Self-Oligomerization of Pigeon Iron-Sulfur Protein Induced by Magnetic Field

Pigeon can recognize geomagnetic information to return home from distances 500 ~ 1,000 km or more. Pigeon iron–sulfur (Fe–S) cluster assembly 1 homolog (clISCA1) is one of the target proteins for research into the magnetoreception mechanism of animals. By using the small angle X-ray scattering (SAXS) technique with a magnetic device, we revealed that clISCA1 molecules self-oligomerize to form columnar oligomers depending on the magnetic field condition such as magnetic flux density. Pigeon may be able to recognize not only the direction but also the strength of the magnetic field, if clISCA1 molecules contribute to the magnetoreception.

Magnetoreception is a sense used by many animals to perceive information about the magnetic field, which is important for behaviors such as migration, homing, feeding, and breeding. In some animal species, cryptochrome (CRY) in the retinal cells can act as a quantum sensor to detect the inclination angle of the geomagnetic field [1]. A recent study reported that pigeon clISCA1 potentially interacts with CRY [2], but its role in magnetoreception is still unclear. To gain insight into the function of clISCA1 in magnetoreception, we investigated the magnetic field effects on the structure and molecular behavior of clISCA1 using SAXS method with an Nd-Fe-B permanent magnetic circuit device [3] optimized for BL-10C.

The scattering curves ($I(q)$s) (Fig. 1(A)) and the distance distribution functions ($P(r)$s) (Fig. 1(B)) obtained by SAXS measurements showed that the increase of the magnetic flux density induced the association of clISCA1 molecules to form the columnar oligomer. Also, the maximum diameter (D_{max}) of the clISCAS1 columnar oligomer estimated from $P(r)$s gradually increased with the magnetic flux density, whereas the cross-section radius of gyration (R_c) estimated from $I(q)$ was almost constant (Fig. 1(B)). From these results, it was demonstrated that the clISCA1 columnar oligomer uniaxially elongated by applying an external magnetic field [4].

The Fe–S cluster assembly 1 homolog was originally known as a protein that transports Fe–S clusters *in vivo*. In the case of pigeon, the clISCA1 oligomer can bind the [2Fe–2S] and [3Fe–4S] clusters [5]. When these Fe–S clusters were removed from clISCA1 with chelating agents, the clISCA1 did not respond to the external

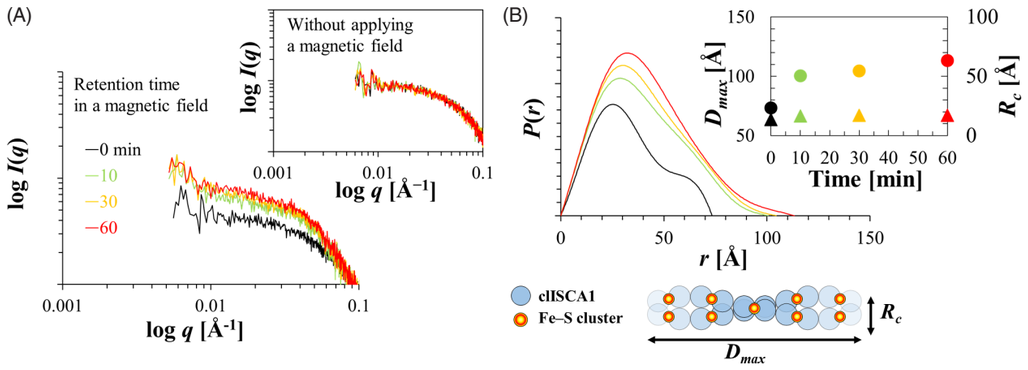

Figure 1: (A) Magnetic response of clISCA1. SAXS curves obtained by applying a 180 mT magnetic field to 6.9 mg/mL clISCA1 solution are shown as an example. The inset shows a control without applying a magnetic field. **(B)** $P(r)$ functions obtained from SAXS curves shown in Fig. 1(A). The inset shows the D_{max} (circles) and R_c (triangles) of the clISCA1 columnar oligomer depending on the magnetic field application time.

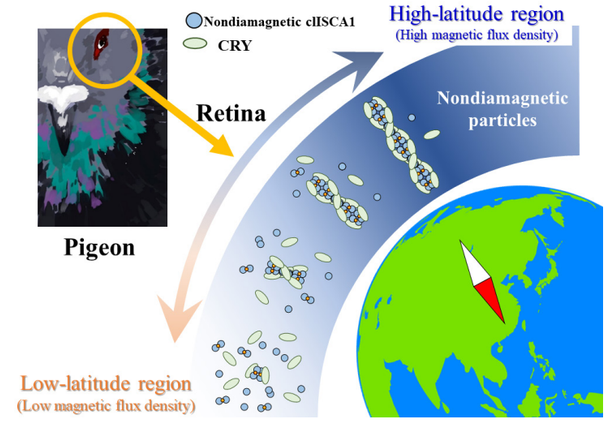

Figure 2: A schematic drawing of the predicted mechanism of CRY/clISCA1 complexation in the geomagnetic field, assuming that clISCA1 molecules are in the nondiamagnetic states.

magnetic field and did not form the columnar oligomer. These properties indicate that Fe–S cluster enhances the magnetic response of clISCA1 and acts as a connector between clISCA1 molecules in the clISCA1 columnar oligomer.

The magnetic features of Fe–S clusters depend on their redox states. For example, $[2Fe–2S]^{1+}$ and $[3Fe–4S]^{0}$ become paramagnetic states. Conversely, $[2Fe–2S]^{2+}$ and $[3Fe–4S]^{1+}$ become a diamagnetic state. Therefore, the magnetic feature of clISCA1 columnar oligomer would be regulated by the overall balance of [2Fe–2S] / [3Fe–4S] mixing binding and their redox states. When an external static magnetic field is applied to a solution, nondiamagnetic particles (ferromagnetic, ferrimagnetic, superparamagnetic, paramagnetic and antiferromagnetic particles) in a solution gather at high magnetic flux density locations. Accordingly, the clISCA1 columnar oligomers formed at high magnetic flux density locations have a nondiamagnetic feature.

Controlling the magnetic flux density in the vicinity of the geomagnetic field (<100μT) is technically difficult, but the length of the clISCA1 columnar oligomer certainly depends on the magnetic flux density. If clISCA1 molecules in retinal cells respond to the geomagnetic field, the non-diamagnetic clISCA1 columnar oligomers may elongate in high magnetic flux density locations such as high-latitude regions of the Earth (Fig. 2). As a result, the amount of CRYs anchored to the clISCA1 columnar oligomers would increase, leading to an increase in the amount of CRYs functioning as magnetic field sensors. Pigeon may be able to perceive not only the inclination angle but also the magnetic flux density reflecting the latitude, when clISCA1 acts as a scaffold for CRY.

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BEAMLINE

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