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(54) **STEM CELL MOBILIZATION AND TISSUE REPAIR AND REGENERATION**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,114,926	A	5/1992	Frindel et al.	
5,939,391	A *	8/1999	Tsyrlova	A61K 38/42 514/13.5
6,610,654	B2 *	8/2003	Tsyrlova	A61K 38/42 424/85.4
8,080,524	B2	12/2011	Bakala et al.	
2003/0104984	A1	6/2003	Tsyrlova et al.	
2007/0098680	A1	5/2007	Kawabe et al.	
2007/0259819	A1	11/2007	Bakala et al.	
2010/0041147	A1	2/2010	Tsyrlova et al.	
2011/0104175	A1	5/2011	Bernstein et al.	
2011/0172155	A1	7/2011	Crockford et al.	
2014/0088006	A1	3/2014	Tsyrlova et al.	
2015/0111238	A1 *	4/2015	Tang	G01N 33/6848 435/23

FOREIGN PATENT DOCUMENTS

WO	9728183	A1	8/1997
WO	9736922	A1	10/1997
WO	2004091661	A1	10/2004
WO	2012159044	A1	11/2012

OTHER PUBLICATIONS

Machine translation of WO 2004/091661, pp. 1-8, Oct. 2004.*
UniProt Direct Submission P19104. Hemoglobin subunit alpha. Jan. 23, 2007. [Retrieved from the Internet Jan. 10, 2014: <http://www.uniprot.org/uniprot/P19104.txt?version=70>]; amino acids 43-55.
Azizi et al., "Acute Angiotensin-converting Enzyme Inhibition Increases the Plasma Level of the Natural Stem Cell Regulator N-Acetyl-Seryl-Aspartyl-Lysyl-Proline", J. Clin. Invest., 97(3): 839-844, Feb. 1996.
Myohanen et al., "Prolyl oligopeptidase induces angiogenesis both in vitro and in vivo in a novel regulatory manner", Br. J. Pharmacol., 163: 1666-1678, 2011.
Shen et al., "The peptide network regulated by angiotensin converting enzyme (ACE) in hematopoiesis", Cell Cycle, 10 (9): 1363-1369, 2011. <http://dx.doi.org/10.4161/cc.10,9.15444>.
Claims in Application No. 14/118,313 as amended Nov. 23, 2015.

* cited by examiner

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(57) **ABSTRACT**

Stem cells are mobilized from bone marrow by administering an amount of Phe-Pro-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Ser-Asp-Lys-Pro (SEQ ID NO: 2) or Phe-Ala-His-Phe-Asp-Leu-Ser-His-Gly-Ser-Ala-Gln-Val-Ser-Asp-Lys-Pro (SEQ ID NO: 3) effective to mobilize the stem cells. This is useful for promoting bodily tissue regeneration in a patient in need of tissue regeneration treatment. Alternatively, the mobilized stem cells can be collected for transplant.

18 Claims, 16 Drawing Sheets