Experimental report

02/06/2020

Proposal: 8-04-852 **Council:** 10/2018

Title: Neutron spin echo spectroscopy study of nanoscale dynamics of the alpha-catenin/beta-catenin complex

Research area: Biology

This proposal is a resubmission of 8-04-837

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Samples: PROTEIN
deuterated or natural alpha-catenin/beta-catenin complex

Instrument	Requested days	Allocated days	From	To
IN15	7	7	28/06/2019	05/07/2019

Abstract:

Cell-cell adhesion is essential for the development, function, maintenance, and transmission of force in the tissues of higher organisms. The multidomain proteins alpha-catenin and beta-catenin are key components of the cell-cell adherens junction complex. Despite the importance of the catenin complex in the adherens junction, the mechanism by which the catenin complex connects the adherens junction to the actin cytoskeleton remains to be determined. A hypothesis is that the catenin complex is the core mechanosensor that allows cells to locally sense, transduce and adapt to environmental mechanical constraints. In our recently published results, we have shown that alpha-catenin is a flexible molecule that is suitable for neutron spin echo (NSE) study (Nicholl et al Biophys J. 2018). Our preliminary structural study indicates that the alpha-catenin/beta-catenin complex can sample different configurations. Here we will extend the study to use NSE to determine the nanoscale dynamics of the alpha-catenin/beta-catenin complex. The study will contribute to our understanding of how the catenin complex functions as a mechanosensor.

We performed the NSE experiments at IN15 in the summer of 2019. The experiments were successful. A manuscript has been submitted, and is currently under review. The award of beam time has been acknowledged as:

Institut Laue-Langevin neutron beam time award citation: Neutron spin echo spectroscopy study of nanoscale dynamics of the α-catenin/β-catenin complex. (2019) Institut Laue-Langevin (ILL) doi:10.5291/ILL-DATA.8-04-85

The abstract of the manuscript is as follows:

As the central component of the adherens junction in cell-cell adhesion, the cadherin-catenin complex senses and transduces mechanical tension between neighbouring cells. In particular, the cadherin-catenin complex binds to intimately juxtaposed actin microfilaments strongly only under mechanical tension that is exerted by actomyosin contractility. Recently we showed that the cadherin-catenin complex exists in an ensemble of flexible conformations, with the actin-binding domain (ABD) of α-catenin adopting a variety of configurations. To further elucidate the mechanosensing mechanism of the cadherin-catenin complex, we have determined the nanoscale protein motion of the complex using neutron spin echo spectroscopy (NSE), selective deuteration, and theoretical physics analysis. The results reveal that the entire ABD becomes mobile as a part of the cadherin-catenin complex. By contrast, in the α-catenin homodimer alone, only the much smaller disordered C-terminal tail of the ABD is moving. This activation in ABD domain motion, together with a gain in conformational entropy, suggests the existence of an entropic trap in the cadherin-catenin complex. Mechanical tension facilitates the reduction in entropy of the mechanosensory portion of the cadherin-catenin complex, and shifts the equilibrium of the conformational ensemble to a narrower configuration space that is competent to bind the moving actin microfilament.