21世紀COE講演会報告書
理学研究科　三木邦夫

講演者：Johann Deisenhofer 教授（1988年ノーベル化学賞受賞者）
米国テキサス大学ダラス校・サウスウエスタンメディカルセンター（ハワードヒューズ医学研究所）
Howard Hughes Medical Institute, University of Texas Southwestern Medical Center at Dallas, USA
演題：Structural Insights into Cholesterol Homeostasis
場所：京都大学百周年時計台記念館２階国際交流ホールⅡ
日時：2006年4月27日（木）10:15ー12:15
参加者：大学院学生，学生，博士研究員，教員（学内，学外）
参加者総数： 80 名

講演内容：
In this seminar, Dr. Deisenhofer gave a talk on the structural studies of the proteins involved in human cholesterol homeostasis. At first, Dr. Deisenhofer presented the structure of HMG-CoA (3-hydroxy-3-methylglutaryl-coenzyme A) reductase, which catalyzes an important step in the biosynthesis of sterols and isoprenoids. In addition to the structures in complex with HMG-CoA and NADP+ molecules, he also showed the structures in complex with six different inhibitors (clinical drugs known as statins, reference [1]). Secondly, Dr. Deisenhofer talked about the structure of LDL (low-density lipoprotein) receptor, which mediates cholesterol homeostasis through endocytosis of lipoproteins (reference [2]). He presented a new mechanism by which the LDL receptor transports lipoproteins utilizing the pH difference between the inside and outside of endosome. He also talked about the latest knowledge of hypercholesterolemia, the collapse of cholesterol homeostasis, caused by several mutations in this protein. During his talk, he also explained how young postdoctoral fellows and students in his laboratory overcame the large difficulties in crystallizing these two proteins. This inside story was very inspirable especially for the young audiences, showing that a lot of efforts always exist behind their excellent works.

[1] E.S. Istvan and J. Deisenhofer: Structural mechanism for statin inhibition of HMG-CoA reductase, *Science* **292**, 1160-1164 (2001).

[2] G. Rudenko, L. Henry, K. Henderson, K. Ichtchenko, M. S. Brown, J.L. Goldstein, and J. Deisenhofer. Structure of the LDL receptor extracellular domain at endosomal pH, *Science* **298**, 2353-2358 (2002).


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