

Chapter 44

Designing Biomedical Stents for Vascular Therapy: Current Perspectives and Future Promises

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ABSTRACT

The breakthrough technologies of stent have revolutionized the medical industry, particularly in the field of percutaneous coronary interventions and other vascular therapies. However, recent concerns of late stent thrombosis and in-stent restenosis have rekindled an interest in developing new and improved therapeutic stent devices. A multidisciplinary approach of regeneration therapy, biomedicine, and nanotechnology is the next frontier for this. The chapter presented here gives a comprehensive overview of the evolving stent technologies for efficient vascular tissue therapy and articulates the potential of these technologies to design the next generation of therapeutic stent. In addition, the chapter also encompasses upcoming technologies to develop bioactive stents for efficient healing and remodeling of damaged local vascular biology.

INTRODUCTION

Coronary artery disease, caused by atherosclerosis, is one of the leading causes of death due to disease in the world. Most of these patients undergo initial angioplasty and stenting to re-establish coronary blood supply prior to considering bypass surgery (Ghosh, Schistek, & Unger, 2004; Windecker, et al., 1999; Paul, Elhayek, Shum-Tim, & Prakash, 2010). Although stents are excellent in providing

early clinical benefits, they have several serious disadvantages resulting from limited biocompatibility, stent blockage, and In-Stent Restenosis (ISR) (Bittl, 1995). The tunica intima consisting of endothelial cells and the tunica media, consisting of primarily smooth muscle cells mainly plays important role in the restenosis process. Following vascular injury due to stenting, the body response by proliferating the nearby smooth muscle cells similar to scarring. Thus, there occurs a vessel lumen narrowing due to excessive neointimal proliferation. Other cells are also recruited in the

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injured region including various inflammatory cells, such as macrophages, T-cells, and a small number of B-cells (Farb, Weber, Kolodgie, Burke, & Virmani, 2002).

Several approaches have been used to improve stent design and durability, such as the use of covered stents to improve biocompatibility of the stent material and intracoronary radiation to inhibit inflammation and proliferation of smooth muscle cells, which cause ISR. Radiation therapy, although effective, has potential side effects and requires specialized infrastructure and is not widely available in many centers, whereas coated stents have not been completely successful in eliminating the problem (Hehrlein, 2002). The introduction of Drug Eluting Stents (DES) has been perceived as a significant improvement in the existing stent design (Degertekin, et al., 2003; Liistro, et al., 2002; Ko, et al., 2009; Lee, et al., 2009). The drugs used are mostly those that target the issues related to the inflammation and subsequent proliferation of smooth muscle cells. The direct use of these pharmacological agents is limited by the problems associated with drug washout and the inadvertent effects on non-target cells, as well as the very high costs. Benefits from Bare-Metal Stents (BMS) have not been conclusively demonstrated in recent clinical trials. Acute thrombosis of drug-eluting stents has been reported alarmingly in the clinical settings (Dehmer & Smith, 2009; Fitchett & Kutryk, 2008; Simon & Jozic, 2008). Therefore, there is an urgent need to develop more biocompatible stents that can offer better long-term results. Several reports in the literature described the use of gene therapy approaches using either genes promoting endothelial cell growth or factors inhibiting smooth muscle cell proliferation (Isner, Vale, Symes, & Losordo, 2001; Yla-Herttuala & Martin, 2000). Naked plasmid DNA or liposome mediated plasmid delivery has been used experimentally, but is limited by the poor uptake and transient expression (Rutanen, Markkanen, & Yla-Herttuala, 2002; Yla-Herttuala & Martin, 2000). Several viral vectors have been tried since

then to overcome the problem of poor transfection efficiencies, but its major disadvantages include poor biosafety profile, immunological, and inflammatory reactions. This book chapter illustrates the current status of stent technology to treat coronary stenosis and explores the rapid shift of research and clinical interests from bare metal to pharmacological and bioengineered stents for future generations of stents.

ETIOLOGY OF VASCULAR STENT RELATED PROBLEMS

Coronary angioplasty followed by stenting is one of the commonly used interventional procedures for the treatment of coronary artery disease (Hoffmann & Mintz, 2000). A major long-term complication of this treatment is ISR, which occurs at the site of the atherosclerotic lesion following stenting (Fischman, et al., 1994; Serruys, et al., 1994). This pathological recurrence is often the result of endothelial cell lining damage (Braun-Dullaues, Mann, & Dzau, 1998; Serruys, et al., 1994). The vascular endothelium provides a non-thrombogenic physical and biochemical barrier which plays an important role in maintaining the structure and normal function of the blood vessels (Folland, Hartigan, & Parisi, 1997). In addition, various autocrine factors produced by these endothelial cells help in controlling the vessel tone and vascular wall remodeling (Shirota, He, Yasui, & Matsuda, 2003). Endothelial dysfunction is one of the mechanisms implicated in the subsequent development of atherosclerosis which then promotes the whole process of stenosis at the site by various mechanisms including inflammation and proliferation of smooth muscle cells (Ross & Glomset, 1973). Another frequently noted medical complication related to stents is thrombosis. Thrombosis could be attributed to various factors including procedure related factors, patient- and lesion-related factors, antiplatelet therapy, and thrombogenicity of the stent. Procedural risk

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