33

TACROLIMUS IMMUNOSUPPRESSION OF NEW ZEALAND WHITE RABBITS FOR AN EXPERIMENTAL MODEL OF OESOPHAGEAL REPLACEMENT.

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Aims: Human stem cells and scaffolds can be used to produce engineered tissues for oesophageal replacement. Human cell-seeded xenografts require recipient immunosuppression to engraft and survive. This study aims to define tolerability and efficacy of tacrolimus immunosuppression in New Zealand White rabbits (NZWR) for the transplantation of engineered constructs.

Methods:
Tolerability
4 NZWR were given tacrolimus subcutaneously (0.08 mg/kg). Induction involved 4 daily doses and maintenance – alternate day dosing for 21 days. Tacrolimus levels, urea, creatinine and full blood count were measured at day 0, 5, 8, 16 and 21. Rabbits were weighed alternate days.
Efficacy
Decellularised scaffolds were seeded with *in vitro* expanded, human oesophageal epithelial cells and cultured for 3 days. 1x1cm sections of seeded scaffold were implanted into a vascularising muscle flap in the neck of 2 immunosuppressed and 2 non immunosuppressed control animals on day 22. Immunosuppressed rabbits continued on tacrolimus. Animals were observed and culled at day 29. Specimens were fixed, sectioned and stained (H&E). *Statistics - Wilcoxon Signed Rank. (SPSS)*

Results: Tacrolimus was well tolerated with no infective complications. Animals showed different degrees of weight loss due to anorexia, but mean weight difference of 3.12 kg (day 0) to 3.04kg (day 22) was not significant (p=0.68). Tacrolimus levels were therapeutic (5-20 µg/L) after induction (day 4 mean 10.2 µg/L) and in 3 animals at day 22, mean 5.05 µg/L. (Fig 1) No significant difference was seen between day 0 and day 22 in levels of urea, creatinine, neutrophil and white cell count.

Animals survived the efficacy study with no local signs of rejection. Histology showed limited epithelial cell survival and differentiation.

Conclusion: NZWR can be safely immunosuppressed with tacrolimus for the implantation of human cell-derived engineered constructs. Further analyses will be required for longer time points to determine whether immunosuppression prevents xenograft rejection.