Translational Research of Hemoglobin-vesicles as a Transfusion Alternative

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A fluid of hemoglobin-vesicles, Hb-V, is being developed as a transfusion alternative that comprises concentrated particle dispersion ([Hb] = 10 g/dL, occupied particle volume = 40%, particle size = 250 nm) with physicochemical characteristics comparable to those of blood. Encapsulation of a concentrated Hb solution with phospholipid vesicles can shield the toxic side effects of cell-free Hb, such as extravasation, NO scavenging inducing vasoconstriction and hypertension, and oxidative damage to the vascular wall. For facilitating translational research of Hb-V, we study efficient production methods, analytical methods, *in vivo* safety and efficacy of Hb-V (**Figure 1**).

Recent results include (i) A new Hb encapsulation procedure has been established that enables a high yield and efficiency of Hb encapsulation for scale-up. (ii) Ferric metHb in Hb-V can be effectively reduced to the ferrous form in blood circulation by using the electron energies produced by RBC glycolysis via transmembrane electron mediators, phenothiazines, including methylene blue [1,2]. (iii) ADME of Hb-V and its minor effects on immunological system and hyperlipidemic condition are clarified [3,4]. (iv) Hb-V showed efficacies as a resuscitative fluid for uncontrolled hemorrhagic shock [5] and as a perfusion fluid for storing an amputated rat hind limb for replantation [6]. (v) Injection of CO-bound Hb-V is effective not only for resuscitation from hemorrhagic shock [7] but also for the treatment of idiopathic pulmonary fibrosis [8], presumably by the released CO that reduces generation of ROS. We also clarified that Hb-V can rescue placental hypoxia and improve fetal development in the rat pre-eclampsia model [9].

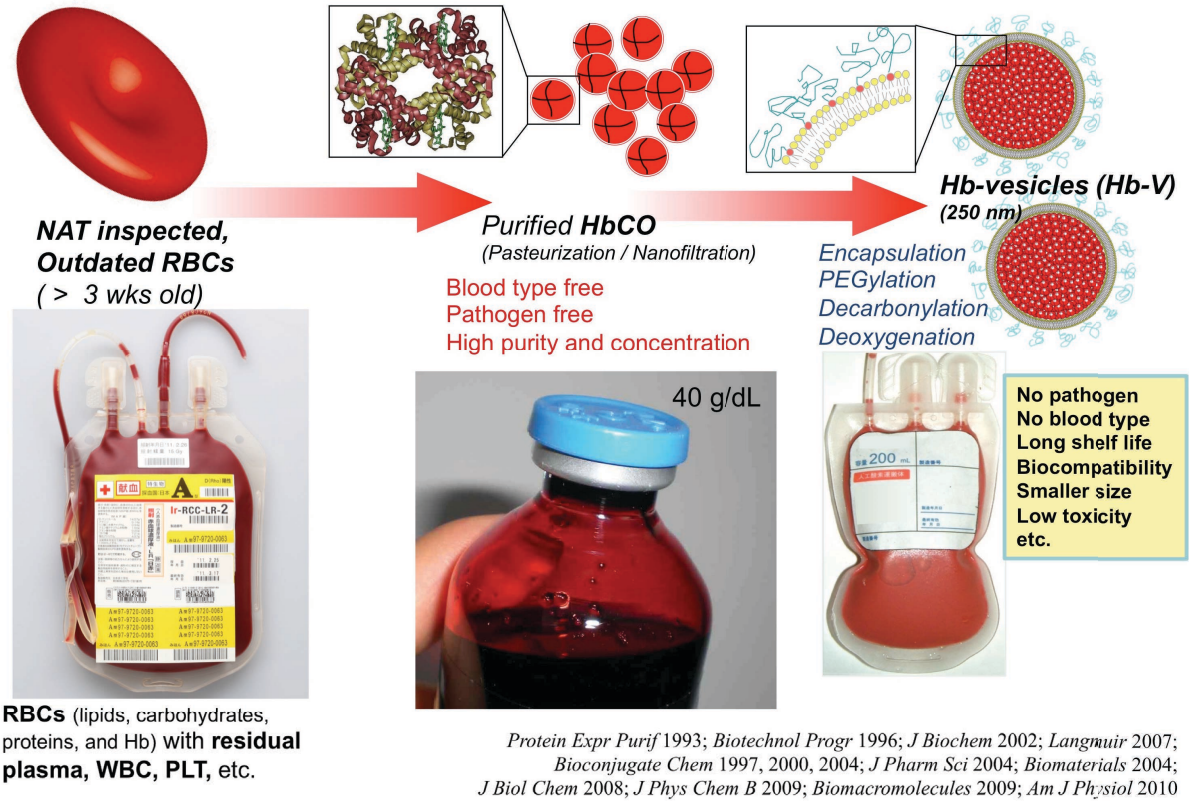

Figure 1. From biological to artificial red cells

Through establishing the production method and confirmation of HbV safety and efficacy step-by-step, we prepare for the next stages of translational research. From the fiscal year 2015 this research has been supported by Japan Agency for Medical Research and Development (AMED) [10].

We strongly wish to find a partner company to develop Hb-V together aiming at eventual realization of Hb-V. Please contact us if you are interested in our project [11].

Keywords: Blood Substitutes, Artificial Red Cells, Oxygen Carrier, Liposomes, Hemoglobin

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