Synthesis of Hemoglobin Oligomer Capable of Structural Changes in Response to O_2 Association and Dissociation

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Considerable interest has arisen recently in protein assemblies as functional biomaterials. We have recently reported a linear coordination polymer of recombinant hemoglobin [rHb(βC93A/βK120C)].[1] Hb consists of an $\alpha_2\beta_2$ tetramer with dissociation equilibrium to two αβ dimers. Hb Kansas [rHb(βN102T)] has unique transformation. The dissociation is promoted by O_2 association because Asn-βN102 which stabilizes the quaternary structure of oxy Hb is lacked in the protein. In this paper, we report synthesis and dynamic structural changes of a rHb(βC93A/βN102T/βK120C) [rHb(2)] oligomer in response to O_2 association and dissociation (Fig. 1).

First, we expressed rHb(di-α/βC93A/βK120C) [rHb(1)] using *Pichia* yeast[2] and combined rHb(1) with a bismaleimide crosslinker, yielding a robust rHb(1) oligomer. Size exclusion chromatography and dynamic light scattering indicated that the oligomer consists of average 8 rHb(1) molecules. In contrast, combining rHb(2) with the same crosslinker yielded $XL[\alpha\beta(2)]_2$. Interestingly, $XL[\alpha\beta(2)]_2$ was polymerized under anaerobic condition to form the similar oligomer made of average 8 rHb(2) molecules. Upon addition of O_2, the oligomer dissociated to $XL[\alpha\beta(2)]_2$. The structural changes were observed reversibly for three cycles. The rHb(2) oligomer is an unique functional biomaterial capable of structural changes in response to O_2 association and dissociation.

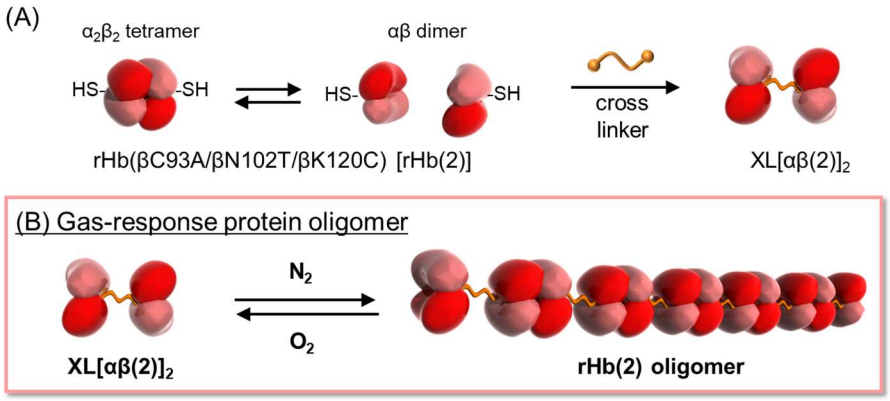

Fig. 1 (A) Synthetic scheme and (B) structural changes of the rHb(2) oligomer.

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2) Y. Morita, A. Saito, J. Yamaguchi, T. Komatsu, *RSC Chem. Biol.* **2020**, *1*, 128

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