抗体 CDR-H3 の構造分類 1P270

○里田 大祐二2 白井 宏樹3 中村 春木二

「阪大・蛋白研、 "阪大・院生命機能、"アステラス製薬・分子医学研究所

New classification of the structures of antibody CDR-H3

Daisuke Kuroda(1,2), Hiroki Shirai(3), Haruki Nakamura(2). (1: Graduate School of Frontier Biosciences., Osaka University; 2: Institute for Protein Research. Osaka University; 3: Molecular Medicine Laboratories, Astellas Pharma Co., Ltd.)

The third complementarity determining region on an antibody heavy chain (CDR-H3) lies in the centre of the antibody combining site and plays important roles for antigen recognition among the six CDRs. The CDR-H3 has enormous diversities in their lengths, sequences, and structures. Therefore the model building of CDR-H3 segment is the most essential but difficult step for the structural modeling of an antibody. The number of antibody structures experimentally determined has increased since we developed "H3-rules", so as to classify the structure of CDR-H3 from its amino-acid sequence. Here, we applied H3-rules to the new antibody sequences and compared the predictions with their real structures. We find that although H3-rules does work for the CDR-H3 structures which have typical hydrogen bonds between the side-chains of Arg and Asp located at the both ends of the CDR-H3 segments, it works poorly for the other cases. Careful inspection of erroneously classified structures enables us to identify several new key residues for characterizing the CDR-H3 structures. Thus, we revise the H3-rules and apply it to the sequences of antibody drugs. Finally, we discuss the concept of "antibody druggability" from the commonality of CDR-H3 features of antibody drugs.

寿命を制御する分子機構の解明

1P272 ○須田 斎¹、正山 哲嗣¹、尾崎 貴美¹

「東海大・開発工・生物工 1pK01

Molecular mechanism of regulation in the lifespan

Hitoshi Suda, Tetsuji Shoyama and Takami Ozaki. (1: Dept. Biological Science and Technology, Tokai Univ.)

In the study of aging and lifespan, to measure survival curves is essential. Generally, force of mortality (or spontaneous death rate) is plotted on the basis of the survival data, and it is analyzed by the Gompertz model. So far, the Gompertz model has played an important role for the analysis of lifespan. Indeed, in human beings, this model fits well with experimental data in the period 40-90 years old. However, this is a mere empirical mathematical model that does not include a biological background. Thus, we present a biophysical model based on the principles of fluctuation and regulation to explain the effect of stochastics on survival. The model is a good fit for the survivorship and mortality rates observed in the nematode Caenorhabditis elegans. A parameter included in the theory, which is called the fluctuation constant, correlates well with a declining rate of respiration with age, which we term the aging rate. The framework involved in the fluctuation theory is compatible with the existence of a regulatory system such as that acting in the insulin/IGF-1 (insulin-like growth factor-1) signaling pathway during adulthood, and that sensing, switching, and memorizing the rate of mitochondrial respiration early in life. Our result shows that the Gompertz model is ruled out in the nematode

昆虫分類学-「古典」と「ゲノム」の良好な一致 1P271

○小森 学¹、宮本 潔²、小作 明則²、西垣 功一¹,3

「埼大院・理工・機能材料、²獨協医・医総研、³埼玉バイオグループ/埼玉県中小企業 振風公社

Insect taxonomy: A good correspondence between classical and novel genomic approaches

Manabu Komori(1), Kiyoshi Miyamoto(2), Akinori Kosaku(2), Koichi Nishigaki(1)(3)(1:Department of Functional Materials Science, Saitama University;2:Institute of Medical Science, Dokkyo Medical University;3:Rational Evolutionary Design of Advanced Biomolecules, Saitama SmallEnterprise Promotion Corporation)

Ecology is the key science to provide prescriptions for sustaining favorable environments with all developing activities for various resources. However, it can not be fulfilled without the knowledge on the whole organisms which constitute the ecosystem: the knowledge dependent on Taxonomy. It has already become clear that classifying organisms based on the genotype is much easier, rapider, and, in cases, even more precise than doing so based on the phenotype. There are only two general approaches presented and realized for this purpose: i.e., ribosomal RNA-sequencing approach (RPD II) and the Genome profiling method (On-web GP). In this study which applied the GP method to classifying insects, we demonstrated not only that the GP method can also applicable to the insect study but also that the well-established entomological knowledge, which has been built up based on the phenotypic traits, could be also confirmed by this genome-based approach. We will discuss both the methodological advantages of GP over ribosomal RNA-sequencing approach and the profound meaning of the high correspondence between the phenotype and the genotype.

精子運動法則の生殖医療への応用 1P273

○磯部 哲也

1鈴鹿回生病院 生殖医療センター 1nK02

Application of Laws of Sperm Motion to Reproductive Medicine Tetsuya Isobe, Reproductive Medical Center, Suzuka Kaisei Hospital

The following equations of sperm motion were derived mathematically from the balance between propulsive forces generated in the tail and resistive forces exerted on the head using a sperm model with a spherical head, spring neck and flexible thin cylindrical tail. Here, A is the amplitude of lateral head motion, f is beat-cross frequency of head motion and V is swimming velocity of the sperm (curvilinear velocity), L is linearity. a, b, c, d is constants.

1/V = a(1/A) + b

f = c

 $L^2 + dV^2 < 1$

The validity of these three equations was demonstrated using computer aided sperm analysis (CASA) on 175 samples of freshly ejaculated semen obtained from 49 patients. Semen from 5 patients was treated using a 90% single-layer Percoll preparation, and various sperm motility parameters were measured over the course of time. Two parameters were hypothesized as a sperm motility index. One is the standard error of 1/V from the regression line in the scatter diagram with 1/V on the vertical axis and 1/A on the horizontal axis. The other is the mean value of (1- L^2)/V^2. The two parameters decreases respectively when mean swimming velocity and percent motility increase by Percoll treatment, and increases respectively when the mean swimming velocity and percent motility decrease with time. The two parameters in all freshly ejaculated semen samples respectively show a negative correlation between mean swimming velocity and percent motility. This suggests that it may be possible to use these two parameters as a sperm motility index.