

Final Report of my TUF fellowship

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Project Title:

Developing pelvic floor repair materials which can stimulate ingrowth of new blood vessels after implantation

Supervisors:

Prof Christopher Chapple

Prof Sheila MacNeil

Host Institution:

University of Sheffield, United Kingdom

Department of Materials Science Engineering

Department of Urology

The aim of my research was to develop the new generation of synthetic materials to be used in pelvic floor repair in women with stress urinary incontinence and pelvic organ prolapse. These materials need to be designed so that they can stimulate a favourable wound healing and promote rapid angiogenesis while providing good structural support. The clinical need for such materials is now increasingly more recognized, as the complications associated with use of current vaginal mesh has come to public attention. This issue has been covered on a BBC television programme twice in the last 6 months [1] and also made the headlines after a parliamentary debate was held in July 2017 [2]. In the UK one in ten women will need a pelvic floor repair surgery during their lifetime for most of which a synthetic material will be needed to reinforce weakened tissues. Thus better synthetic materials that can integrate better into patients tissues are urgently needed to replace the vaginal mesh in pelvic floor.

In this project I worked on a Poly-L-lactic acid (PLA) polymer which is a highly biocompatible material that is commonly used in biomedical applications. I have constructed the scaffolds using a technique called 'electrospinning' which allowed fabrication of scaffolds with micro/nano sized fibres to mimic the organization of the natural tissue matrix. The resulting synthetic material, the electrospun PLA with random fibres, had mechanical properties close to those of healthy vaginal tissues. I have also functionalized these materials by incorporating drugs into them. I have used the female sex hormone, estradiol, in my scaffolds as it plays the most crucial role in maintaining normal structure and function of pelvic tissues in women. Additionally estradiol is known to stimulate new blood vessel formation.

My results demonstrated that estradiol can effectively be integrated into the synthetic materials without compromising mechanical properties and that estradiol can be gradually released from these materials to stimulate new blood vessels formation and a favourable tissue integration. The next step to take this research forward is to evaluate the estradiol releasing PLA scaffold in an appropriate pre-clinical model. The sheep model appears to be the most appropriate animal model to evaluate implants used in vaginal surgery. A sheep has a near clinical size vagina with 3 levels of supporting structures just like in humans.

With regards to my professional development as clinical academic, these studies have made a huge contribution towards completion of my PhD and I am hoping to submit my PhD thesis by December 2018.

Publications within the duration of TUF fellowship (The contribution of TUF has been acknowledged);

1. Mangir N, Hillary CJ, Chapple CR, MacNeil S: **Oestradiol-releasing Biodegradable Mesh Stimulates Collagen Production and Angiogenesis: An Approach to Improving Biomaterial Integration in Pelvic Floor Repair.** European Urology Focus 2017.
2. Eke G*, Mangir N*, Hasirci N, MacNeil S, Hasirci V: **Development of a UV crosslinked biodegradable hydrogel containing adipose derived stem cells to promote vascularization for skin wounds and tissue engineering.** Biomaterials 2017; 129: 188-198. (*joint first authors)
3. Mangir N, Turkeri L: **Stem cell therapies in post-prostatectomy erectile dysfunction: a critical review.** Can J Urol 2017; 24(1): 8609-8619.

Presentations made within the duration of TUF fellowship;

1. Medical School Research Day, University of Sheffield, 16th June 2017
Title: **An estradiol releasing, proangiogenic mesh can improve biomaterial integration in pelvic floor repair**
2. The Canadian Urology Association/ European Association of Urology International Exchange Programme Meeting, 20th March 2017, Royal Hallamshire Hospital, Sheffield.
Title: **Tissue engineering applications in urology**
3. EPSRC funded GRCF workshop on Affordable Healthcare in Pakistan - Developing Biomedical Materials for Clinical Impact, 9-13th Jan 2017, the Leopold Hotel Sheffield.
Title: **Developing Pelvic Floor Support Materials For Women With Stress Urinary Incontinence and Pelvic Organ Prolapse**
4. 3rd National Congress of Turkish Urological Surgery Association, 2-6 November 2016, Antalya-Turkey.
Title: **Take Home Messages in Functional Urology**
5. COST ReST Meeting – Biomaterials, Biomechanics of the Lower Pelvic Floor and Surgical Interventions. Holiday Inn Royal Victoria Hotel, Sheffield UK, 27-28 November 2016.
Title: **Developing Pelvic Floor Support Materials For Women With Stress Urinary Incontinence and Pelvic Organ Prolapse**

References

1. **The Victoria Derbyshire programme** [<https://www.youtube.com/watch?v=ebmjbcouHNY>]
2. Devlin H: **Senior doctors call for public inquiry into use of vaginal mesh surgery in UK.** In: *The Guardian.* 2017.