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From Cell Biology to Tissue Engineering

An immunohistochemical study of cytokeratins distribution of the human adult male and female urethra

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Summary. Surgical treatment of diseases affecting long urethral areas represents a challenge in urology. Recent developments of tissue-engineered urethral substitutes represent a hope for patients. However finding an ideal tissue source for urethral reconstruction first requires proper understanding of the native human urethra physiology and a deep knowledge of the histological and molecular features of the native human urethra. Here we present a comprehensive characterization of male and female urethra by histological, histochemical and immunohistochemical methods with a panel of 15 antibodies. The results demonstrated that the histology of the male and female urethra depend on the area where the sample is taken along its length. Proximal areas of male and female urethra have differential expression of the epithelial basal and suprabasal layer markers CK14 and CK10 which distinguished the prostatic/membranous and proximal female urethra from the bulbar/penile and distal female areas of the urethra. The distal male (penile) and female may be further divided by the distinct expression pattern of CK19. On the other hand, the expression of CK5/6 and CK19 also make a distinction of the proximal and distal female urethra. These results should facilitate a more informed selection of donor graft tissues for urethral replacement. Besides, novel bioengineered urethral tissue approaches should take into account the characterization of the different areas of the urethra presented in this work.

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Introduction

The urethra is a tubular structure that connects the urinary bladder to the urinary meatus. The male urethra, with a length of about 18-20 cm, is divided into a distal (penile and bulbar) and a proximal (membranous and prostatic) portion (Schenkman and Manger, 2013; del Pozo-Jimenez et al., 2014). The urethra in females is about 4 cm and it may be divided as distal (near to the meatus) and proximal (near to the bladder) (Schenkman and Manger, 2014).

Surgical treatment of diseases affecting long urethral areas is still a challenging problem in urology. Current clinical therapies are based on the utilization of autologous grafts (McAninch, 2014). Various tissues such as preputial mucosa, genital and extragenital skin, buccal mucosa, lingual mucosa, small intestinal submucosa, and bladder mucosa have been proposed for urethral reconstruction (Hampson et al., 2014). However several problems arise when using donor tissue: i) limited donor tissue supply, ii) problems of morbidity in the area of tissue harvesting and damage to the tissue to be grafted, iii) deterioration of the grafted tissue at long term, and iv) healing process of grafted tissue is not equal in all patients and may suffer fibrosis before the final urethral closure proceeds (Barbagli et al., 1995; Mundy, 1995; Dublin and Stewart, 2004). For all of these reasons, better substitutes for urethral