Laboratory of Computational Biology

Institute for Protein Research

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We use computational methods to study biological systems and diseases with applications to drug discovery. As expectations for artificial intelligence (AI) increase in various fields, we recognize that the availability of data organized in a form suitable for computer analysis will have a significant impact on the success or failure of AI development. Our research is focused on integrating a wide array of data, including genes, proteins, chemical compounds and diseases. We are also developing methods to predict protein structure, function, and interaction, and applying these methods to specific data analysis.

Data integration for relating molecular-level events to higher-order biological systems

A large amount of experimental data related to various branches of life sciences are already stored in public databases. However, many common issues need to be resolved before they can be analyzed and utilized as “big data”. For example, information on experimental conditions is not structured sufficiently, making it difficult to select the necessary data, and terminology and units are unstandardized. We are building databases and developing technologies as a basis for connecting molecular-level events to higher-order biological systems. For example, to develop predictive models for pharmacokinetic parameters, we are building an integrated database of data extracted from several public data sources, which have been manually curated by examining experimental conditions and converting units appropriately. Our TargetMine (https://targetmine.mizuguchilab.org) data warehouse can assist discovery research in the early stages of drug discovery, and stores data from numerous databases, concerning many relationships such as those between genes and diseases/phenotypes, and genes and tissues in which they are expressed. To integrate those data into an effective analysis platform, we are adopting unified terminologies and concepts, and developing new analysis tools.

Understanding and predicting protein-mediated interactions and modeling biological responses

The increasing amounts of experimentally-determined protein structures and interations have made it possible to predict the structure, function, and interaction of proteins from their amino acid sequence alone. We develop novel comutaiontal methods using machine learning and other techniques, but also focus on the analysis of specific biological systems, aiming to present hypotheses testable by direct experimentation. For example, we predicted the structure and binding-sites of BIG3, a novel gene exclusively overexpressed in breast cancer cells. A peptide designed based on this knowledge has been shown to block the interactions between BIG3 and its partner protein, and suppress the growth of breast cancer cells both in vitro and in vivo. Protein-protein intractions are attractive targets both in drug discovery and basic research, and remain one of our major research themes.

Transcriptome analysis of early human embryos

In early human embryos, transcription is initiated at the 4-cell stage, which leads to the production of new proteins and cell differentiation. Recent studies have revealed that a transcription factor called DUX4 is expressed prior to zygotic genome activation and induces the expression of various genes and retrotransposons. We investigate the mechanism of activation of specific retrotransposons in early embryos by integrating single-cell transcriptome dataset with epigenetic datasets such as ATAC-Seq and ChIP-Seq data. We also aim to identify conserved and divergent elements of the retrotransposons among primates by comparing human, macaque, and marmoset embryos. Furthermore, we explore the transcriptional activity of the retrotransposons in a wide range of somatic cells, in which some of the retrotransposons might be adapted as regulatory elements.

Figure 1: High Performance Computer System

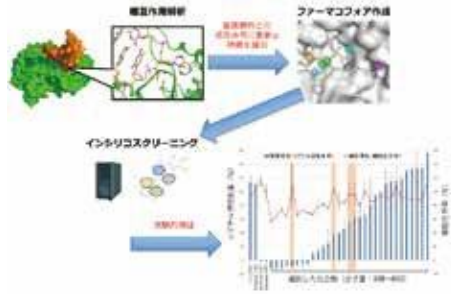

Figure 2: Drug Design Based on Structural Information

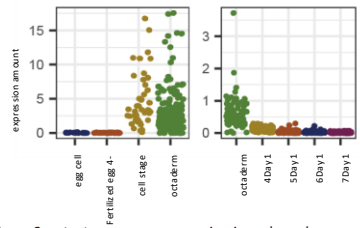

Figure 3. retrotransposon expression in early embryos.

We aim to create an environment where members of diverse nationalities and backgrounds can work together.

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