. 43%, HR 0.40, 95% CI 0.20–0.82, p = 0.01] and lower two to five-year re-graft survival for re-PK vs. re-EK [53% vs. 78% HR 4.60 95% CI 1.10–19.30, p = 0.037]. However, multivariate Cox regression analysis with correction for recipient age, donor-gender match and year of re-graft, showed no significant difference in two to five-year re-graft survival for primary indication [FED v. PBK; HR 0.62, 95% CI 0.28–1.38, p = 0.25] and re-graft technique [re-PK vs. re-EK; HR 4.03, 95% CI 0.86–18.87, p = 0.077].

Conclusion: Our results show a significant increase in repeated corneal grafts in the Netherlands between 2007 and 2015. While univariable Cox regression analysis indicates similar early- and better long term re-graft survival for FED vs. PBK and re-EK vs.re-PK, multivariate analysis, indicates similar early and late re-graft survival, irrespective of primary indication, re-graft technique and year of re-graft. Considering the clinical benefits of EK (faster recovery, tectonic stability and lack of suture related complications) it should be considered the procedure of choice for repeated keratoplasty for FED and PBK.

Long-term clinical outcomes following deep anterior lamellar keratoplasty

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Introduction: Deep anterior lamellar keratoplasty (DALK) may be a suitable lamellar keratoplasty technique in patients with corneal stromal pathologies not affecting the endothelium. The main advantage is to prevent long-term endothelial cell loss and to promote graft survival.

Patients and Methods: 71 eyes of 69 patients who received a DALK between November 2002 and April 2016 were included in this retrospective study. Indications for surgery were: keratoconus ($n = 39$ eyes), stromal scar ($n = 20$), herpes simplex virus keratitis ($n = 10$), post-LASIK ectasia ($n = 1$) and corneal stromal dystrophy ($n = 1$). Postoperatively, best (spectacle) corrected distance visual acuity (LogMAR; BDVA), refractive and corneal astigmatism, endothelial cell loss, complications and graft survival were evaluated at 3 months, 6 months, 1 year, 3 years and 5 years.

Results: Mean age at the time of surgery was 39 ± 15 years. Mean follow-up was 3.5 ± 1.6 years; 34 eyes completed a follow-up of 5 years. Ten eyes (14%) were lost to follow-up. Mean BDVA improved from 0.98 ± 0.58 LogMAR preoperatively to 0.19 ± 0.32 at the last follow-up visit. Postoperative mean spherical equivalent and mean