

LIFE SCIENCE:



Remarkably diverse types of research are included in the Life Science II section for this year. Some are directly related to medical problems and others are on the basic analysis of biomedical specimens including methodologies.

The report most closely related to clinical medicine is that by Schwenke *et al.* who studied the mechanism of pulmonary arterial hypertension (a disease that increases the blood pressure of pulmonary artery) by angiography. They develop rat models of the disease by two methods: by prolonged exposure to a low oxygen concentration and by drug (monocrotaline) use. Both models had fewer branches of blood vessels than normal rats. By high-resolution synchrotron angiography, they found that the 100-200 μm blood vessels of the former model are more sensitive to a sympathetic stimulus than those of the latter model. The results suggest the presence of different types of pulmonary hypertension in humans.

The work on the mouse lung by Hooper *et al.* used a technique called particle image velocimetry (PIV) in combination with propagation-based phase-contrast imaging, which enhances the contrast of the lung much better than conventional projection imaging. PIV reveals a motion in each part of the lung during respiration. In this study, abnormal movements were observed in a mouse with bleomycin-induced pulmonary fibrosis, which induces the formation of excess fibrous tissues in the lung. Thus, PIV has potential as a novel method for disease detection.

The study by Ochala *et al.* is quite medically related but not based on imaging; it uses small-angle X-ray diffraction analysis. Human muscle samples were collected by biopsy from patients who suffer from genetic diseases of the skeletal muscle. These diseases are caused by the mutation of a protein (tropomyosin) that regulates muscle contraction. X-ray diffraction analysis can tell how the protein undergoes a conformational change during contraction. The results show that the mutated molecule does not change its conformation sufficiently to cause complete contraction. The approach used in this study shows that X-ray diffraction can be utilized for better understanding of the inherited muscle diseases at the molecular level.

MEDICAL BIOLOGY

Kanzaki *et al.* also used small-angle X-ray scattering to study the molecular change of a protein classified as a chaperonin that assists the folding of other proteins. Since proper folding of proteins is essential for the normal function of cells, the dysfunction of this class of proteins is related to a variety of diseases such as Alzheimer's and Parkinson's. The chaperonin studied here was from a thermophilic bacterium that has the highest activity at high temperatures. Three mutant proteins were prepared to study their activities at low temperatures. Although all the mutants retained intact folding capability at 60°C, unlike the wild-type protein, two of the mutants kept the high conformational change ability even at 40°C, which correlated with their higher folding ability. The difference seems to originate from the locations of the mutations in the protein, showing that these amino acids are crucial to the conformational stability of the protein.

The study by Matsuyama and Yamauchi is performed at the cellular level; they carried out high-resolution mapping of elements in NIH/3T3 cells using Kirkpatrick-Baez mirrors. The probe size can be as small as 29 nm × 48 nm, but is adjustable so that a larger area can be quickly scanned to find the most interesting regions. All elements between Na (Z=11) and Pb (Z=82) were studied and interesting results were obtained: elements like S and Cu are relatively evenly distributed in a cell, and P, Ca and Fe are much more concentrated in the nucleus. The non-uniform distribution of the elements suggests the different roles of these elements in a cell.

The imaging of soft biomedical samples such as brain, breast and abdominal organs is challenging, and synchrotron radiation has been used to overcome this difficulty. Yashiro and Momose developed a new imaging technique for low-contrast objects suitable for biological imaging. The technique uses a combination of two optical devices, a zone plate and a grating which is a unique idea. Although this technique is still in the early stage of development, it has a potential to be employed as a clinical imaging modality.

Both clinical and basic studies are required for future advancement in medicine. Although the methods used in these reports are not directly applicable to the diagnosis of human diseases, they will contribute to a better understanding of these diseases that are indispensable to conquer them.

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