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(54) **HYDROGEL BIOSCAFFOLDINGS AND BIOMEDICAL DEVICE COATINGS**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,512,569	A	6/1950	Saffir
3,144,868	A	8/1964	Jascalevich
3,584,624	A	6/1971	de Ciutiis
3,780,733	A	12/1973	Martinez-Mangor
3,804,097	A	4/1974	Rudie
3,890,976	A	6/1975	Bazell et al.
4,141,973	A	2/1979	Balazs
4,617,186	A	10/1986	Schafer
4,794,931	A	1/1989	Yock
4,818,291	A	4/1989	Iwatsuki et al.
4,842,590	A	6/1989	Tanabe et al.
5,000,185	A	3/1991	Yock
5,024,234	A	6/1991	Leary et al.
5,026,350	A	6/1991	Tanaka et al.
5,049,130	A	9/1991	Powell
5,092,848	A	3/1992	DeCiutiis
5,100,185	A	3/1992	Menke et al.
5,109,859	A	5/1992	Jenkins
5,116,317	A	5/1992	Carson et al.
5,128,326	A	7/1992	Balazs et al.
5,171,217	A	12/1992	March et al.
5,202,745	A	4/1993	Sorin et al.
5,203,338	A	4/1993	Jang
5,242,427	A	9/1993	Bilweis
5,270,300	A	12/1993	Hunziker
5,291,267	A	3/1994	Sorin et al.
5,306,250	A	4/1994	March et al.
5,321,501	A	6/1994	Swanson et al.
5,328,955	A	7/1994	Rhee et al.
5,336,252	A	8/1994	Cohen
5,354,279	A	10/1994	Hofling
5,365,325	A	11/1994	Kumasaka et al.
5,372,138	A	12/1994	Crowley et al.
5,380,292	A	1/1995	Wilson
5,419,777	A	5/1995	Hofling et al.
5,437,632	A	8/1995	Engelson
5,455,039	A	10/1995	Edelman et al.
5,459,570	A	10/1995	Swanson et al.
5,464,395	A	11/1995	Faxon et al.
5,465,147	A	11/1995	Swanson
5,485,486	A	1/1996	Gilhousen et al.
5,499,630	A	3/1996	Hiki et al.
5,516,532	A	5/1996	Atala et al.
5,540,912	A	7/1996	Roorda et al.
5,546,948	A	8/1996	Hamm et al.
5,554,389	A	9/1996	Badylak et al.
5,575,815	A	11/1996	Siepian et al.
5,580,714	A	12/1996	Polovina
5,580,856	A	12/1996	Prestrelski et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP	0331584	9/1989
EP	0835667	4/1998

(Continued)

OTHER PUBLICATIONS

Agocha A. et al. "Hypoxia regulates basal and induced DNA synthesis and collagen type I production in human cardiac fibroblasts: effects of transforming growth factor-beta 1, thyroid hormone, angiotensin II and basic fibroblast growth factor," *J. Mol. Cell. Cardiol.* 29(8): 2233-2244. (Apr. 1997).

(Continued)

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(57) **ABSTRACT**

Bioscaffoldings formed of hydrogels that are crosslinked in situ in an infarcted region of the heart (myocardium) by a Michael's addition reaction or by a disulfide bond formed by an oxidative process are described. Each of the bioscaffoldings described includes hyaluronan as one of the hydrogel components and the other component is selected from collagen, collagen-laminin, poly-1-lysine, and fibrin. The bioscaffolding may further include an alginate component. The bioscaffoldings may have biofunctional groups such as angiogenic factors and stem cell homing factors bound to the collagen, collagen-laminin, poly-1-lysine, or fibrinogen hydrogel component. In particular, the biofunctional groups may be PR11, PR39, VEGF, bFGF, a polyarginine/DNA plasmid complex, or a DNA/polyethyleneimine (PEI) complex. Additionally, the hydrogel components may be injected into the infarct region along with stem cells and microspheres containing stem cell homing factors. The bioscaffolding may be formed on a stent or a cardiac medical device.

6 Claims, 31 Drawing Sheets