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Molecular Imaging: Contributing to Drug Research and Development

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"Molecular imaging" is a recently developed approach that unites bioimaging engineering showing marked recent advances and the results of molecular/cellular biology for application to biochemistry/biology/clinical diagnosis/and treatment. Molecular imaging is in vivo imaging of the spatial/temporal distribution of biological/molecular biological processes (events) at the cellular/molecular level. This imaging allows the dynamic observation of life phenomena based on the movement of molecules, and has been contributing to the promotion of studies on the basis of life science, biological functions and causes of diseases, genetic/regenerative medicine, tailor-made medicine, drug discovery, and new clinical diagnostic methods, attracting attention as a novel approach opening the new field of the post-genome period.

There are some molecular imaging methods. Among them, methods using radiation such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) play a major role. Their applications to drug discovery include: (1) measurement of the in vivo behavior of labeled drugs or preparations themselves, and (2) measurement of the receptor occupation rate, enzyme activity or inhibition rate, or changes in biomolecules after drug administration using appropriate radioligands or substrates.

Drugs and preparations that can be labeled with radioisotopes (such as 11-C, 18-F, 123-I, 99m-Tc, 111-In) allow the direct visualization of their in vivo behavior. When drugs themselves can be labeled, pharmacokinetic and pharmacodynamic data can be obtained by measuring their in vivo changes in humans, particularly their distribution behavior at the site of action. In such measurements, basic data supporting drug efficacy and safety in humans can be directly confirmed, which is the final goal of the development of medical drugs. This direct confirmation can provide useful data to help in the decision-making process for the selection of new drug candidate compounds. A similar method is applicable to the assessment of drug delivery, called drug delivery imaging.

On the other hand, using radiological compounds involved in physical, biochemical, and pharmacological responses as the subjects of evaluation are used as probes for analysis, biological functions involving these compounds can be quantitatively analyzed by measuring their in vivo behavior. This is a basis of clinical diagnosis by nuclear medicine imaging, and facilitates the direct in vivo imaging of various receptors, transporters, and the expression state, density, and activity of enzymes and the measurement of their quantitative changes. Probes that are objectively measured and evaluated as parameters reflecting normal biological processes, disease development processes, or pharmacological responses to treatment interventions are called biomarkers. Therefore, data obtained by molecular imaging that allow the in vivo evaluation of local changes are regarded as biomarkers (imaging biomarkers), and provide information useful for the clarification of biological functions, causes of diseases, and the evaluation of medical drugs. In addition, when this method is used in combination with drug administration, the rate of receptor occupancy by the drug, enzyme activity and inhibition rate, and treatment effects can be evaluated.

Thus, molecular imaging by PET/SPECT, which allows the direct evaluation of the in vivo behavior and interactions of specific molecules, has wide potentialities, and is expected to markedly accelerate drug discovery research in the future.