INBIOSIS SEMINAR SERIES (14)

INSTITUT BIOLOGI SISTEM
INBIOSIS
INSTITUTE OF SYSTEMS BIOLOGY

Protein Disulfide Isomerase does not Control Recombinant IgG4 Productivity in Mammalian Cell Lines

by

Dr. Peter Klappa
University of Kent, United Kingdom

13 August 2010 (Friday)
9.00 am ~ 10.15 am

Seminar Hall
Institute of Systems Biology (INBIOSIS)
Universiti Kebangsaan Malaysia

TENTATIVE SCHEDULE

13/08/2010 (Friday)

9:00 am – 9:15 am
Registration

9:15 am – 9:20 am
Welcome Speech

9:20 am – 10:00 am
Seminar : Protein Disulfide Isomerase does not Control Recombinant IgG4 Productivity in Mammalian Cell Lines

10:00 am – 10:15 am
Conclusion, Q&A and Wrap-up

Dr. Peter Klappa

PhD in Biology

Transport of Secretory Proteins into the Endoplasmic Reticulum of Higher Eukaryotes

University Goettingen (1991)

Staatsexamen [corresponds to PGCE]

Teaching Biology and Chemistry in Higher Education

University Muenchen (1987)

Diplom [corresponds to M.Res. In Biology]

Teaching Biology and Chemistry in Higher Education

University Muenchen (1987)

Research Interests:

- *Protein Folding and the Role Molecular Chaperones and Folding Catalysts Play*
- *Structure, Function and Specificity of Protein Disulphide Isomerase and Peptidyl Prolyl cis-trans Insomerase.*
- *Cell Biology*
- *Biochemistry*
- *Protein Chemistry*
- *Proteomics/Metabolics/Transcriptomic*

Abstract

Protein Disulfide Isomerase does not Control Recombinant IgG4 Productivity in Mammalian Cell Lines

Posttranslational limitations in the endoplasmic reticulum during recombinant monoclonal antibody production are an important factor in lowering the capacity for synthesis and secretion of correctly folded proteins. Mammalian protein disulfide isomerase (PDI) has previously been shown to have a role in the formation of disulfide bonds in immunoglobulins. Several attempts have been made to improve the rate of recombinant protein production by overexpressing PDI but the results from these studies have been inconclusive. Here we examine the effect of a) transiently silencing PDI mRNA and b) increasing the intracellular levels of members of the PDI family (PDI, ERp72 and PDIp) on the mRNA levels, assembly and secretion of an IgG4 isotype. Transiently silencing PDI in NS0/2N2 cells suggests that PDI is involved in disulfide bond formation of this subclass of antibody. From the knock-down experiments the flux control coefficient for PDI can be calculated as = 0.25. This value indicates that although PDI contributes to a certain extent towards the flux control of disulfide bond formation, it is not the rate-limiting step in the formation of fully assembled IgG4 antibodies in NS0 cells. Furthermore, overexpression of members of the PDI family in a CHO cell line does not improve productivity and hence we conclude that the catalysis of disulfide bond formation is not rate limiting for IgG4 production. We therefore propose that PDI is not a suitable target for rational cell engineering in NS0 and CHO cell lines in order to increase IgG4 productivity.

Registration Form
(INBIOSIS Seminar Series 14)

Name : _____

Institution : _____

Address : _____

Tel No. : _____

Fax No. : _____

Email : _____

Attendance confirmation should be made before **10 Aug 2010 (Tues)** and sent to

Institute of Systems Biology
Universiti Kebangsaan Malaysia
43600 UKM Bangi or
faxed to **03-8921 3398**

**As places are limited, early registration is recommended.*

Enquires

For more information please contact:
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(Nur Hasrina Mohar / Emelda Rooseleena Rohani / General)
Or email:
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