様式Ｃ－１９

科学研究費助成事業（科学研究費補助金）研究成果報告書

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研究課題名（和文）　自然免疫蛋白質の機能アノテーション

研究課題名（英文）　Functional annotation of innate immunity proteins

研究代表者
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研究成果の概要（和文）：

研究成果の概要（英文）：A pipeline (SFAS) was constructed that predicts the location of functional domains based on several tools. Intrinsically disordered domains can be analyzed IDD Navigator. Structual domains can be analyzed using several novel methods have been developed by our group and integrated. In particular, sequence alignment (SEEKQUENCER, MAFFTash) and structure refinement (Spanner, OSCAR) show significant improvement over existing methods. The pipeline has been validated using large-scale benchmarks as well as case studies.

交付決定額

（金額単位：円）

	直接経費	間接経費	合　計
２００９年度	2,900,000	870,000	3,770,000
２０１０年度	300,000	90,000	390,000
２０１１年度	400,000	120,000	520,000
年度			
年度			
総　計	3,600,000	1,080,000	4,680,000

研究分野：生物学
科研費の分科・細目：生物科学・生物物理学
キーワード：Protein structure, protein function, threading, alignment

１．研究開始当初の背景

Previously we had developed a method for structure alignment (ASH) that was extended to include evolutionary information in order to predict the function of hypothetical proteins solved as part of structural genomics efforts. We implemented the method in the package SeSAW, and found it could be used to predict the function of homology models. We therefore decided to develop our own structure prediction pipeline and to integrate this pipeline with SeSAW. This enabled use to propose a “sequence to function annotation service” (SFAS).

２．研究の目的

There are two purposes of SFAS. The first is to provide a tool to the scientific community for identification of

functional domains in any amino acid sequence. SFAS is fully automated, but allows human interaction at several levels (e.g., selecting domain boundaries, structural templates, or threading method). The second purpose is to identify the functions of novel proteins that are part of the innate immune response. Approximately 2,000 proteins are known to be involved in the innate immune response, but many of these have not been functionally characterized.

３．研究の方法

Each stage of the pipeline is an independent module that performs a specific task. The modules work together and are integrated by a graphical user interface (GUI). The key modules are as follows:

(1) 2D prediction. This module predicts intrinsic disorder (iupred or disopred) and secondary structure (psipred or jpred) and presents the predictions as a 2D graph. The user can select a sequence range and submit it to one of two downstream modules (Threading meta server or IDD Navigator).

(2) Threading meta server. This module takes a sequence as input and submits it to one or more threading methods. The available methods include HHPred, FFAS, FORTE, PSIBLAST, and BLAST. The results for a given threading method are displayed on a single page and can be viewed in 3D or submitted to the Spanner module.

(3) IDD Navigator. This module predicts pfam domains and gene ontology (GO) identifiers--indicators of protein function--for intrinsically disordered domains (IDDs). This is accomplished by matching the amino acid composition with IDDs with associated pfam domains and GO identifiers stored in our database.

(4) Spanner. This module builds a continuous 3D structure from a sequence-structure alignment. Gaps are filled by “spanning” them with fragments of known structure. The filed gaps are refined by restrained energy minimization and scored using OSCAR. Spanner models can be submitted to SeSAW for function prediction.

(5) SeSAW. This module begins by structurally aligning the 3D model to known structures. Those that score above a given threshold are then scored using profile-profile alignment (which includes evolutionary information on the input structure and each similar domain).

４．研究成果

The software described above is available to the scientific community for free via the internet. In order to publicize the pipeline, we applied our pipeline to: 1) modeling of regnase-1, an essential regulator of inflammatory cytokines; 2) modeling polymorphic positions in ROP16, a pathogenic kinase that interferes with innate immune responses by phosphorylating STAT3; 3) modeling a polymorphism in LMP7, a component of the immunoproteosome in humans; 4) modeling of AOX in the intestinal parasite Blastocystis, an intestinal parasite.

５．主な発表論文等

（研究代表者、研究分担者及び連携研究者には下線）

〔雑誌論文〕（計 18 件）

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⑦ Standley DM, November, 2009, Osaka, Japan: MEI Center lecture series “Functional Annotation using SeSAW”

〔その他〕
ホームページ等
http://sysimm.ifrec.osaka-u.ac.jp/

６．研究組織

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