特別講演会

日時　　平成２４年１０月１６日（火）14:00～15:00

場所　　北海道大学理学部５号館低層棟大講堂 (2-03 室)
〒062-8517 札幌市北区北 10 条西 8 丁目

講演者　　Prof. Brian D. Sykes
Department of Biochemistry, University of Alberta, Canada

講演題目　　Using NMR to unravel aspects of cardiovascular function: Drug design and schema

講演要旨

Mutations in the contractile proteins of the heart are known to give rise to familial hypertrophic, dilated, or restrictive cardiomyopathies. It is believed that mutations that increase the calcium sensitivity of cardiac myofilaments give rise to hypertrophic cardiomyopathy, while those that decrease calcium sensitivity give rise to dilated cardiomyopathy. The myofilament calcium regulatory protein troponin is a promising therapeutic target in this regard. Our aim is to elucidate the underlying mechanism(s) of how this protein works. We have used high resolution NMR spectroscopy to determine the three-dimensional solution structures of calcium sensitizers and calcium desensitizers bound to the crucial troponin C-I interface. We used the regulatory domain of troponin C and its interaction partner, the switch region of troponin I containing the ischemia-protecting Ala162His substitution, to elucidate the structural details of their interaction under normal and acidic conditions using high resolution NMR spectroscopy. Our structures indicate that both calcium sensitizers and desensitizers are characterized by hydrophobic groups that are able to intercalate between the hydrophobic interfaces of troponin C and I. We show that the binding of troponin I to troponin C is reduced under acidic conditions, and that the presence of the His162 mutation markedly increases its affinity both at normal pH, and especially in the acidic environment.

＊ブライアン・サイクス教授は、筋肉蛋白質トロポニンを始めとする数多くの生体物質の構造機能解析を NMR 法を駆使して進められてきた世界屈指の研究者です。どなたにも分かり易い講演内容ですので、ぜひ多くの方々の御参加を賜りますようにお願い申し上げます。

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