Laboratory of Dynamic Cell Biology

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The enigma of chromosome structure

Well over a century after the discovery of chromosomes during a cell division in 1842, the enigma of their higher order structure remains. We have been studying the higher order structure of chromosomes using several methods.

Fig. 1. A human chromosome and its structural models (A to C, Fukui and Uchiyama 2007, *Chem. Rec.*)

Image analysis and new microscopy for chromosomes

Image analysis systems, CHIAS1 to 4, have been developed and employed to obtain precise quantitative chromosome image data. The chromosome image parameter has been proven to be effective for the objective characterization and identification of plant chromosomes, especially the condensation pattern (CP) at the prometaphase stage. As a result, the chromosomes of several cultivated plants have been identified for the first time. Now, in collaboration with Prof. Itoh of our Division, we are developing a new optical microscope technique: stimulated parametric emission (SPE) microscopy, which allows three-dimensional and live imaging without staining chromosomes with any dye. The plant cell image obtained is shown in Fig. 2.

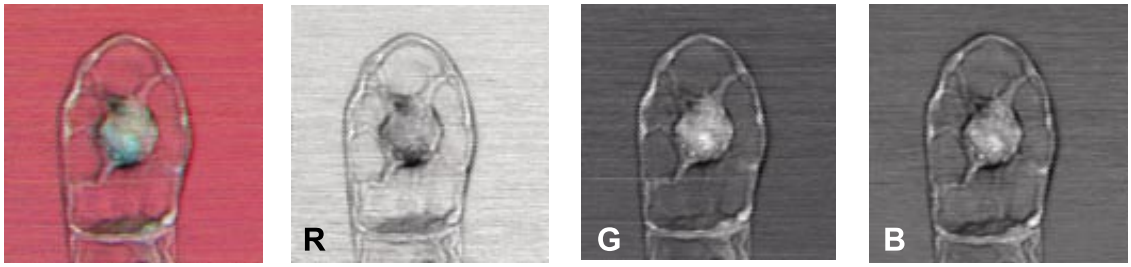

Fig. 2. Color image composition using R, G, B monochrome images.

Proteome analysis of human chromosomes

We have already completed a proteome analysis of human metaphase chromosomes and identified more than 200 chromosomal proteins. Based on a comparison of the chromosomal proteins among the

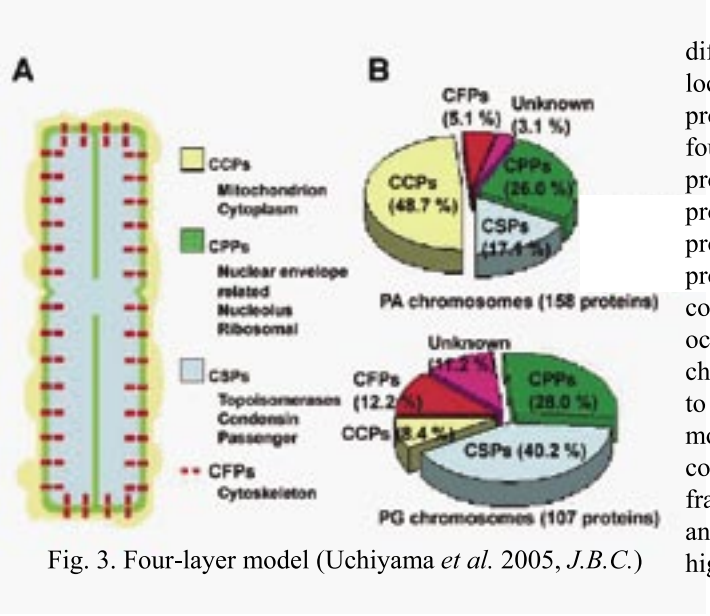

Fig. 3. Four-layer model (Uchiyama *et al.* 2005, *J.B.C.*)

differently prepared chromosomes, and localization analyses of the proteins, each protein has been classified into one of the four protein groups, chromosome coating protein (CCP), chromosome peripheral protein (CPP), chromosome structural protein (CSP) and chromosome fibrous protein (CFP). Each of the four groups consists of different sets of proteins and occupies a specific region of the chromosome. These findings have led us to develop the chromosome "Four-layer model" (Fig. 3). This model is the first comprehensive chromosome protein framework that is not inconsistent with any existing models of chromosome higher order structure.

Dynamic analysis of chromosomal proteins

We have been analyzing the function and localization of the newly identified chromosomal proteins by developing antibodies against the proteins. Among the 200 chromosomal proteins that have been identified by proteome analysis, the function of several has not been identified. Application of RNA interference (RNAi) methods has revealed new functions of these proteins, especially the functions in the cell cycle, chromosome dynamics, nuclear morphology, *etc*. For example, prohibitin 2 (PHB2) has been shown to be involved in the regulation of sister chromatid cohesion during mitosis in human cells. Although PHB2 was known to have multiple functions, its function in mitosis has now been demonstrated for the first time.

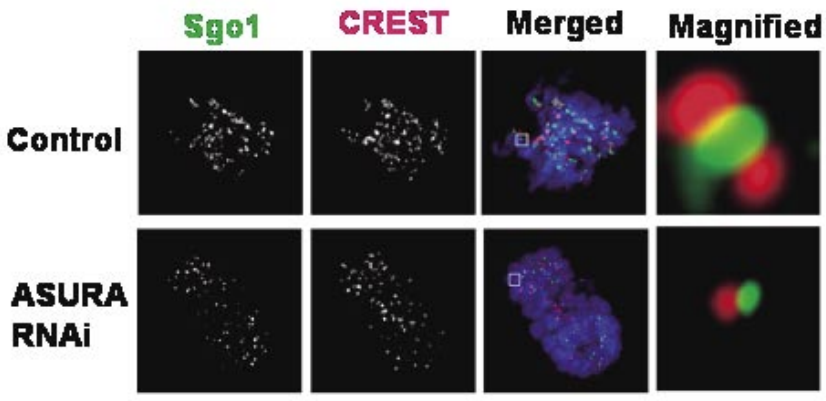

Fig. 4. Prohibitin RNAi (Takata *et al*. 2007, *Curr. Biol.*)

References (Selected papers in 2007)

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