Development of a Hyperpolarized Molecular Probe for Aminopeptidase N Activity Applicable *in vivo*

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Magnetic nuclear resonance imaging (NMR/MRI) is a powerful method to visualize molecular information *in vivo*. However, its application is strongly limited because of its low sensitivity. To overcome this limitation, hyperpolarization techniques have been studied vigorously. Dynamic nuclear polarization (DNP) is one of the most well-developed methods.[1]

In contrast to the high potential of DNP-MRI, chemical probes applicable *in vivo*, such as [1-^{13}C]pyruvate are very few. This is because there is no general guideline for designing DNP-MRI molecular probes applicable *in vivo*. To establish broadly useful design guidelines and expand the scope of DNP-MRI probes, it is necessary to provide examples of the development of DNP-MRI molecular probes applicable *in vivo* through rational molecular design. Various requisites must be satisfied so that DNP-MRI molecular probes function *in vivo*. Generally, the most important factor is hyperpolarized lifetime. In addition, when aiming at enzymatic activities, enzymatic reaction rate, the difference of chemical shift values, and selectivity to the target enzyme are important. Therefore, designing probes that satisfy all these requisites is highly challenging.

Herein, we report the development of DNP-MRI molecular probes applicable *in vivo* targeting aminopeptidase N activity by precise molecular design.[2] We carefully considered what is needed for molecular probes to function *in vivo* as DNP-MRI molecular probes and precisely designed molecular structures from various aspects such as organic chemistry, biochemistry, calculation, and nuclear physics (Figure 1).

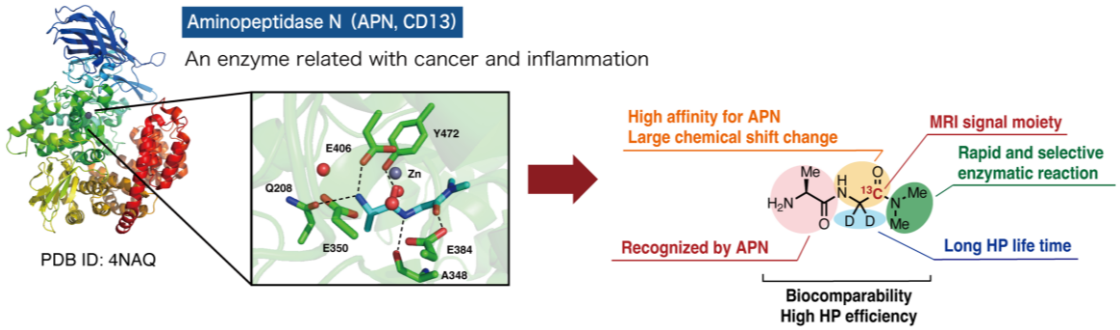

Figure 1. Development of a DNP-MRI molecular probe for aminopeptidase N (APN) activity through precise molecular design.

References

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