Introduction

Regenerative medicine holds the promise of fulfilling unmet medical needs, especially in the area of restoration of organ function and organ replacement (transplantation). Development of tissue engineered regenerative medicine products requires a multidisciplinary effort involving cell biology, biomaterials, bioprocess development, engineering, preclinical development, clinical translation, and manufacturing. Strategies should be evaluated early in development with input from Clinical, Regulatory, and Marketing to improve the probability of success. For example, use of autologous cells can provide early entry into the clinic but may present challenges in manufacturing scale-up and not be commercially acceptable. Biomaterials used to formulate biologically active components may involve a more complicated regulatory approval pathway. Tengion has created a unique integrated technology platform to develop regenerative medicine products from research to commercialization.

Applications

Tengion developed its first regenerative medicine product, the Neo-Bladder Augment (NBA), using bladder-derived autologous smooth muscle cells (SMC) and urothelial cells (UC) in an integrated scaffold. Advancements in understanding the regenerative biology of the NBA allowed the next generationNeo-Bladder Replacement product to be composed of only SMC (no UC) on the scaffold, thereby simplifying manufacturing and reducing cost of goods. Further optimization of the bioprocess enabled development of the Neo-Urinary Conduit (NUC) using SMC derived from autologous adipose tissue, avoiding use of bladder cancer tissue as a cell source. The technology platform has been applied to other tubular organs including the Gastrointestinal system. SMC-seeded tubular scaffolds (NGI) have shown promise in augmenting the small intestine in rats. The platform technology has also been successfully extended to solid organ regeneration in the Neo-Kidney Augment (NKA). Selected regenerative renal cells (SRC) provided a significant regenerative stimulus in rodent models of chronic kidney disease, resulting in delayed disease progression, preservation of functional renal mass, and reduced disease-related mortality.

Neo-Urinary Conduit (NUC)

A tissue engineered Neo-Urinary Conduit provides an alternative to using gastrointestinal tract in patients who require a urinary diversion post-cystectomy. Use of GI tissue requires GI tissue resection and exposes gut mucosa to urine, leading to multiple acute and chronic complications, including GI and metabolic derangements, complications that a NUC capable of regeneration would be expected to reduce.

Neo-Gastrointestinal Augment (NGI)

A tissue engineered Neo-Gastrointestinal augment provides patients suffering from small bowel syndrome and related diseases an alternative to lengthening of small bowel or transplantation with their associated complications and poor quality of life including lifelong immunosuppression. An NGI augment capable of regeneration presents a viable option that would be expected to provide a functional organ and reduce complications.

Neo-Kidney Augment (NKA)

A Neo-Kidney Augment product using selected regenerative renal cells and biomaterials can be used for catalyzing kidney tissue regeneration to restore renal function thereby delaying or eliminating the need for dialysis and transplant.

Conclusions

- Neo-Urinary Conduit seeded with autologous SMC sourced from adipose tissue was capable of establishing a patent incontinent urinary diversion for post-cystectomy management of urine elimination in pigs and is currently being evaluated in Phase I clinical trials.
- Neo-Gastrointestinal Augment product prototypes implanted into small intestines of Lewis rats elicited a functional regenerative response.
- Neo-Kidney Augment product prototype implantation into healthy rat kidneys was well-tolerated and elicited neo-kidney tissue regeneration at site of implantation.
- Implantable regenerative medicine products developed using tissue engineering principles can be used in reconstructing tubular organs (e.g., bladder, GI) and solid organs (e.g., kidney).