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Dopamine-loaded blood exosomes targeted to brain for better treatment of Parkinson's disease

Mengke Qu, Qing Lin, Luyi Huang, Yao Fu, Luyao Wang, Shanshan He, Yu Fu, Shengyong Yang, Zhirong Zhang, Ling Zhang, Xun Sun



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3 Mengke Qu,<sup>1</sup> Qing Lin,<sup>1</sup> Luyi Huang,<sup>2</sup> Yao Fu,<sup>1</sup> Luyao Wang,<sup>1</sup> Shanshan He,<sup>1</sup> Yu Fu,<sup>1</sup> Shengyong  
4 Yang,<sup>2</sup> Zhirong Zhang,<sup>1</sup> Ling Zhang,<sup>3,\*</sup> Xun Sun,<sup>1,\*</sup>

5 1, Key Laboratory of Drug Targeting and Drug Delivery Systems of Ministry of Education, West  
6 China School of Pharmacy, Sichuan University, Chengdu, 610041, China

7 2, The State Key Laboratory of Biotherapy/Collaborative Innovation Center, West China Hospital,  
8 Sichuan University, Chengdu, 610041, China

9 3, College of Polymer Science and Engineering, Sichuan University, Chengdu, 610065, China

10 \*Corresponding author. E-mail address: [femcivrogner@gmail.com](mailto:femcivrogner@gmail.com) (Ling Zhang);

11 [sunxun@scu.edu.cn](mailto:sunxun@scu.edu.cn) (Xun Sun)

12 **Abstract**

13 Parkinson's disease (PD), one of the most common movement and neurodegenerative  
14 disorders, is challenging to treat, largely because the blood-brain barrier blocks passage of most  
15 drugs. Here we find exosomes from blood showing natural brain targeting ability which involved  
16 the transferrin-transferrin receptor interaction. Thus, we develop a biocompatible platform based on  
17 blood exosomes for delivering drugs across the blood-brain barrier. Blood exosomes show sizes  
18 between 40-200 nm and spherical morphology, and dopamine can be efficiently loaded into blood  
19 exosomes by a saturated solution incubation method. Further *in vitro* and *in vivo* studies  
20 demonstrates these exosomes successfully delivered dopamine to brain, including the striatum and  
21 substantia nigra. Brain distribution of dopamine increased more than 15-fold by using the blood  
22 exosomes as delivery system. Dopamine-loaded exosomes show much better therapeutic efficacy in

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